Catalytic Effect
Of
Indium - Tri - Chloride
On The Electrophilic Substitution Reactions
Of Indole With Aromatic Aldehydes

By

S. Geetha

A DISSERTATION SUBMITTED TO THE AVINASHILINGAM INSTITUTE FOR HOME SCIENCE AND
HIGHER EDUCATION FOR WOMEN - DEEMED UNIVERSITY, COIMBATORE - 641 043
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE IN

APPLIED CHEMISTRY

APRIL - 1999

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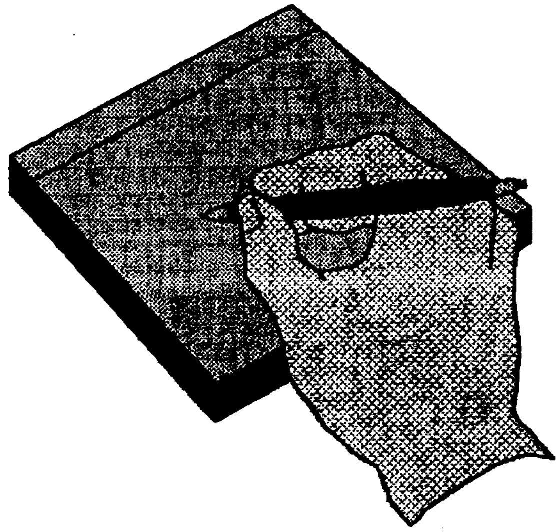
Certified As Bonafide Research Work.

S. Sivakamasundari
29/4/99
Signature of Head of the Department

29.4.99
Signature of Guide



ACKNOWLEDGEMENT

ACKNOWLEDGEMENT

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LIST OF ABBREVIATIONS

^{1}HNMR - PROTON NUCLEAR MAGNETIC RESONANCE SPECTRUM

CMR - CARBON NUCLEAR MAGNETIC RESONANCE SPECTRUM

IR - INFRA RED SPECTRUM

UV - ULTRA VIOLET SPECTRUM

Rf - RETENTION FACTOR

tlc - THIN LAYER CHROMATOGRAPHY

r.t - ROOM TEMPERATURE

3°C - TERTIARY CARBON

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PROCEDURE FOR COLUMN CHROMATOGRAPHY

INTRODUCTION

1 INTRODUCTION

Indole nucleus plays a significant role in pharmacology. Various psychopharmacological activities such as hallucinogenic, hypnotic, sedative antidepressive etc. have been found to be associated with Indole nucleus.

It has been noticed that the introduction of phenyl group at 2-position of the indole ring enhances biological activities, like mono amino oxidase inhibition. Alkyl amino (substituted phenyl) indoles have shown potent mono amino oxidase inhibitory activity.

Aniconvulsant activity has been reported in 3-acylindole derivatives. Bis-indolyl methane derivatives have shown potent central nervous system depressant activities.

These observations have prompted the synthesis of substituted indoles. In the present work, three indole derivatives have been successfully synthesized.

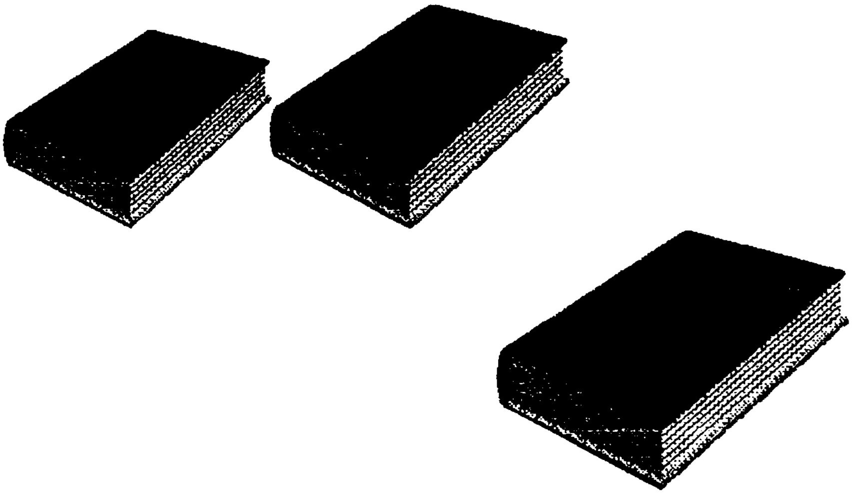
The eletrophilic substitutions of indoles with aromatic aldehydes and Schiff's bases result in interesting heterocyclic compounds such as bis-indolyl methanes. They provide greater yield when they are catalysed by Lewis acids such as Aluminium chloride, Lanthanide triflates etc.

The present work is concerned with the synthesis of Indole derivatives using Indium tri chloride as a Lewis acid to catalyse the reaction. Indium tri chloride is a catalyst used widely in polymerisation reaction, chlorination of chloro phenyl silanes, sulphide synthesis, Friedel craft's acylation, hydrode chlorination and condensation of silyl enol ethers. The fast coordination-dissociation tendency of Indium tri chloride prompted me to investigate its catalytic activity in the electrophilic substitution reactions of Indole.

Acetonitrile has been used as solvent medium for this synthesis of Indole derivatives. The products have been separated by column chromatography. Various spectral techniques such as IR, ^{1}HNMR, CNMR and Mass spectra have been utilised for the analysis and interpretation of the expected structures.

1.1. OBJECTIVES OF THE STUDY

1. To study the electrophilic substitution reactions of Indole with
   - a. Benzaldehyde
   - b. Tolualdehyde
   - c. Vanillin
2. To investigate the effectiveness of Indium tri chloride as catalyst in the above reaction.
3. To find out the optimum requirement of the catalyst to get better yield.
4. To make use of column chromatography technique for the separation and purification of the synthesized compounds.
5. To make the synthesis of Indole derivatives economical.
6. To carry out various spectral studies such as IR, ^{1}HNMR, CNMR and Mass spectra of the synthesized compounds.
7. To study and interpret the spectral results.

