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Synthesis Characterization, Biological Evaluation of Acetyl Substituted Heterocyclic Isatin Derivatives

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KEYWORDS

Isatin, acetyl substituted products, IR, NMR, MASS Spectroscopy

ABSTRACT:

Isatin-1H-Indole-2,3-dione and its derivatives are group of indole derivatives that contain one nitrogen at the first position and two ketone groups at second and third position and is able to involve in electrophilic and nucleophilic substitution reaction at various positions.

In this research Acetyl substituted Isatin products are prepared. It is a broad range of heterocyclic molecule that can be used as precursor for drug synthesis and research in the discipline of pharmaceutical chemistry. The chemical compounds can be identified using chemical tests. Structures of acetyl substituted heterocyclic compounds can be confirmed by IR, NMR, MASS spectroscopy. Acetyl substituted heterocyclic Isatin derivatives has broad spectrum of activity against fungi, helminthes, mycobacterium, HIV virus and also possesses anti-hypertensive, anti-parkinsonism, anticonvulsant and anti-oxidant activity.

A new series of Isatin molecules were synthesized from aniline, chloral hydrate and hydroxyl amine to form intermediate isonitrosoacetanilide that was further treated with sulphuric acid to give Isatin.

1. Introduction

There is immense presence of medicinally useful heterocyclic compounds in the nature and are exploited for drug synthesis and development in the field of pharmaceuticals. The field of medicinal chemistry explains the connecting link between structure of target protein and ligand activity for the purpose of healing human and zoonotic diseases. Multitude of heterocyclic moieties such as furan, thiophene, pyridine, pyrrole, quinolone, thiazole are contained in Isatin derivatives that were used in the formation of new compounds for treatment of different ailments.[1] a variety of Isatins were derived from multiple sources such as human brain parotid gland secretions from Bufo frogs, as well as from plants like Melochia tomentosa and fungi like streptomyces albus [2][3].Isatins undergo various chemical rearrangements like N-alkylation, formation of 1,2,3 triazole hybrid compounds [4]. It inhibits the protease enzyme in SARS-CoV-1 and SARS-CoV-2. In synthetic chemistry this molecule is highly reactive and undergoes electrophilic and nucleophilic substitution [6]. Aromatic electrophilic substitution reaction takes place at C-5, C-7 part of benzene ring of this compound [7]. The nucleophilic addition involves carbonyl group. Along with these reactions this precious moiety is involved in acylation, alkylation, oxidation, reduction and ring expansion. Its antioxidant and cytotoxic properties are appreciable against HL60 cells that can also be used as prophylactic agent to free radical induced cytotoxicity [9]. Anticonvulsant activity has been exhibited against minimum electro shock and subcutaneous metrazole by the Schiff bases of Isatin with different benzothiazole amines [10]. There is broad spectrum antiHIV, anticancer, antimicrobial action and anti tubercular activity to amino pyrimididinimio Isatin congeners[11,12]. All different forms of this active ligand were screened for antifungal, antiviral, antibacterial, antiparasitic, analgesic and anti-

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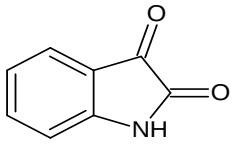
inflammatory as well as anthelminthic activity [13,14,15,16,17].

2. Structure Of Isatin



1*H*-indole-2,3-dione

COMMON NAME	**ISATIN**
MOLECULAR FORMULA	**C8H5NO2**
MOLECULAR WEIGHT	**147.1308G/MOL**
COMPOSITION	**C (65.3155%) H (3.43%) N (9.52%) O (21.75%)**

3. Physical Properties

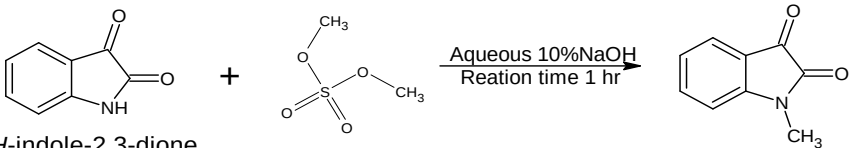
COLOUR	**ORANGE RED**
Odour	characteristic.
Melting Point	203℃-205℃
Boiling point	360℃
Flash Point	341℃
Solubility	soluble in acetic acid, ethyl acetate, ethanol. Insoluble in benzene, toluene and water.

4. Reactions of Isatin

It undergoes electrophilic aromatic substitution reaction at positions C-5 and C-7 of benzene ring and nucleophilic addition takes place at carbonyl group. This molecule also undergoes reduction, oxidation and ring expansion reactions.

N-Substitution Reaction

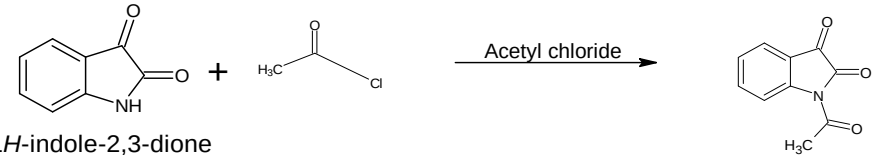
N-Alkylation of Isatin can be done by direct synthesis from N-Alkyl anilines like in Gassmann procedure or by treating Isatin with dimethyl sulphate in 10% dil. Aqueous sodium hydroxide for one hour.



1*H*-indole-2,3-dione + dimethyl sulfate → 1-methyl-1*H*-indole-2,3-dione

N-Acylation Rection:

N-Acyl Isatin was obtained by treating Isatin with acyl chloride or anhydrides under reflux.



1*H*-indole-2,3-dione + → 1-acetyl-1*H*-indole-2,3-dione

Electrophilic Substitution Reaction:

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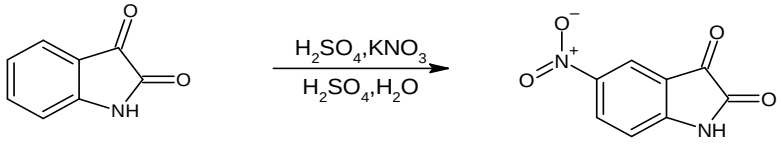
Nitration of Isatin at C-5 position is done by using fuming nitric acid in conc. Sulphuric acid.

