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Synthesis of Indole, Derivatives of Indole and Mono-Substituted Indole

Sharif A. Kazi[1], Shahabaj M. Bagwan[2] and Sandip A. Nirwan[3]
Loknethe Gopinathji Munde Arts, Commerce & Science College, Mandangad, Ratnagiri, Maharashtra, India[1,3]
Karmveer Hire Arts, science, Commerce & Educational College, Gargoti, Bhudargad, Kolhapur, Maharashtra, India[2]
Address for Correspondence: kazisharifa1988@gmail.com

Abstract: *Indoles are occurs both naturally and synthetically. Indoles are most important heterocycles in organic chemistry. Indoles & its derivative exhibit wide range of biological activity such as anti-Alzheimer's disease, anti-Bacterial, anti-cancer, anti-diabetic, anti-inflammatory, anti-oxidant, anti-fungal & anti-corona virous. [1,2] In presence research work involve synthesis of Indole, derivative of Indole & substituted Indole is characterized by Chemical/Physical test & Two, Indole & 3nitro-indole is characterized by IR Spectra.*

Keywords: Indol, Organic compound, Heterocycles, Biological active etc

I. INTRODUCTION

In organic chemistry, cyclic compounds that contain at least one ring atom that is not a carbon are called heterocycles. However, the rings of most heterocycles that Pertain to organic chemistry contain more carbons than heteroatoms. However, "heterocycles" that do not contain any carbon, such as the S_8 ring, are also known in inorganic chemistry, but that is exactly why they are classified under in organic chemistry. In organic chemistry, carbocyclic compounds that contain at least one ring atom that is not a carbon are called "heterocycles".

The most frequently occurring heteroatoms in heterocycles are nitrogen, oxygen, and sulphur. However, heterocycles with other heteroatoms. Such as phosphorus and selenium, also appear. In nature heterocycles are of great importance. Roughly more than one held of all natural products contains heterocyclic components. Many of them have important functions in the human organism. In additions, many natural compounds are pharmacologically active. Nitrogen-containing heterocycles are particularly widespread in nature. The alkaloids, for instance, are a special class of nitrogen containing, naturally occurring heterocycles. Furthermore, deoxyribonucleic acid (DNA), which is the carrier of genetic information in all living beings, contains the nitrogen-containing heterocycles adenine and guanine (purine bases), as well as cytosine and thymine (pyrimidine bases)-Ribonucleic acid (RNA) additionally contains the pyrimidine base uracil. Genetic information is saved in the sequence of these purine and pyrimidine bases in the DNA and RNA chains. There are several nomenclature systems of heterocycles that are in use. Aside from systematic nomenclature, trivial names are also frequently applied.

II. MATERIALS AND METHODS

All the commercial reagent and solvent were used AR-grade. Melting point were recorded in laboratory using capillary tube. All the reaction is monitored by chemical & physical methods such as melting point, boiling piont & functional group detection test.

2.1 Synthesis of 1H-Indole

Step 1: (N-Formyl-o-Toluidine) Mix. Together 43gm (0.4 mol) of o-toluidine & 21gm of 90% formic acid in a 100ml round bottom flask fitted with a reflux condenser, & heat the mixture on a boiling water both for three hours. Replace the reflux condenser by a Claisen steel head & an air condenser arranged for distillation under reduced pressure & distilled the product using a water pump, collecting the formyl-o-toluidine as a fraction of B.P-173^{0}C. which solidified on cooling M.P-57^{0}C the yield is (80%). A pure specimen M.P-61^{0}C may be obtained by crystallization from the mixture of benzene & light petroleum (B.P-48^{0}C).