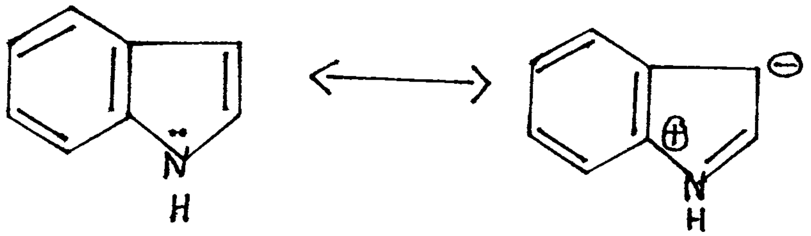


REVIEW OF LITERATURE

2. REVIEW OF LITERATURE

2.1 Structure and reactivity of Indoles

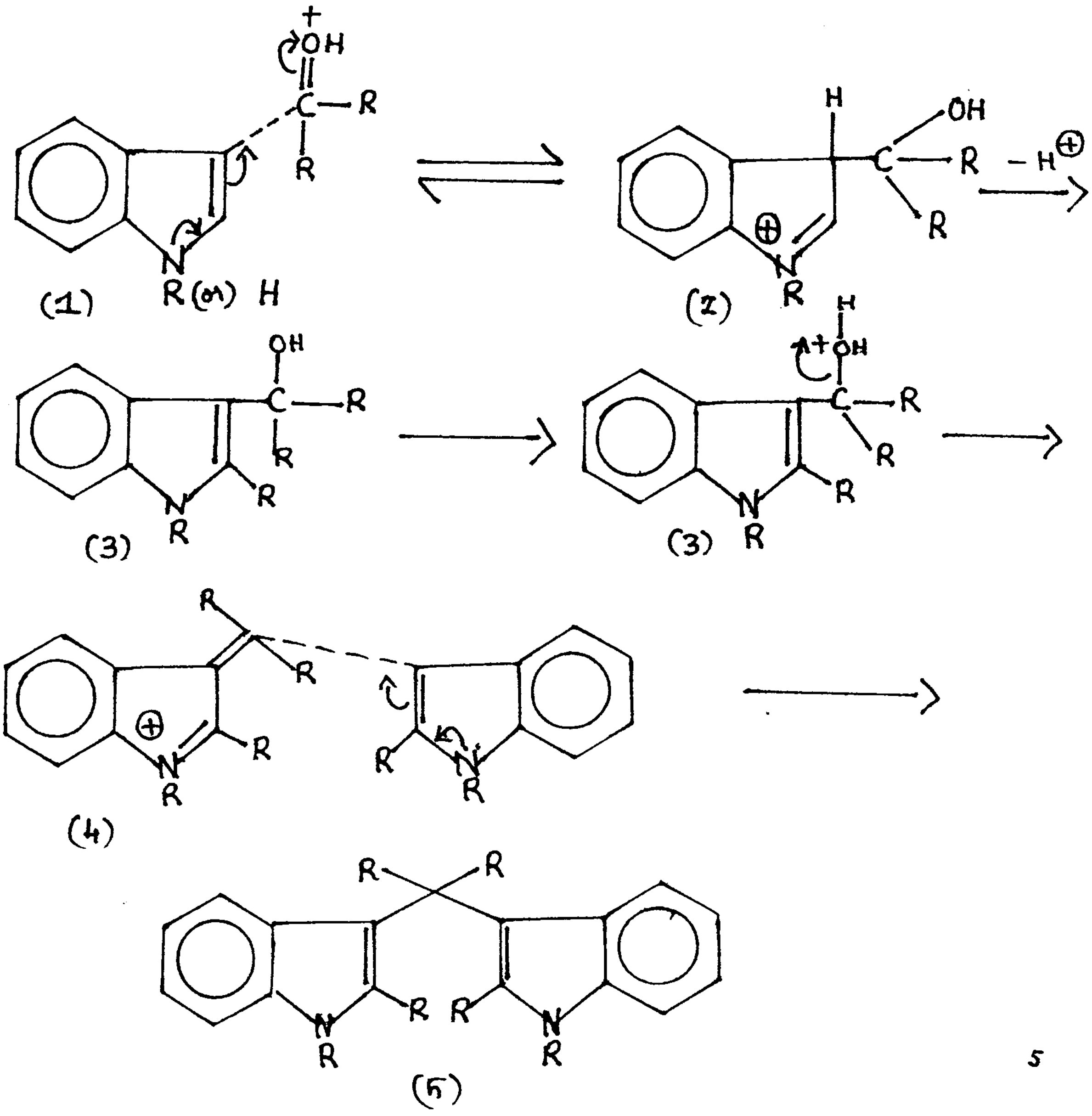
Indole is a planar hetero aromatic molecule. The ten-electron pi-system is formed by a pair of electrons from the Nitrogen atom and eight electrons from the Carbon atoms of the ring. In accord with the familiar description of Indole in terms of resonance concept in that there is significant delocalization of electron density from Nitrogen to the Carbon atoms of the ring, particularly to C-3. The most fundamental chemical properties of the indole ring are correctly predicted by the structural picture.