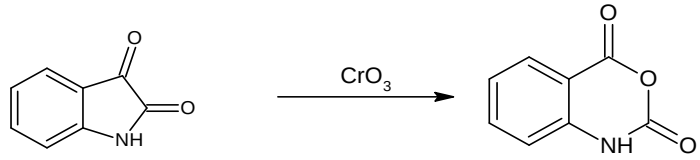


1*H*-indole-2,3-dione

5-nitro-1*H*-indole-2,3-dione

Oxidation Rection:

Isotonic anhydride which is the oxidation product of Isatin, can be obtained by treating Isatin with hydrogen peroxide or chromic anhydride. The resultant molecule abundantly used in herbicide production and for medicinal chemistry. Isatin reacts with chromic acid to yield isotonic anhydride by peroxidation under mild and neutral conditions.



1*H*-indole-2,3-dione

2*H*-3,1-benzoxazine-2,4(1*H*)-dione

5. Nucleophilic Addition Reaction

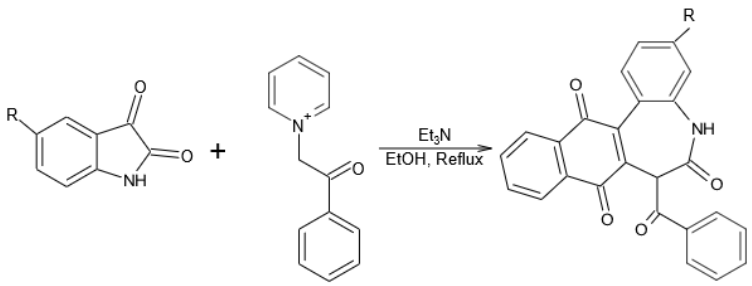
Isatin and its yields can undergo nucleophilic attack at C-2 andC-3 positions. This selectivity towards C-2 or C-3 depends on nature of nucleophile, types of substituents attached to it, solvent and temperature used and especially on the bonds of nitrogen atom. The initial product obtained suffers further reaction in the presence of a second nucleophilic group to give a cyclization product. Due to didactic reasons, these reactions are sorted based on the nature of nucleophile.

Reduction:

Reduction of Isatin with lithium yields indoles in moderate quantity and use of THF as a solvent lead to higher yields of the same. Chemo selective alkylation of Isatine at C-3 or N-1 in presence of metal hydrates gives rise to 1or 3 alkyl indoles.

Ring Expansion Reaction:

This type of reaction is valuable in the field of organic synthesis that forms larger ring and is difficult to be synthesized by other means for the formation of 2-quinoline derivatives through the electrophilic nature of C-3 of Isatin by catalytic asymmetric ring expansion reaction of Isatins and alpha alkyl diazo esters.



6. Structural Activity Relation

Addition of nucleophile to the C-3 keto group is the most well-known reaction of Isatin like the electrophiles.

Electrophilic substitution on aromatic ring leads to ring expansion, oxidation and aldol condensation etc.

Oxidative deamination of biogenic and xenobiotics amine is catalyzed by the enzyme that alters their leves in the brain.

Substitution of 5,6,7 postions of the aromatic ring of Isatin, seems to increase its MAO inhibitory action.

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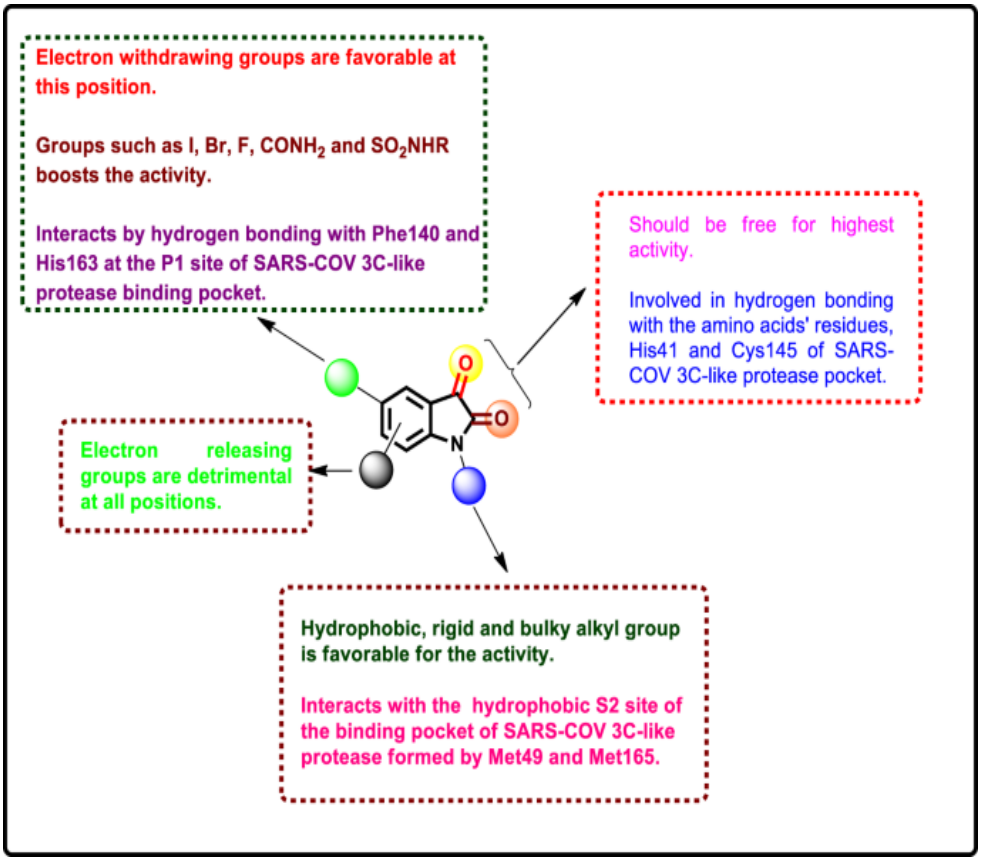
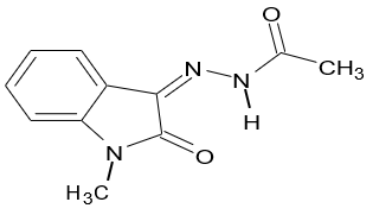


7. Properties of Isatin

Isatin derivatives such as Hydrozoan exhibit extensive biological activity against microbes, tumors, malarial parasites, HIV viruses, bacteria, mycobacterium tuberculosis, helminthes and also decreases inflammation, convulsions and exhibits benefits with its anti-oxidant properties.