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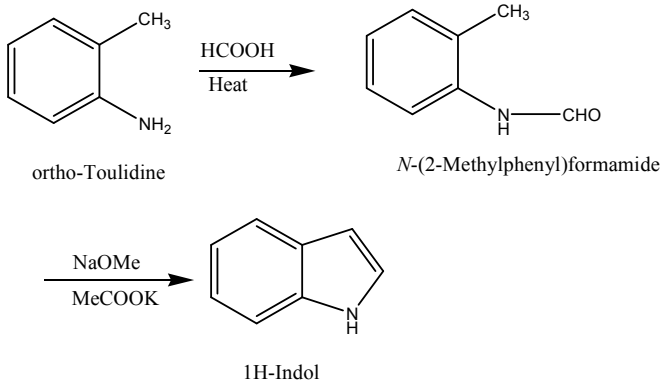
Step 2: -Prepare the solution of sodium methoxide in 125ml anhydrous methanol using 5.75 gm (0.25 mol) of sodium in a 250 ml flask fitted with a reflux condenser protected by a calcium chloride guard tube and add 35gm of N-formyl-o-toluidine then add rapidly 50gm coarsely ground, freshly fused potassium acetate & heat under reflux with shaking until all has dissolved. Remove the methanol under reduced pressure transfer a flask to a fume cupboard & fit a steal head & condenser set for downward distillation surround the flask with a both of molten woods metal & raise the temp. Steadily to about 300-350^{0}C. The subsequent reaction is accompanied by the distillation of o-toluidine & the evolution of carbon monoxide, continue the head until no further distillation occurs (about 30 min) & finally remove traces of o-toluidine by carefully applying partial vacuum. Remove the heating both allow the flask to cool & decompose the residue by adding 100ml of water & steal distilling. Colourless plate of Indole separates from the cooled distillate, make the latter slightly acidic with HCL. Collect the filtrate the section filtration & wash them with a little cold water. The yield of indole M.P-48^{0}C is 5gm. A purer specimen (M.P-52^{0}C) may be obtained by crystallization from light petroleum (B.P-48^{0}C)[1,3]



ortho-Toulidine

N-(2-Methylphenyl)formamide

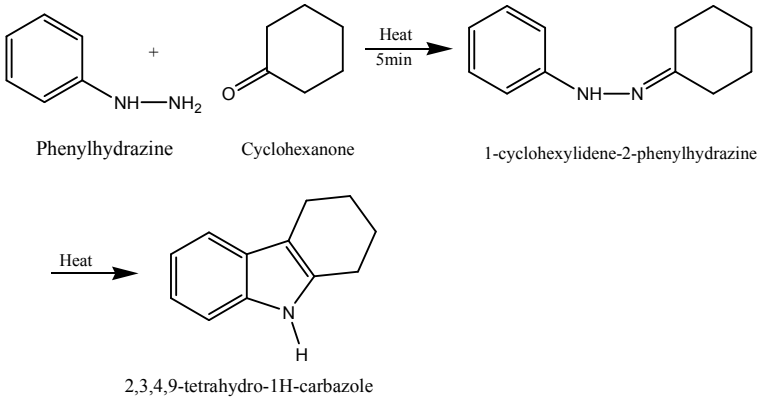
1H-Indol

Scheme-1: Synthesis of 1H-Indole

2.2 Synthesis of 2,3,4,9-tetrahydro-1H-carbazole

Cyclohexanone 9ml, phenyl hydrazine 8gm. (0.07mol) Dissolve the cyclohexanone in 50ml of glacial acetic acid, add 8gm of phenyl hydrazine & boil the solution under reflux for 5 Min. Cool the solution when the tetrahydro carbazole will crystallize out. Filter the pump, drain well & recrystallize from ethanol. The recrystallization should be performed rapidly, for the tetrahydro carbazole undergo atmospheric oxidation in a hot solution after recrystallisation, the compound should be dried in a vacuum desiccators & not in an oven. Repeated recrystallisation should be avoided. The tetrahydro carbazole after through drying is obtained as colourless crystals M.P-118^{0}C the yield of recrystallize material 11gm.

If cold saturated ethanolic solution a recrystallisation tetrahydro carbazole & of picric acid are mixed & stirred the chocolate-brown picrate of the carbazole slowly crystallize. After it has been filtered at the pump, washed with small quantity of ethanol & dried, it has (M.P-145^{0}C)[9,12]