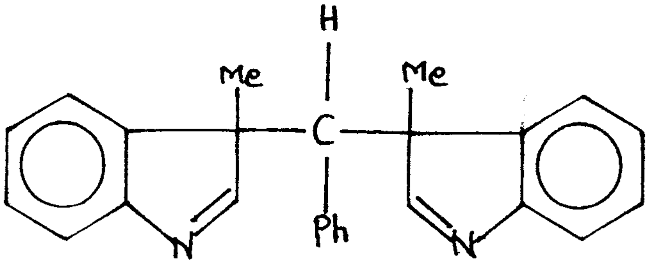
The Indole ring is reactive towards electrophilic substitution, the 3- position being the most reactive site for substitution. The high reactivity of the 3-position can be predicted on the basis of pi-electron density - informations obtained from molecular orbital calculations. Due to the high reactivity of the-3-position the substition takes place only on the 3-position. Hamlet and Dacons have also concluded from the UV- spectra of 2- arylIndoles in 85% phosphoric acid that protonation must occur predominantly at the 3- position.

2.1.1. Reactions of Indole with Ketones and Aldehydes:

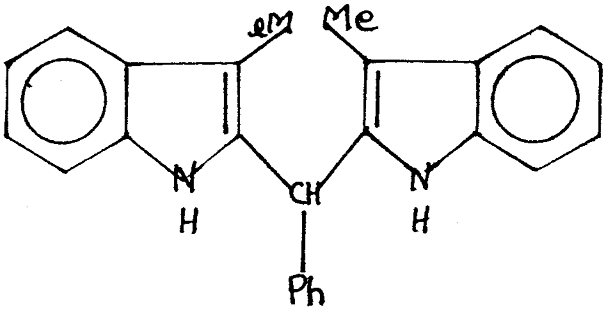
Reactions between Indoles and aldehydes or ketones are ordinarily initiated by acid. The carbonyl compounds attack at the 3-position of the indole ring. Most such reactions however proceed beyond this initial stage. The most commonly observed reaction is the reaction of 2 moles of an Indole with an aldehyde or ketone to give a bisindolyl methane. (5). This transformation depends upon the instability of the carbinol (3) in acidic solution Indolyl carbinols lose water, generating electrophilic alkylidiene indolenines (or the conjugate acid 4) which act as electrophiles toward a second molecule of the Indole.



The structures of the products derived from aldehydes and 3-substituted Indoles caused some difficulty prior to the advent of the modern spectroscopic methods and an indolenine (a) structure was orginally assigned. The presence of typical Indole ultraviolet absorption and the presence of N-H absorption bands in the infra red clearly show that the products are actually 2, 2'- di indolyl methanes. (b)

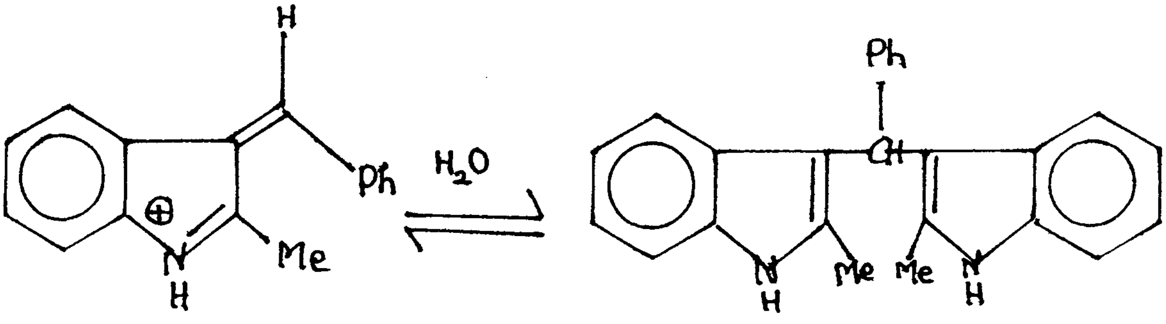


[a]



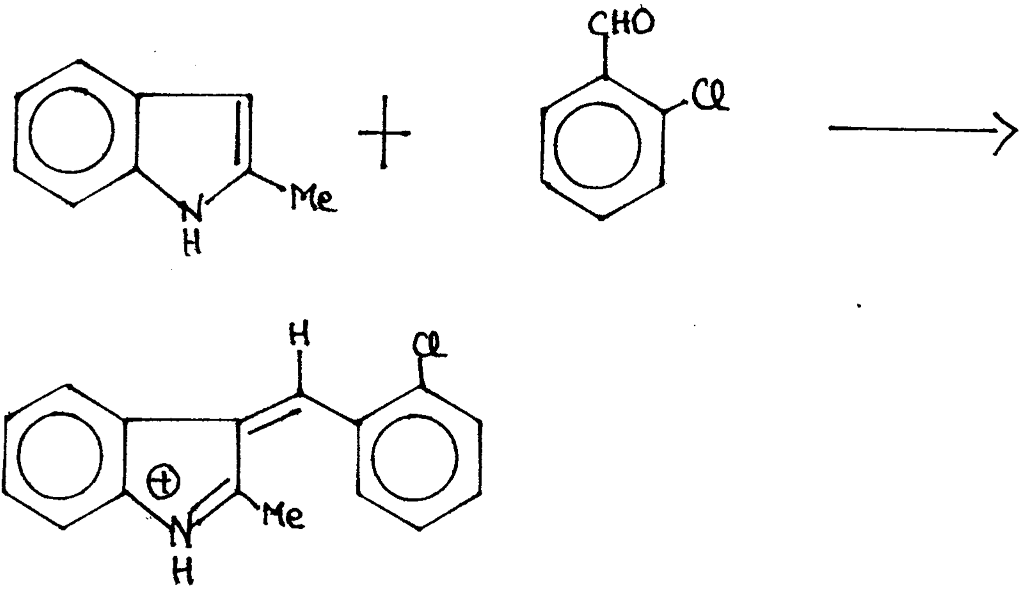
[b]

Burr and Gortner have demostrated qualitatively that the position of the equilibrium between the di indolyl methane (ii) and the alkylindene 3–H indole (i) is a function of the acidity of the solution. Strongly acidic media favours the condensation of aromatic aldehydes with Indoles. Strongly acidic solution can be used as a preparative route to 3-arylidene 3H-indoles, the synthesis being an example for this.