8. Discovery of Pharmacological Activity of Isatin

In 1965 an I satin -2,3-dionebased compound Metis zone was discovered it is an antiviral agent used against viral infection as a prophylactic agent. Food and drug administration, USA (FDA) approved.

S. No	Drug	Activity
1	 ***N*'-[(3*Z*)-1-methyl-2-oxo-1,2-dihydro-3*H*-indol-3- ylidene] acetohydrazide**	**ANTI-VIRAL ACTIVITY**

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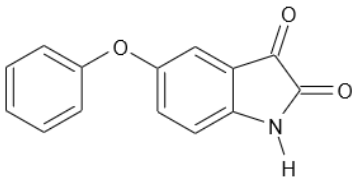
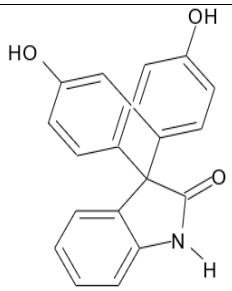
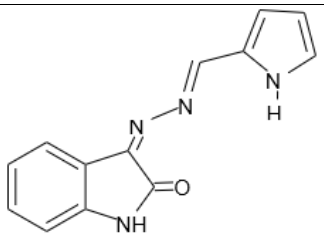
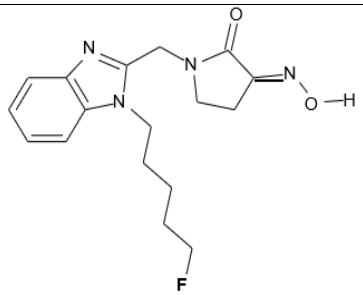
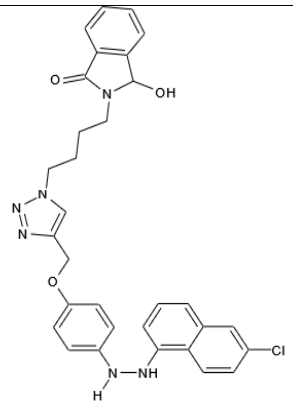
2	 **5-phenoxy-1*H*-indole-2,3-dione**	**MOA INHIBITOR**
3	 **3,3-bis(4-hydroxyphenyl)-1,3-dihydro-2*H*-indol-2-one**	**ANTIVIRAL ACTIVITY**
4	 **(3*Z*)-3-{(2*E*)-[(1*H*-pyrrol-2-yl) methylidene] hydrazinylidene}-1,3-dihydro-2*H*-indol-2-one**	**ANTIPROLIFERATIVE**
5	 **(3*E*)-1-{[1-(5-fluoropentyl)-1*H*-1,3benzimidazol-2-yl] methyl}-3-(hydroxyamino) pyrrolidin-2-one**	**ANTIPROLIFERATIVE**
6		**ANTIMALARIAL**

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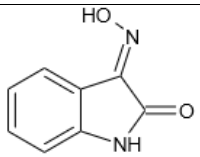
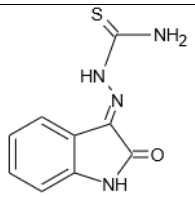
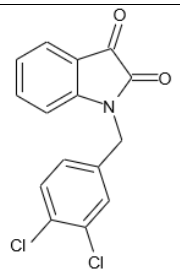
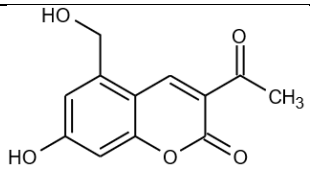
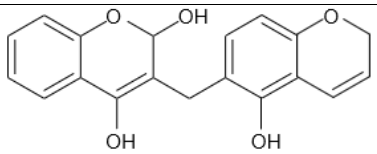
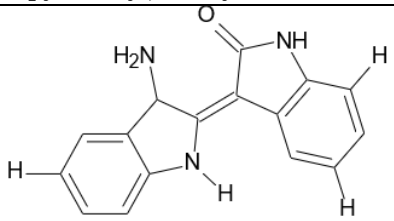
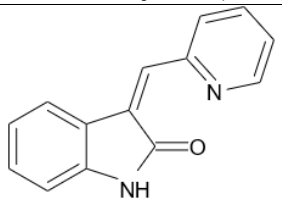
	1-(4-(4-((4-(2-(7-chloroquinolin-4-yl) hydrazonyl) phenoxy) methyl)-1H-1,2,3-triozal-1-yl) butyl)-3- hrdroxyindolin-2-one	
7	 **(3*E*)-3-(hydroxyamino)-1,3-dihydro-2*H*-indol-2-one**	**ANTICHOLINESTERASE**
8	 **(2*E*)-2-(2-oxo-1,2-dihydro-3*H*-indol-3-ylidene) hydraz1- carbothioamide**	**ANTIVIRAL**
9	 **1-[(3,4-dichlorophenyl) methyl]-1*H*-indole-2,3-dione**	**APOPTOSIS**
10	 **3-acetyl-7-hydroxy-5-(hydroxymethyl)-2*H*-1- benzopyran-2-one**	**ANTIBIOTIC**
11	 **3-[(5-hydroxy-2*H*-1-benzopyran-6-yl) methyl]-2*H*-1- benzopyran-2,4-diol**	**ANTI-COAGULANT**
12	 **(3*E*)-3-(3-amino-1,3-dihydro-2*H*-indol-2-ylidene)-1,3- dihydro-2*H*-indol-2-one**	**ANTI- HIV**
13		**GLYCOGEN SYNTHASE KINASE**