Phenylhydrazine Cyclohexanone 1-cyclohexylidene-2-phenylhydrazine

2,3,4,9-tetrahydro-1H-carbazole

Scheme-2: Synthesis of 2,3,4,9-tetrahydro-1H-carbazole

2.3 Synthesis of 3-Formyl-1H-Indol (Formulation of Indole)

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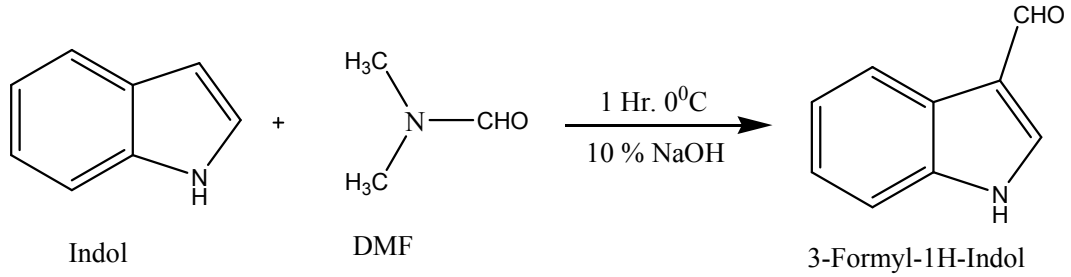
Indole 3.38gm (0.0235mol) was added drop wise to N-N-Dimethyl formamide 15ml under stirring at 0^0C. the reaction mix. Was stirring for 1 hour at same temp. To the reaction mix. added solution of N-N-Dimethyl formamide at 0^0 C. The reaction mix. was stirred at 35^0 C for 1 hour & then poured in ice cold water 90ml a clear solution is obtained which on basify with 10% NaOH solution. Solid ppt. Out. Then clear crystal was separated by washed with water (M.P-144^0C)[1,15]



Indol DMF 3-Formyl-1H-Indol

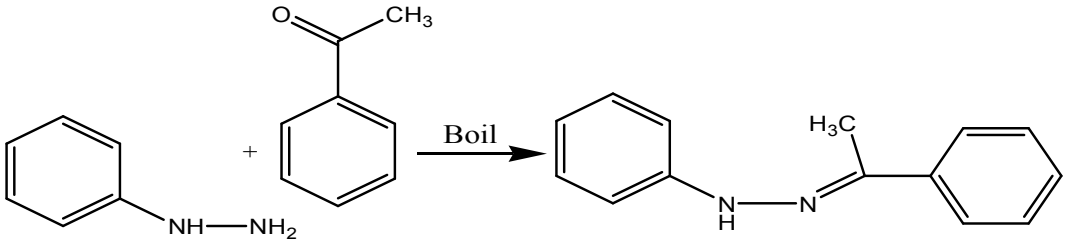
Scheme-3: Synthesis of 3-Formyl-1H-Indol (Formulation of Indole)

2.4 Synthesis of 2-phenyl-2,3-dihydro-1H-indole

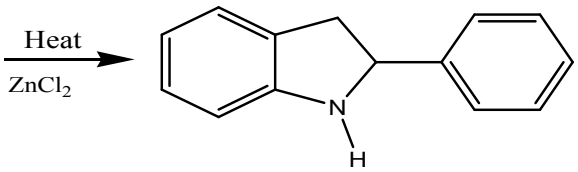
Step 1: Dissolve 5ml of acetophenone in 12ml of glacial acetic acid contained in a boiling tube for which a well-fitting cork is available. Dissolve 6.8gm of phenyl hydrazine in a mixture of 12.5 ml of glacial acetic acid & 20ml of water & add this solution to that of the acetophenone at once corking & vigorously shaking the boiling tube. The mixture becomes slightly warm & the phenyl hydrazine rapidly separate as colourless crystals. After 5 min. Shaking, cool and the tube in cold water & then filter the content at the pump.

Wash the crystal on the filter with dil. Acetic acid & then with water. Recrystallize the phenyl hydrazine from ethanol & dried thoroughly.

Step 2: The phenyl hydrazine of acetophenone (Step-1) 1.05gm, with Zinc chloride 0.68gm in a 100ml beaker & heated in 15 minutes in water bath, cool the solution & add small amount of ice-cold water. Filter it, ppt. is obtained. Dry the product & recrystallization in ethanol. [2,3]