[i]

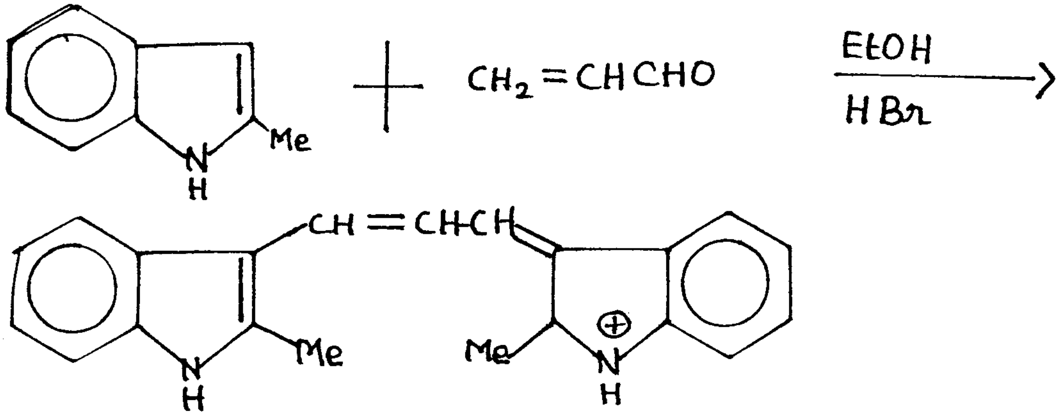
[ii]



2.1.2 Reactions with α, β-unsaturated Carbonyl compounds

The reaction of 2-methyl indole and certain α,β unsaturated carbonyl compounds in alchoholic hydrogen bromide proceeds by reaction with indole at both the β- Carbon and the carbonyl group followed by oxidation to give alkylidiene 3-H-indolium salts.

[i]



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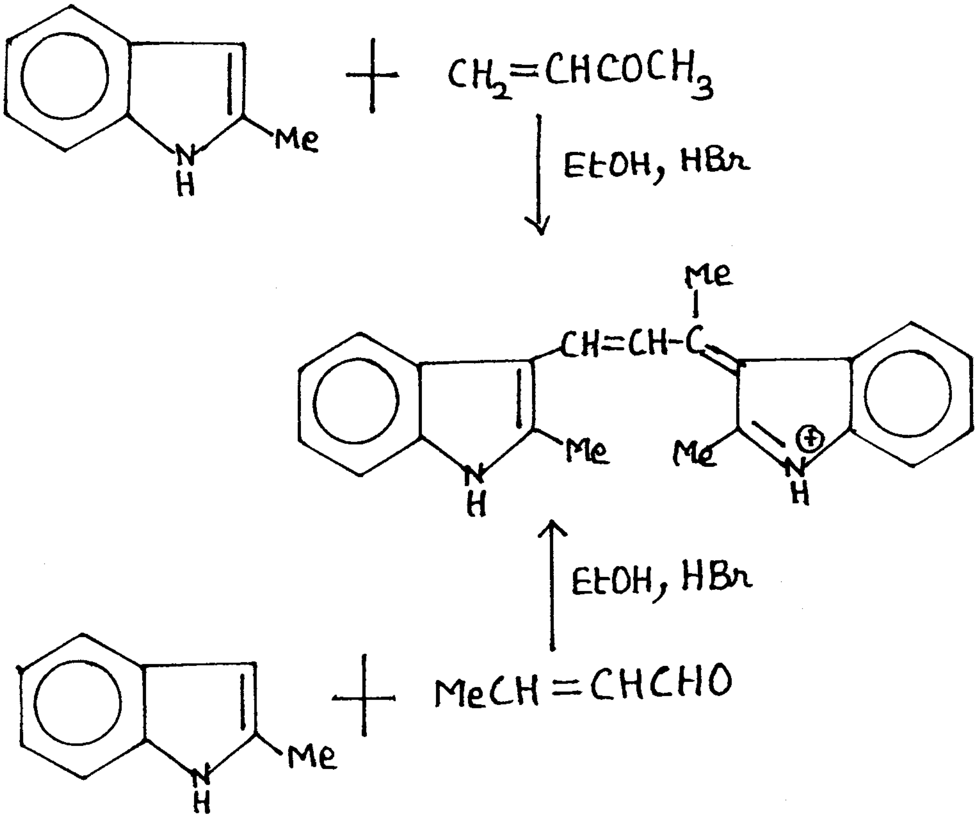
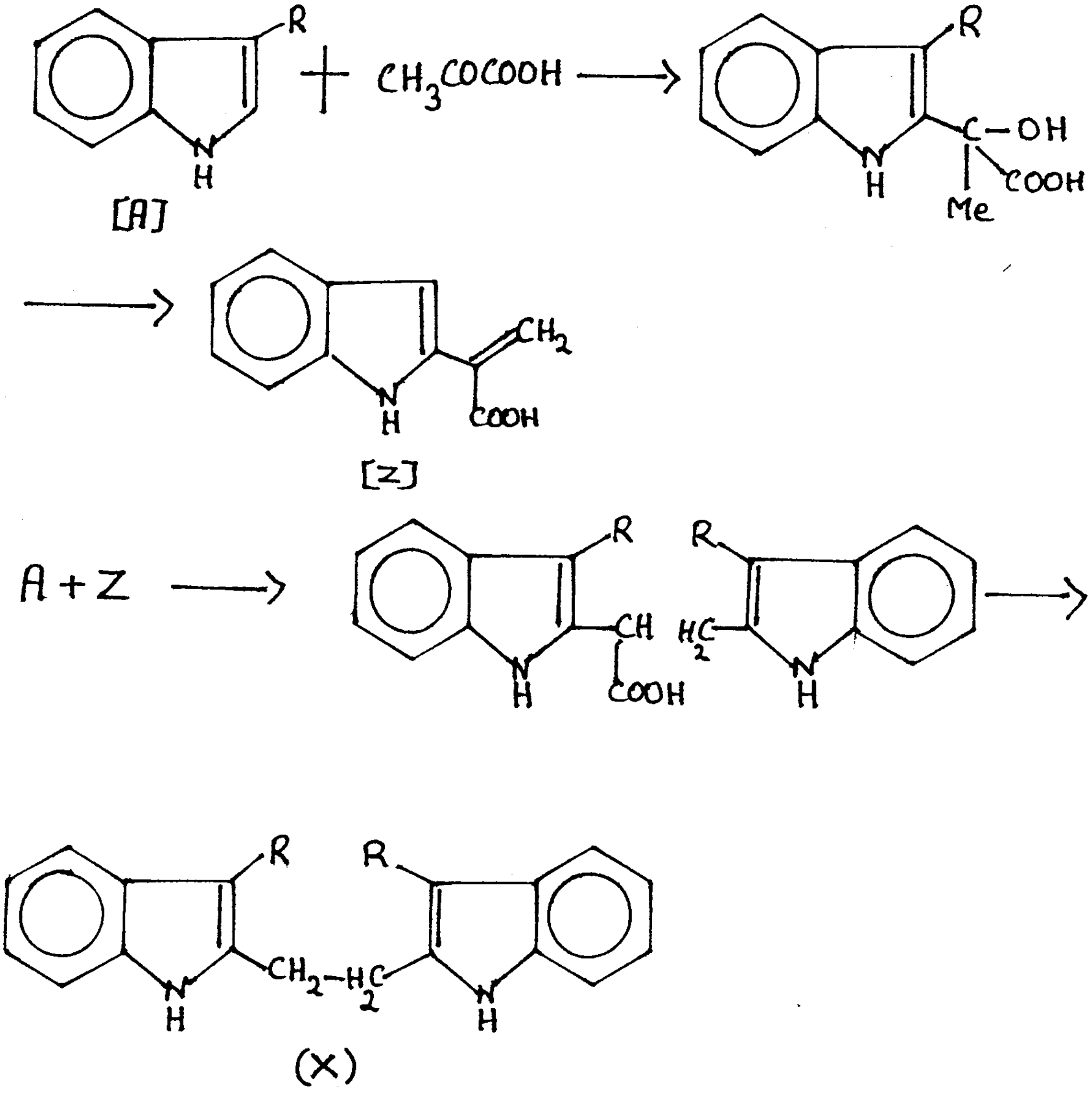