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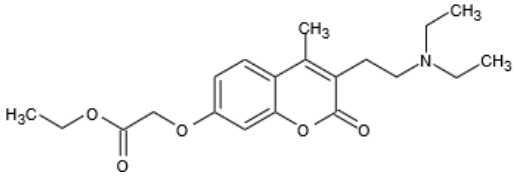
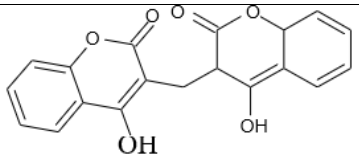
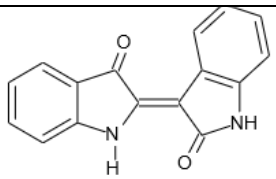
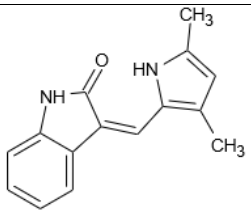
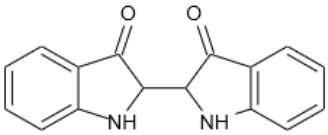
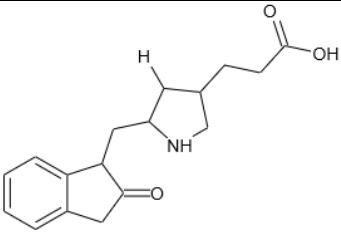
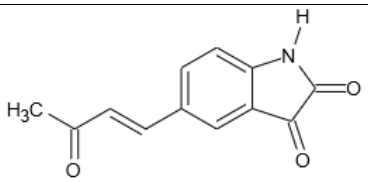
	(3*Z*)-3-[(pyridine-2-yl) methylidene]-1,3-dihydro-2*H*-indol-2-one	
14	 **7-[(2E)-3,7-Dimethyiocate-2'6-dien-1-yl] oxy)-2H-1- benzopyran-2-one**	**CORONARY DISEASE**
15	 **4-hydroxy-3-[(4-hydroxy-2-oxo-3,8 dihydro- 2zbenzopyran-3-yl)methyl]-2*H*-1-benzopyran-2-one**	**ANTI-COAGULANT**
16	 **(3Z)-3-(3-Oxo-1,3-dihydro-2H-indol-2-ylidene)-1, dihydroindone**	**ANTI-INFLAMMATORY**
17	 **MULTIPLE TYROSINE KINASE INHIBITOR**	
18	 **1,1',2,2'-tetrahydro-3*H*,3'*H*-[2,2'-biindole]-3,3'-dione**	**ANTI-MICROBIAL**
19	 **3-{5-[(2-oxo-2,3-dihydro-1*H*-inden-1-yl) methyl] pyrrolidin-3-yl} propanoic acid**	**SMALL MOLECULE INHIBITOR**
20	 **5-[(1*E*)-3-oxobut-1-en-1-yl]-1*H*-indole-2,3-dione**	**ANTI-CANCER**

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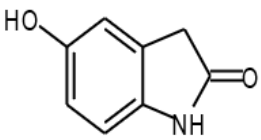
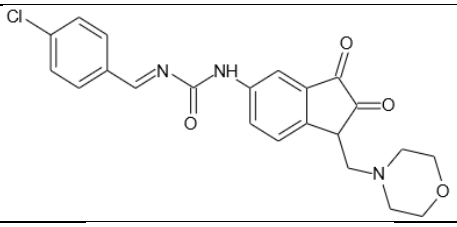
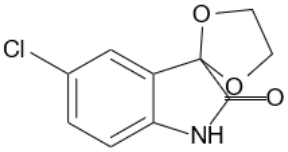
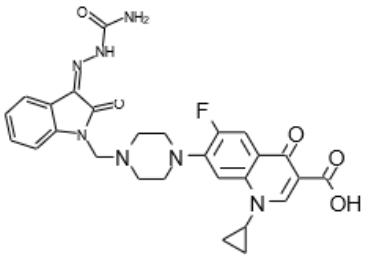
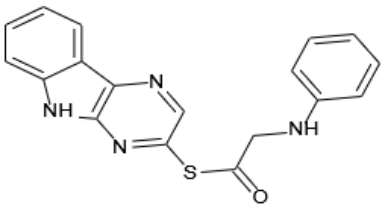
21	 **5-hydroxy-1,3-dihydro-2*H*-indol-2-one**	**MONOAMINE OXIDASE INHIBITOR**
22		**ANTI-EPILEPTIC**
23	 **5'-chlorospiro [[1,3] dioxolane-2,3'-indol]-2'(1'*H*)-one**	**SEDATIVE AND HYPNOTIC**
24		**ANTI-BACTERIAL**
25		**ANTI-DEPRESSANT**

9. Aim and Obtectives

Based on literature review heterocyclic acetyl substituted Isatin has attached attention to various biological activity. The versatile synthesis applicable and biological activity of this heterocyclic compound will help the research to plan, organize and implement new approaches towards the discovery of acetyl substituted Isatin derivatives.

Aim:

Synthesis, characterization and biological evaluation of acetyl substituted heterocyclic Istine derivatives

Objective:

To perform a very simple and facile procedure for the synthesis and characterization of acetyl substituted heterocyclic Isatin derivatives. Purification of final compound using appropriate recrystallization method. Using of ^{13}C- NMR and Mass spectroscopy to characterize the compounds. Finally, evaluation the anti-helminthic activity through earthworms as target.

Scheme-1

STEP-1: SYNTHESIS OF ISATIN (1H-INDOLE-2, 3-DIONE)

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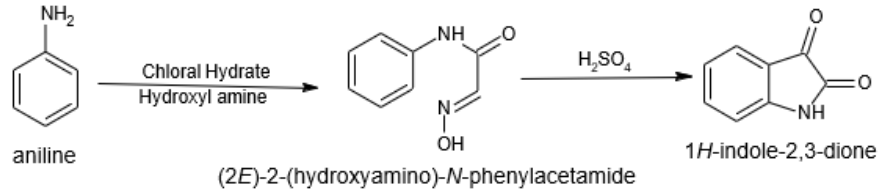
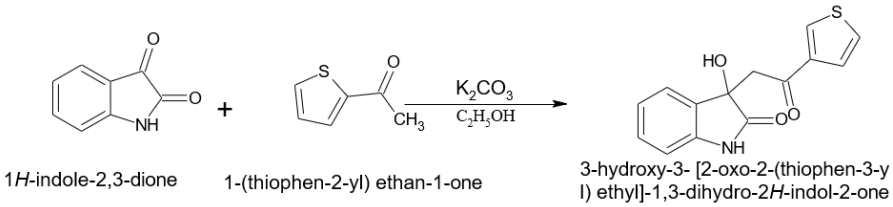