Phenylhydrazine Phenylethanone 2E-1-Phenyl-2-(1-Phenylethylidene)hydrazine



2-phenyl-2,3-dihydro-1H-Indole

Scheme 4: Synthesis of 2-phenyl-2,3-dihydro-1H-Indole

2.5 Synthesis of 1H-indole-3-yl(phenyl)methanone

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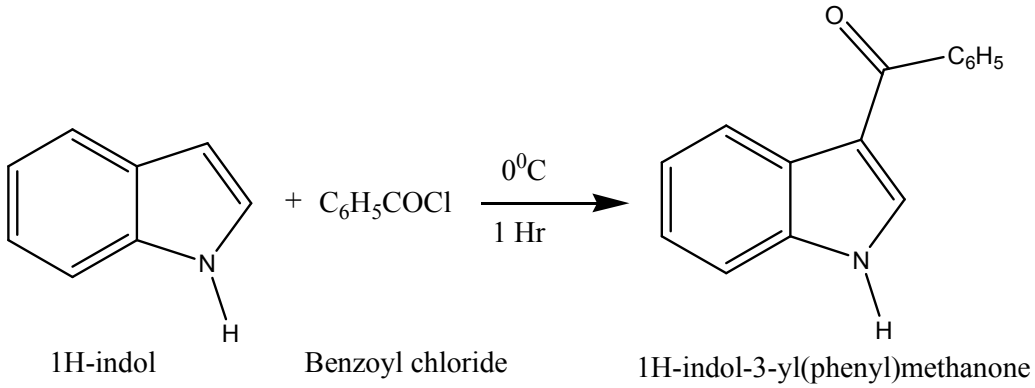
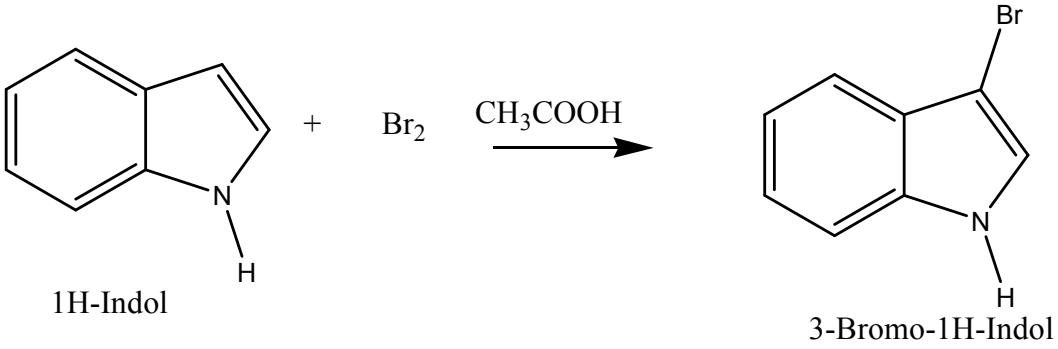
In 250ml of conical flask take 2gm of Indole 20ml of 10% NaOH solution & 2.4ml of Benzoyl chloride (0.017mol). Cool the flask & shake vigorously till the smell of benzoyl chloride disappears which generally requires 14 min. Dilute the content with cold water & water filter off the ppt. product. Wash with cold water & recrystallize from alcohol. (M.P-158^0 C)[1,10]



Scheme 5: Synthesis of 1H-indole-3-yl(phenyl) methnone

2.6 Synthesis of 3-bromo-indole

Dissolve 2.4gm of indole in glacial acetic acid (0.0201mol) about 18ml in 100ml flask. Now add bromine dissolve in glacial acetic acid drop by drop by means of dropping funnel and with constant shaking till mixture becomes yellow wish oranges, allow it to stand for about half an hour and then pour the reaction mixture in to excess of water. Filter of the product at the pump, wash with cold water and dry. Recrystallisation may be done from alcohol (MP.147^0 C)[9,14]



Scheme 6: Synthesis of 3-Bromo-1H- Indole

2.7 3-nitro-1H-indole

Take 4.2gm (0.072 mol) of indole and 4.2ml of glacial acetic acid in 200ml beaker stir and warm the content to obtained the clear solution and add 8c.c conc. Sulphuric acid portion wise with steering. Now place the reaction mixture in a freezing mixture bath (ice + salt) to have temp in a vicinity of 0 to 5^{0}C and add 1ml of nitric acid drop wise and constant steering. Remove the beaker from the freezing mixture bath, allow it to stand at room temp for half an hour. Pour the content to 100gm of crushed ice and allow the product to stand for 15min filter the product add the pump wash the product with cold water and recrystallized product from alcohol (MP.165^{0}C) [9,14]

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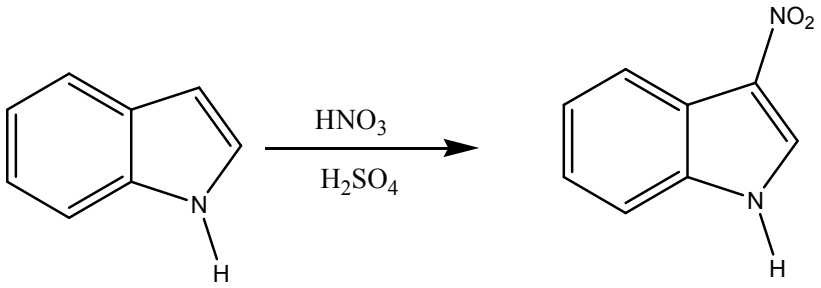