3-Position blocked

The 3 substituted Indole (A) has been found to condense with pyruvic acid to give the 1,2-bis (2-indolyl) ethane (X). This transformation can be satisfactorily rationalised by the steps shown below. The addition of the second Indole ring occurs by reaction with acrylic acid. (Z).

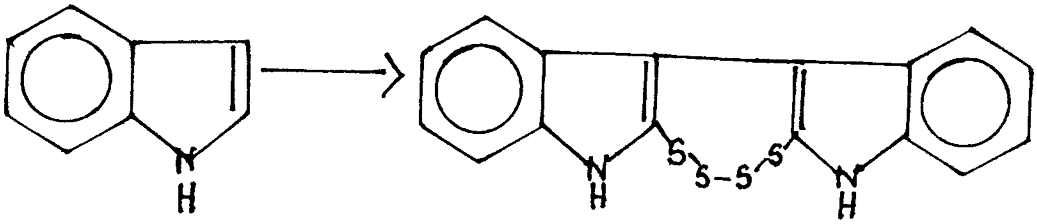


The electrophile can attack C-2 directly or it can attack the more electron rich-3-position and subsequently rearrange intramolecularly to C-2.

2.1.3 Miscellaneous Electrophilic Substitutions

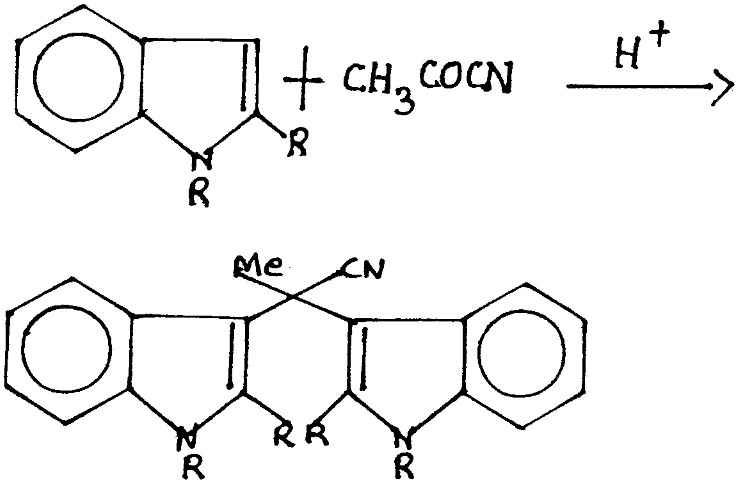
Reaction of sulphur in dimethyl formamide gives a compound containing two Indole rings and four Sulphur atoms. The following structure has been proposed; but the evidence presented is not unequivocal.