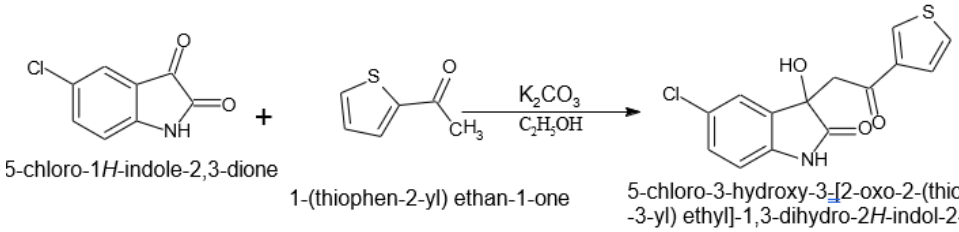
Scheme -2

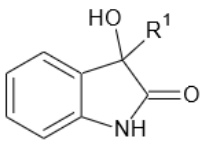
STEP-2: SYNTHESIS OF 3 –HYDROXY 3[2-OXO-2(THIOPHENE-3-YL) ETHYL] 1, 3- DIHYDRO 2H-INDOLE-2-ONE



Scheme-3

STEP-3: SYNTHESIS OF 5-CHLORO-3-HYDROXY 3-[2-OXO2-(THIOPHENE-3YL) ETHYL]1,3-DIHYDRO2H-INDOLE-2-ONE

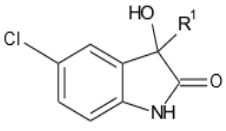




R1= 1(1H-PYRROLE -2YL) ETHAN-1-ONE, 1-ACETYL-1H-INDOLE 2, 3-DIONE,

1-(PYRIDINE-2YL) ETHANE-1-ONE,

1-(4H-IMIDAZOLE-5-YL) ETHANE-1-ONE



R1= 1(1H-PYRROLE -2YL) ETHAN-1-ONE, 1-ACETYL-1H-INDOLE 2, 3-DIONE,

1-(PYRIDINE-2YL) ETHANE-1-ONE,

1-(4H-IMIDAZOLE-5-YL) ETHANE-1-ON

Scheme -1

It involves condensation of aniline with chloral hydrate and hydroxylamine hydrochloride in aqueous sodium sulfide to form isonitrosoacetamide and its subsequent electrophilic cyclization in the presence of strong acid such as conc. Sulphuric acid results in an Isatin derivative. This reaction is named as Sandmeyer Isatine synthesis. Quinolines, acridines, indophenazines are all made from Isatin by this reaction. Isatin act as useful intermediate in the heterocyclic and pharmaceutical chemistry.

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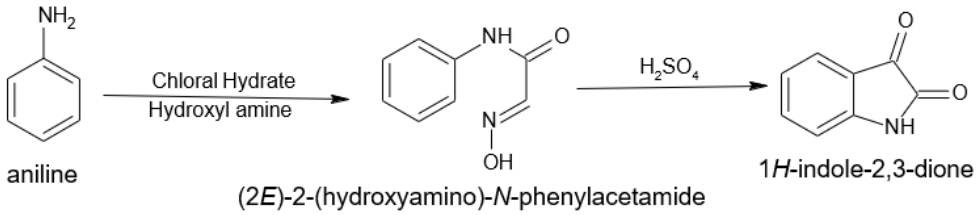
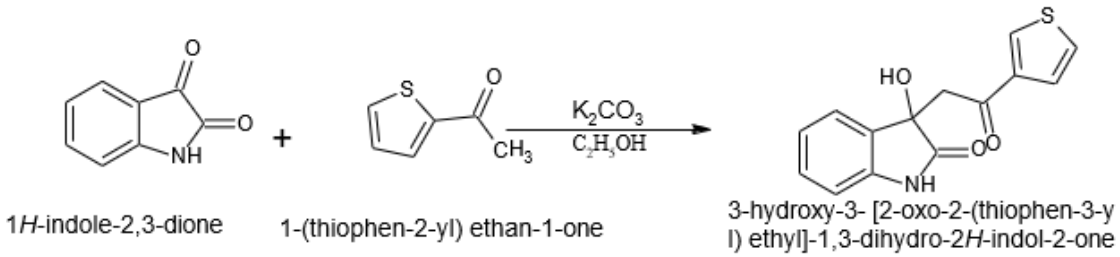


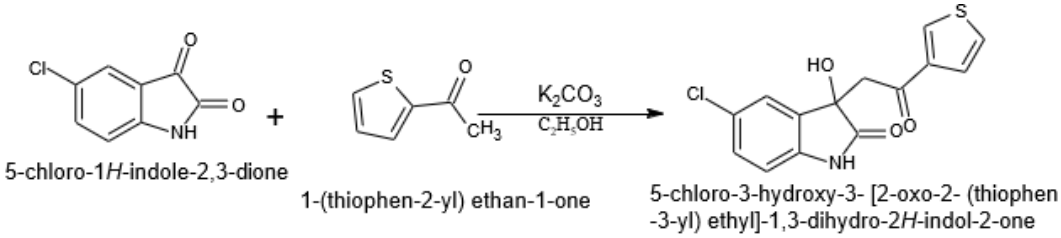
Scheme-2

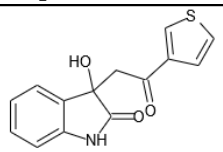
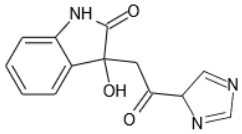
Synthesis of acetyl substituted heterocyclic Isatine yields was carried out in scheme-1. In this step 2 mole (0.02) (2.5236 grams) of 2-Acetyl thiophene was mixed with 1 mole (0.01) (1.4713 grams) of Isatin in ethanol as solvent and sodium carbonate as catalyst is refluxed for about 22-24hours. The completion of the reaction is checked by thin layer chromatography. After completing the reaction, the crude mixture was filtered and washed with ethanol. Finally, the solid precipitate of pure product was obtained.