1H-Indole 3-Nitro-1H-Indole

Scheme 7: Synthesis of 3-nitro-1H-indole

IV. RESULT AND DISCUSSION

Compound	M.P.	Yield in gm	% Yield	Appearance
1] Indole	48^0C	2.1gm	42.00%	Solid
2] Derivatives	145^0C	3.3gm	41.25%	Solid
3] Derivatives	105^0C	2.4gm	40.81%	Solid
4] Formulation	144^0C	1.4gm	41.42%	Solid
5] Benzylation	158^0C	0.68gm	34.00%	Solid
6] Brominaion	147^0C	1.0gm	41.50%	Solid
7] Nitration	165^0C	1.6gm	38.00%	Solid

4.1 Functional Group Test

A. Aromatic Secondary Amines:

1. Reaction with Nitrous Acid

Dissolve nearly 1.g of compound in the 5ml of dilute HCI and cool it in ice cold water. To the above solution add 4-5 ml of 10% sodium nitrite solution drop wise and with constant Shaking, allow the solution to stand for five minutes when a yellow precipitate is produced.

Add nearly about 10ml of water to the above solution and transfer it to the separating funnel. Extract the yellow oily layer with ether, dilute alkali solution and finally with water. Evaporate of the ether, take 1 drop of the oily nitro compound in a test tube and add to it 0.05g of Phenol. Warm the resulting product, cool and add 1ml of conc. Sulphuric acid an intense green colour changing to red on dilution and then back to greenish blue on addition of an excess of alkali.

2. Simmons Test

Take a few drops of the compound and add to it dilute solution of sodium nitro prusside followed by a few drops of dilute Acetaldehyde solution, deep blue colour will be appeared within five minutes.

B. Aromatic Nitro Compound

1. Reduction in Acidic Medium

Take 0.5g of the nitro compound in 5ml of conc. HCI and 2ml of alcohol. Add small pieces of grunted Tin and control the reaction by cooling. Reflux the mixture in a water bath until the entire original compound passes into solution. Filter the product when the reaction ceases and test for the amino group in the filtrate.

2. Reaction in Neutral Medium

Dissolve nearly 0.5g of the substance in an equimolar mixture of alcohol and water by warming. Add it some amount of zinc dust and solid NH_4Cl. Heat the mixture to boil and allow the reaction to complete. Filter the solution and add Tollen's reagent to the filtrate a black Precipitate will be developed.