[i]



OTHER REACTIONS YIELDING BIS INDOLES

[ii]



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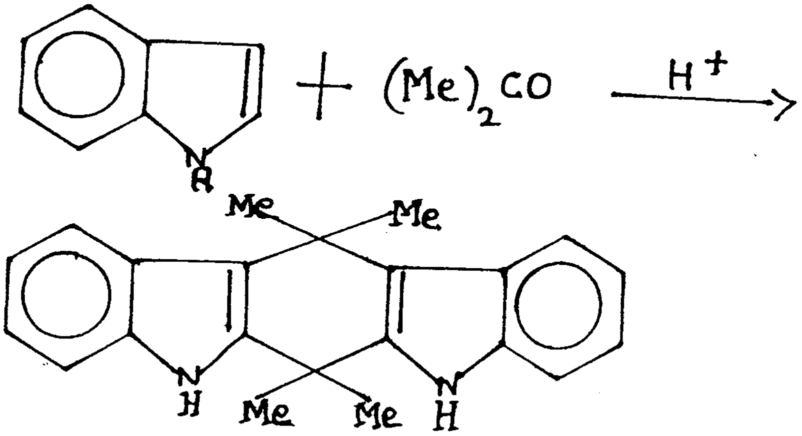


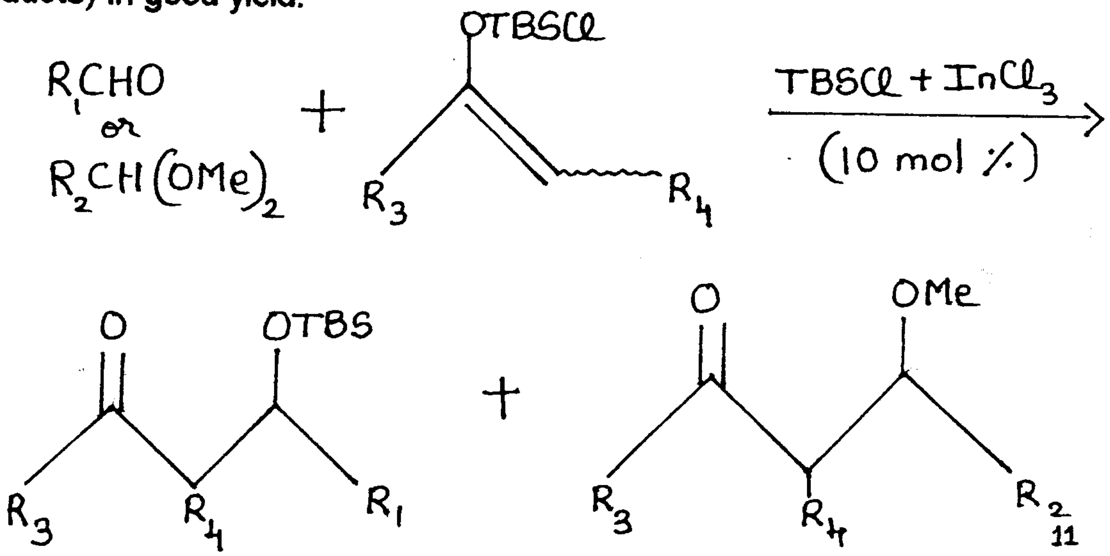
2.2 Catalytic Activity of Indium trichloride

These electrophilic substitution reactions of Indole take place efficiently in the presence of the Lewis acid catalyst. Indium trichloride is proved to be one of the Lewis acid catalysing the electrophilic substitution reaction.

Recent researches predict that Indium tri chloride has wide application in the field of organic synthesis. In literature Indium tri chloride is used. as catalyst for polymerisation reactions, chlorination of chloro phenyl silanes, sulphide synthesis ,Friedel Craft's acylation, hydrode chlorination and Aldol condensation of silyl enol ehers. Recently Indium tri chloride has been found to catalyze Mukaiyama's Aldol reactions and Diels Alder reactions in water owing to its high coordination number and a fast coordination - dissociation equilibrium in aqueous solutions. Indium tri chloride has fast coordination - dissociation tendency.

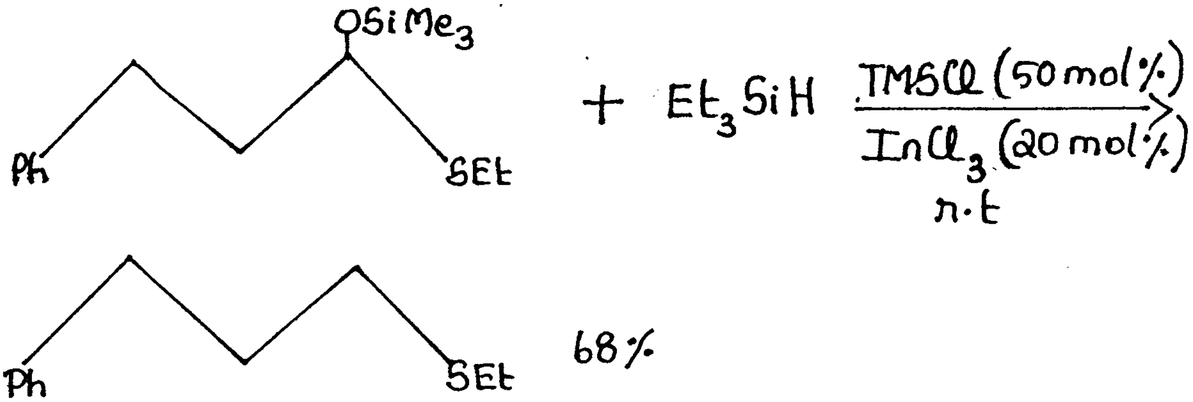
2.2.1 Aldol Condensation

In the presence of a catalytic amount of t-butyl di-methyl silyl chloride (TBSCl) and Indium tri chloride, aldehydes smoothly react with butyl dimethyl silyl enol ethers to afford the corresponding aldol products (adducts) in good yield.