Scheme-3

The synthesis of Acetyl substituted heterocyclic Isatine derivatives was carried out in step-1 reaction. In step-2 5-chloro1H-indolin-2,3 Dione 1 mole (0.01) 1.8158 of was mixed with Isatine 1 mole (0.01)1.4713 grams in ethanol as solvent in the presence of sodium carbonate as a catalyst and refluxed for 22-24hours.The reaction completion checked by using thin layer chromatography after completion of reaction the crude mixture was filter and then washed with ethanol. The solid Precipitate of pure product was obtained.



S. No	Compound Code	Compound Structure
1	SIS-1	
2	SIS-2	

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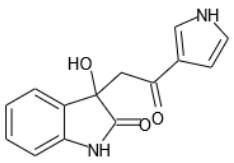
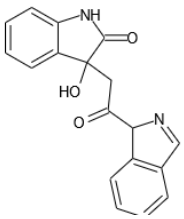
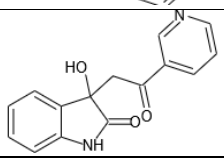
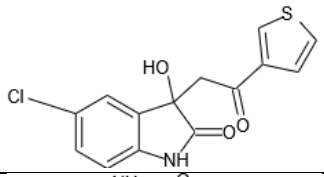
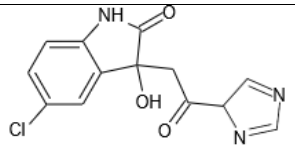
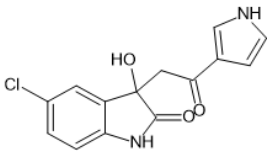
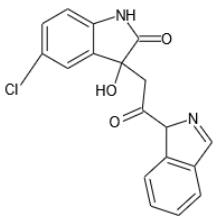
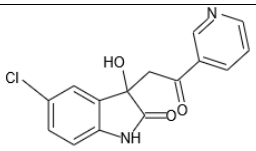
3	SIS-3	
4	SIS-4	
5	SIS-5	
6	SIS-6	
7	SIS-7	
8	SIS-8	
9	SIS-9	
10	SIS-10	

S. No	Compound Code	Synthesized Compound
1	SIS-1	3-hydroxy-3-[2-oxo-2-(thiophen-3-yl) ethyl]-1,3-dihydro-2*H*-indol- 2-one
2	SIS-2	3-hydroxy-3-[2-(4*H*-imidazol-4-yl)-2-oxoethyl]-1,3-dihydro-2*H*- indol-2-one
3	SIS-3	3-hydroxy-3-[2-oxo-2-(1*H*-pyrrol-3-yl) ethyl]-1,3-dihydro-2*H*-indol- 2-one
4	SIS-4	3-hydroxy-3-[2-(1*H*-isoindol-1-yl)-2-oxoethyl]-1,3-dihydro-2*H*- indol-2-one

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5	SIS-5	3-hydroxy-3-[2-oxo-2-(pyridin-3-yl) ethyl]-1,3-dihydro-2*H*-indol-2- one
6	SIS-6	5-chloro-3-hydroxy-3-[2-oxo-2-(thiophen-3-yl) ethyl]-1,3-dihydro- 2*H*-indol-2-one
7	SIS-7	5-chloro-3-hydroxy-3-[2-(4*H*-imidazol-4-yl)-2-oxoethyl]-1,3- dihydro-2*H*-indol-2-one
8	SIS-8	5-chloro-3-hydroxy-3-[2-oxo-2-(1*H*-pyrrol-3-yl) ethyl]-1,3-dihydro- 2*H*-indol-2-one
9	SIS-9	5-chloro-3-hydroxy-3-[2-(1*H*-isoindol-1-yl)-2-oxoethyl]-1,3- dihydro-2*H*-indol-2-one
10	SIS-10	5-chloro-3-hydroxy-3-[2-oxo-2-(pyridin-3-yl) ethyl]-1,3-dihydro- 2*H*-indol-2-one

10. Characterization of synthesized compounds

Physical characterization

The physical properties like molecular formula (MF)Melting point (M.P) Molecular weight (MW) Elemental analysis was given below

Code	MF	MP(^{0}C)	MW (Gm/Mole)	Elemental Analysis
SIS-1	C14H11NO3S	9 - 11°C	273.30704	C (61.52%) H (4.06%) N (5.12%) O (17.56%) S (11.73%)
SIS-2	C13H11N3O3	99 - 105°C	257.24474	C (60.70%) H (4.31%) N (16.33%) O (18.66%)
SIS-3	C14H12N2O3	90-90.5°C	256.25668	C (65.62%) H (4.72%) N (10.93%) O (18.73%)
SIS-4	C18H14N2O3	151-155°C	306.31536	C (70.58%) H (4.61%) N (9.15%) O (15.67%)
SIS-5	C15H12N2O3	200-210°C	268.26738	C (67.16%) H (4.51%) N (10.44%) O (17.89%)
SIS-6	C14H10ClNO3S	154-158°C	307.7521	C (54.64%) H (3.28%) Cl (11.52%) N (4.55%) O (15.60%) S (10.42%)
SIS-7	C13H10ClN3O3	268-270°C	291.6898	C (53.53%) H (3.46%) Cl (12.15%) N (14.41%) O (16.46%)
SIS-8	C14H11ClN2O3	60-70°C	290.70174	C (57.84%) H (3.81%) Cl (12.20%) N (9.64%) O (16.51%)
SIS-9	C18H13ClN2O3	69.02-73.0°C	340.76042	C (63.44%) H (3.85%) Cl (10.40%) N (8.22%) O (14.09%)
SIS-10	C15H11ClN2O3	160-165°C	302.71244	C (62.84%) H (4.00%) Cl (5.98%) N (8.27%) O (16.20%) S (2.71%)

11. Melting Point

Melting and boiling point estimation helps in identification and establishing the purity of any substance. The temperature at which a solid melts and becomes a liquid is known as melting point. A sharp and characteristic melting point of usually 0.5-1.0 is present for pure non-ionic, crystalline organic compound.