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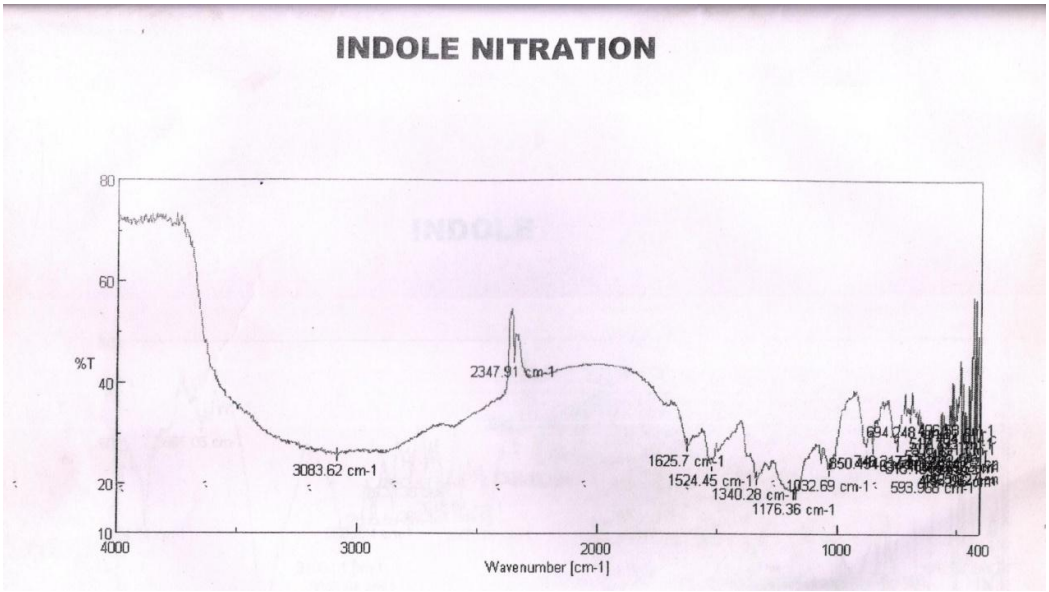
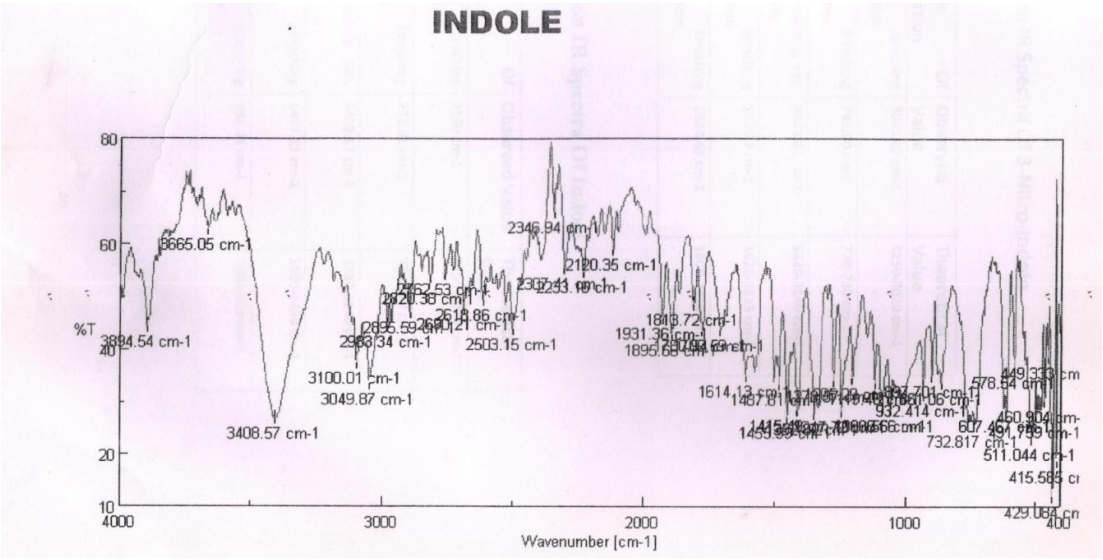
IR SPECTRA



Interpretation IR Spectra of *3-Nitro-1H-Indole*

Sr. No.	Types Of Vibration	Observed Value	Theoretical Value
1	=C-H Stretching Vibration	3083.62 cm^{-1}	3150-3020 cm^{-1}
2	C-H Stretching Vibration	740.00 cm^{-1}	770-730 cm^{-1}
3	N-H Stretching Sec. Amines	3083.62 cm^{-1}	3330-3140 cm^{-1}
4	N=O Stretching Vibration	1625.7 cm^{-1}	1620-1450 cm^{-1}
5	C=C Stretching Vibration	1524.45 cm^{-1}	1600-1450 cm^{-1}



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Interpretation IR Spectra of *1H-Indole*

Sr. No.	Types Of Vibration	Observed Value	Theoretical Value
1	=C-H Stretching Vibration	3100 cm^{-1}	3150-3020 cm^{-1}
2	C-H Stretching Vibration	732.81 cm^{-1}	770-730 cm^{-1}
3	N-H Stretching Sec. Amines	3408.57 cm^{-1}	3330-3140 cm^{-1}
4	C=C Stretching Vibration	1487.81 cm^{-1}	1600-1450 cm^{-1}
5	C-C stretching Vibration	932.41 cm^{-1}	1300-800 cm^{-1}

V. CONCLUSION

Indole and substituted indole are very important part of medicinal drug. In this research work a successful attempt is made for the synthesis of different substituted indole. The products are confirmed by chemical/physical test and IR spectra. The yield is reported for each compound. The percentage yield for indole and substituted indole is given below.

Sr. No	Compound	Yield (gm)	% Yield
01	Indole	2.1	42
02	Derivatives	3.3	41.25
03	Derivatives	2.4	40.81
04	Formulation	1.4	41.42
05	Benzylation	0.68	34
06	Bromination	1.0	41.50
07	Nitration	1.6	38

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