2.2.2 Sulphide Synthesis

Mukaiyama et al (1991) have reported that TMSCl and Indium tri chloride effectively catalysis, the reaction of o-tri methyl silyl mono thio acetals with tri ethyl silyl and silylated carbon nucleophiles respectively to afford the corresponding sulphide derivatives.



2.2.3 Indium tri chloride in Organic Synthesis

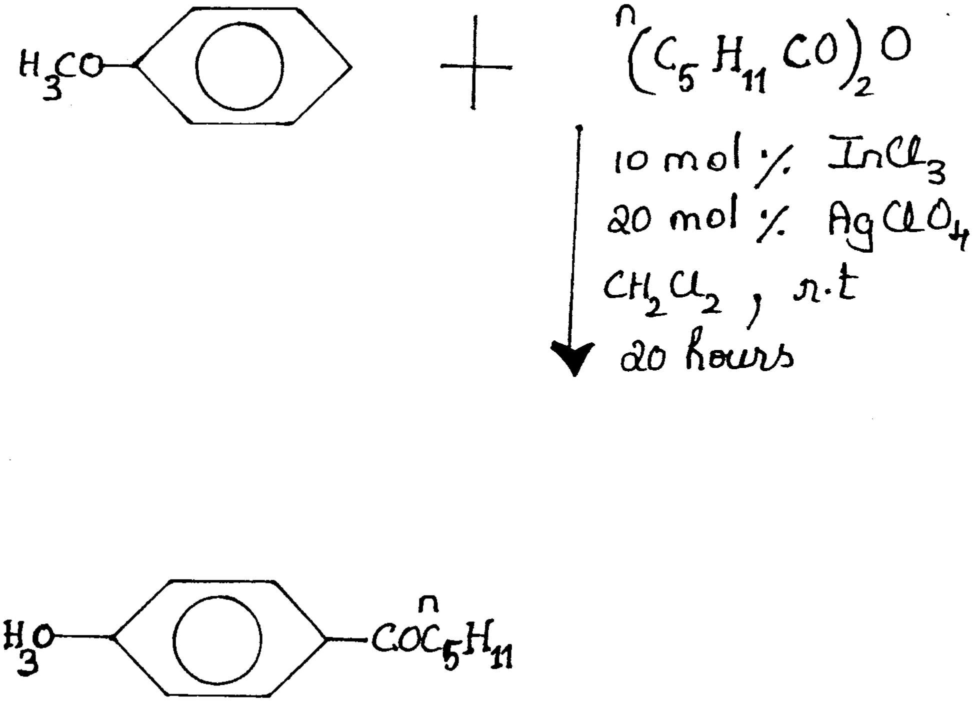
The use of Indium tri chloride as Lewis acid catalyst, is exploited to a less extent in organic synthesis. Literature survey reveals that Indium tri chloride is used, as catalyst for polymerisation reactions, Friedel Crafts acylation, hydrode chlorination, Aldol condensation of silyl enol ether, Mukaiyama Aldol condensations and Diels-Alder reactions in water as well as in non-aqueous solvents.

Polymerisation

Indium tri chloride is used as a catalyst for polymerisation of bi phenyl chloropthalide with t-butyl hydro peroxide for vinyl monomers, methyl methacrylate, aryl chloropthalides and t-butyl acetylene.

2.2.4 Friedel Crafts Acylation:-

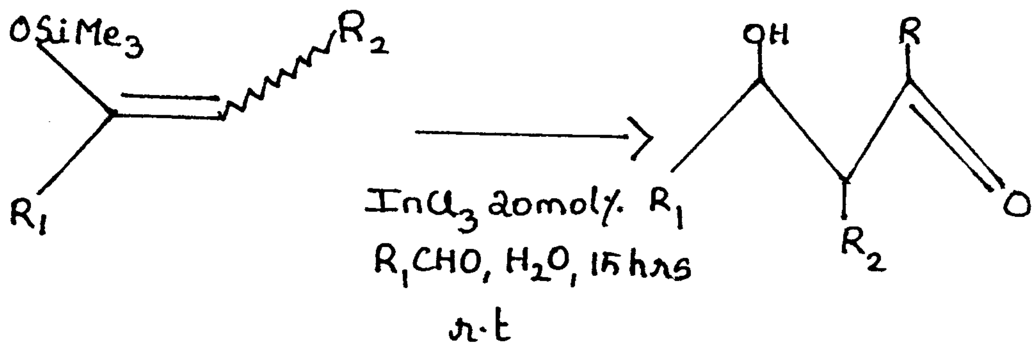
Mukaiyamma et al have reported that Indium tri chloride catalyses Friedel Crafts Acylation of Anisole.