Procedure:

The powder or crystalline substance was taken in a capillary tube after heating it to seal.

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Fill through the open end up to 2-3mm and attach it to thermometer with the help of a thread. take liquid paraffin in a beaker, place it over piece of wire gauge over tripod stand. Clamp thermometer that is carrying the test tube to an iron stand and immerse them in the batch of liquid paraffin and see that thermometer and capillary tubes are held in place with a thread.

Maintain the temperature within 15◦C. Following melting of pure substance the flame is reduced. when temperature raises slowly note it as T1 starting point and T2 is recorded when melting of pure substance takes place. The average of these two temperatures reveals the correct melting point of the substance.

S. No	Compound	Melting Point
1	ISATIN	193℃ - 195℃
2	SIS-1	9 - 11℃
3	SIS-2	99 - 105℃
4	SIS-3	90.0 - 90.5℃
5	SIS-4	151 – 152 ℃
6	SIS-5	200 - 210℃
7	SIS-6	154 - 158℃
8	SIS-7	268℃
9	SIS-8	60-70℃
10	SIS-9	69.0 – 73.0℃
11	SIS-10	160℃

12. Solubility

Acetyl Pyrrole Chloro Substituted

Solvent	**Solubility**
Water	Soluble
Chloroform	Soluble
Aniline	Soluble
Formaldehyde	Soluble
Ethanol	Soluble

Acetyl Pyridine Chlorosubstituted

Solvent	**Solubility**
Water	Soluble
Chloroform	Soluble
Aniline	Soluble
Formaldehyde	Soluble
Ethanol	Soluble
Solvent	**Solubility**
Water	Soluble
Chloroform	Soluble
Aniline	Soluble
Formaldehyde	Soluble
Ethanol	Soluble

Acetyl Pyridine

13. Introduction to Nmr &Mass Spectroscopy

NMR was invented by collaboration of scientists from Harvard and Stanford university in the year1946. This spectroscopy is specific to a nucleus that has wide applications in physical sciences and industry. It uses a large magnet as to probe intrinsic spin properties of atomic nuclei. The electromagnetic radiation is used for transition and resonance of atomic nuclei.

Mass spectroscopy is a sophisticated tool to identify and quantify a wide range of clinically used analytes. The analytical scope gets increased when we combine gas or liquid chromatography with mass spectrometer. The results of mass spectroscopy is expressed as m/z ratio. Where m is the molecular weight of ion in Daltons and Z is the number of charges located on the molecule.

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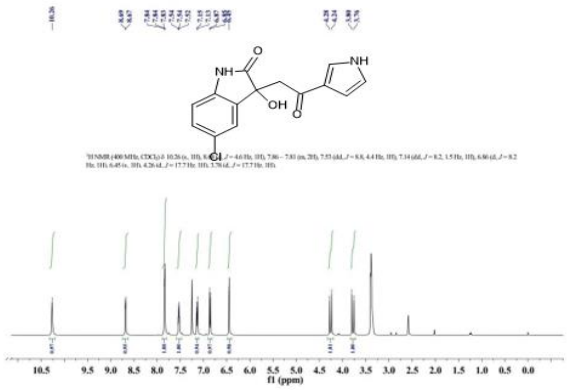
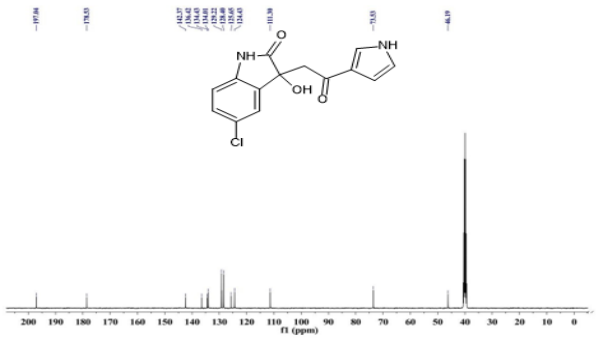
Proton NMR



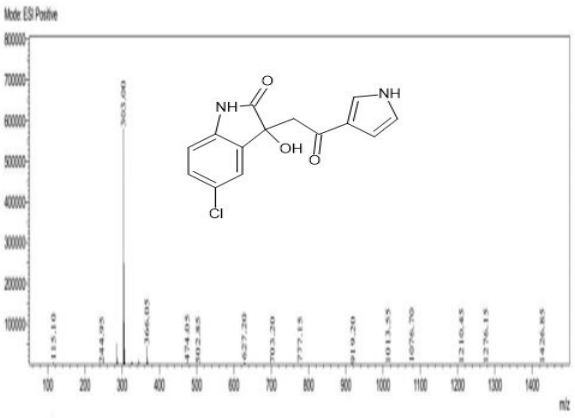
1H - NMR Spectrum of 5-chloro-3-hydroxy-3-[2-oxo-2-(pyridin-3-yl) ethyl]-1,3-dihydro-2*H*- indol-2-one

C^{13} NMR



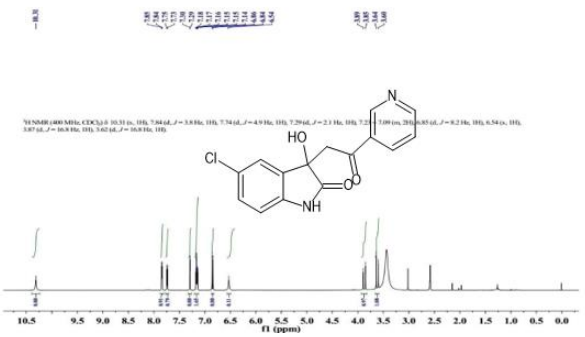
^{13}C- NMR Spectrum of 5-chloro-3-hydroxy-3-[2-oxo-2-(pyridin-3-yl) ethyl]-1,3- dihydro-2*H*-indol-2-one

MASS SPECTROSCOPY



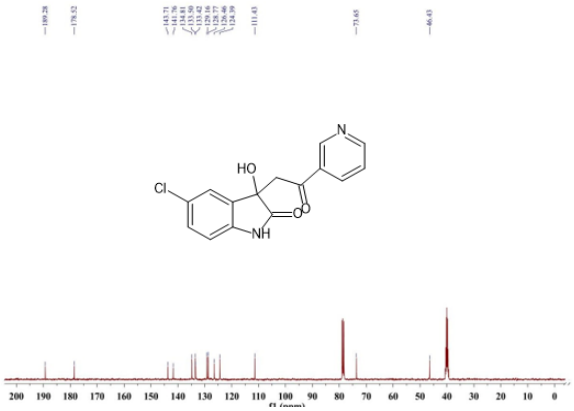
Massw Spectroscopy 5-chloro-3-hydroxy-3-[2-oxo-2-(pyridin-3-yl) ethyl]-1,3- dihydro-2H-indol-2-one

Proton NMR



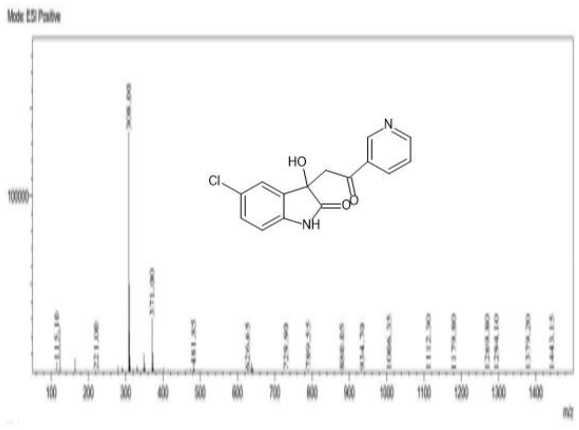
1H-NMR Spectrum of 5-chloro-3-hydroxy-3-[2-oxo-2-(1*H*-pyrrol-3-yl) ethyl]-1,3- dihydro-2*H*-indol-2-one

C^{13} NMR



^{13} C NMR Spectrum of 5-chloro-3-hydroxy-3-[2-oxo-2-(1*H*-pyrrol-3-yl) ethyl]-1,3-dihydro- 2*H*-indol-2-one

MASS SPECTROSCOPY



Mass Spectrum of 5-chloro-3-hydroxy-3-[2-oxo-2-(1*H*-pyrrol-3-yl) ethyl]-1,3-dihydro- 2*H*-indol-2-one

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Code	^{1}h-Nmr	13 C Nmr
SIS-8	Arh 7.3 (4H), C=C 6.5 (1H) C-CL (3.5), CH2OH (3.5 – 4) C-NH2 (1.5 – 5.5)	Ar (123.7,132.1,142.2,144.2) C=O (179), C=C (144), C-CL (40), C-O (74), C-OH (79), C-N (46)
SIS-10	Ar 7.3 (4H), C=C 6.5 (1H) C-CL (3.5), CH2OH (3.5 – 4) C-NH2 (1.5 – 5.5)	Ar (123.7,132.1,142.2,144.2) C=O (179), C=C (144), C-CL (40), C-O (74), C-OH (79), C-N (46)

14. Anthelmintic Activity

The synthesized products are screened for anthelminthic activity using six earthworms of nearly equal size by placing them in the solutions of standard and test drug compounds solution at room temperature and the normal saline was used as a control.

The standard and the test drugs were prepared by dissolving them in minimal quantity of dimethyl sulfoxide (DMSO). volume was adjusted to 10ml by adding normal saline and the concentrations obtained should be 0.1%w/v 0.2% w/v 0.5%w/v.

Albendazole is used as standard. The newer compounds were evaluated by comparing the time taken for complete paralysis and death of earthworms with that of the albendazole. The death of these organisms was concluded by applying external stimuli that can able to induce movement in them and by fading away of their body colour.

Compound	**Time taken for paralysis (P) and death (D) (Mean ±SD) %concentration Paralysis time (Minutes) Lethal time (Minute)**					
	0.1	0.2	0.5	0.1	0.2	0.5
Control	-	-	-	-	-	-
Albendazole	15	12	8	44	34	26
SIS-5	20	23	20	41	56	59
SIS-10	17	15	12	48	37	30
SIS-8	18	14	10	47	37	29

Docking Results:

In this work, ligands against the **BCL-2 protein** (4LXD) were subjected to molecular docking using AutoDock4.2. Initially, the Open Babel program was used to prepare the ligands' 3D structures for docking following their acquisition from PubChem. Docking preparations were also made for the receptor, **BCL-2 protein**. The AutoDock4.2. docking protocol was configured, with the search space and grid box dimensions set to 60 x 60 x 60. Additionally, the docking runs for triplicate docking were started. The binding affinities of the resultant docking positions were examined, and the best poses were chosen for additional examination. PyMOL software was used to examine the ligand-receptor interactions and binding mode. The potential of the drugs and phytochemicals as inhibitors of the **BCL-2 protein** was assessed using the docking study data.

Table 1: Docking score:

Protein-Ligand Complex	**Docking score**
SIS-1	-7.46
SIS-2	-10.91

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Protein-Ligand Complex	Docking score
SIS-3	-10.90
SIS-4	-11.44
SIS-5	-7.70
SIS-6	-7.53
SIS-7	-7.78
SIS-8	-7.88
SIS-9	-8.16
SIS-10	-8.17

15. Result and Discussion

The newer Isatin structures were synthesized and were screened for the anthelminthic action. structures of novel compounds were characterized as sis-1to sis-10 on the basis of analytical and spectral data that includes NMR along with MASS data. Through conducting multiple reactions Isatin reacted with 2-acetylthiophene in the presence of sodium bicarbonate when ethanol was used as a solvent that resulted in 3-hydroxy3[2-oxo-2(thiophene-3-yl) ethyl]2,3-dihydro 2h-indole-2-one. All the denovo molecules have shown the pharmacological activity by invitro studies using earthworms.

16. Conclusion

Isatin and its products gives a new hope for the synthesis of several useful medicines that are effective as anti-bacterial, anti-helminthic, anti-viral and cytotoxic principles. The synthesis of new compounds from Isatin was made possible by modification of core molecule through alkyl, acyl, Friedel craft, nucleophilic addition and substitution reactions. Moreover, these compounds are more potent than the substances that have electron donating moiety.

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