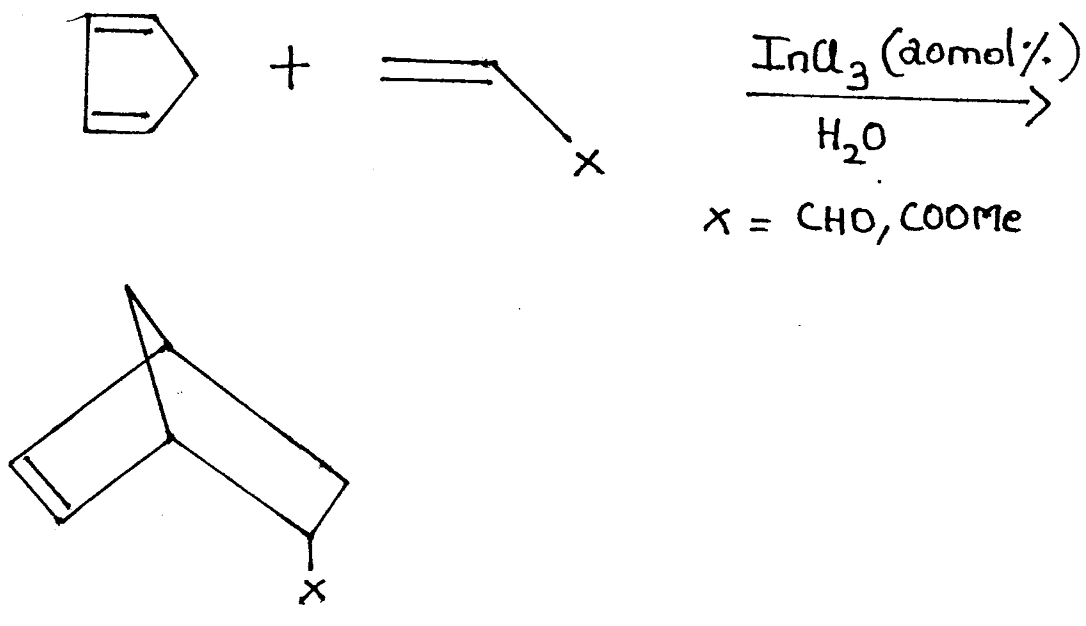


Zhun et al (1990) have reported that treatment of $Me_nPh\,Si\,Cl_3$ (n=0-2) with Cl in the presence of Indium tri chloride affords chloro phenyl silane.

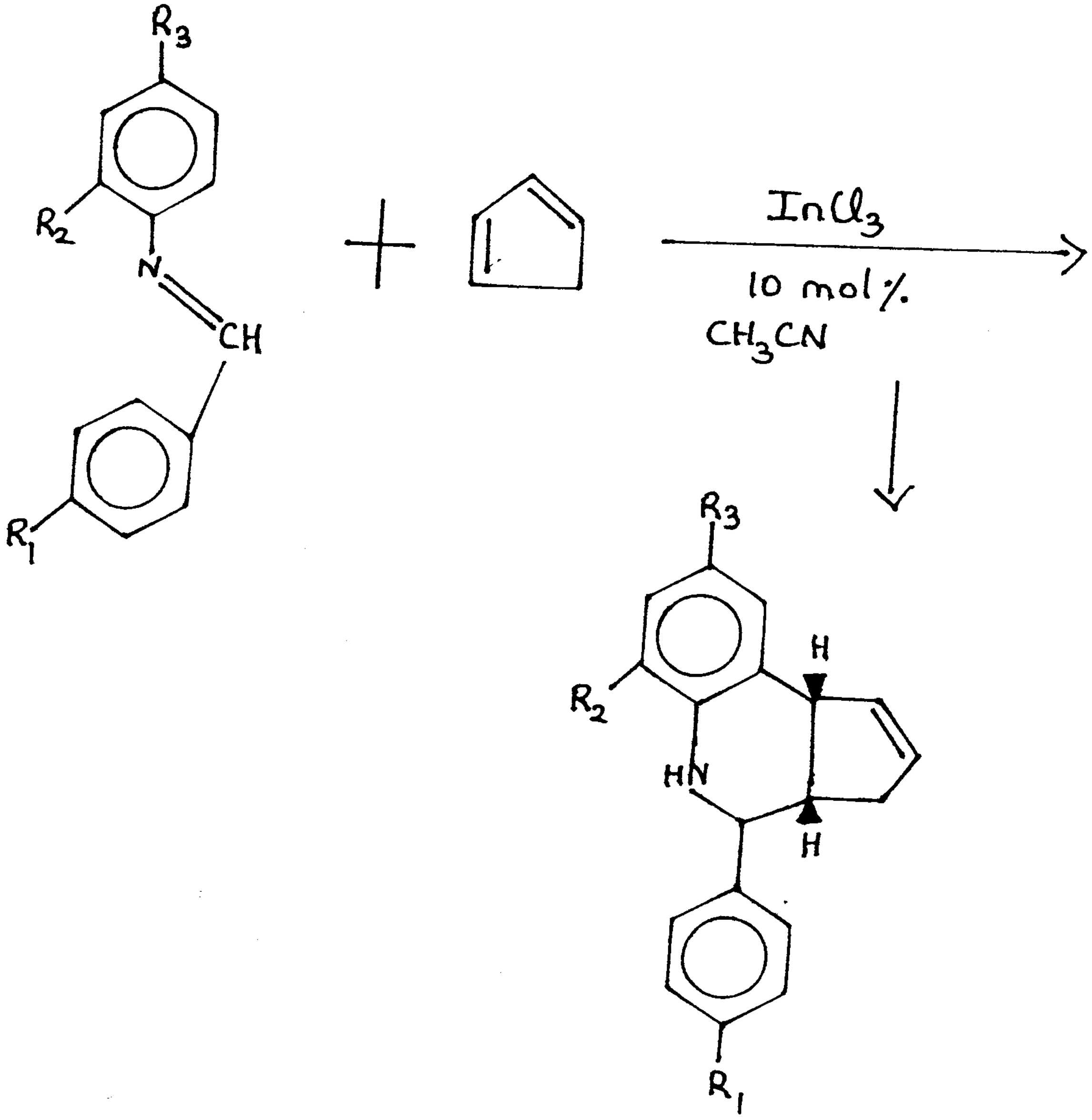
Indium tri chloride also catalyses dehydro chlorination of dichloroethane, promoters for hydro dechlorination of low molecular weight poly isobutylenes and allylation of carbonyl compounds.

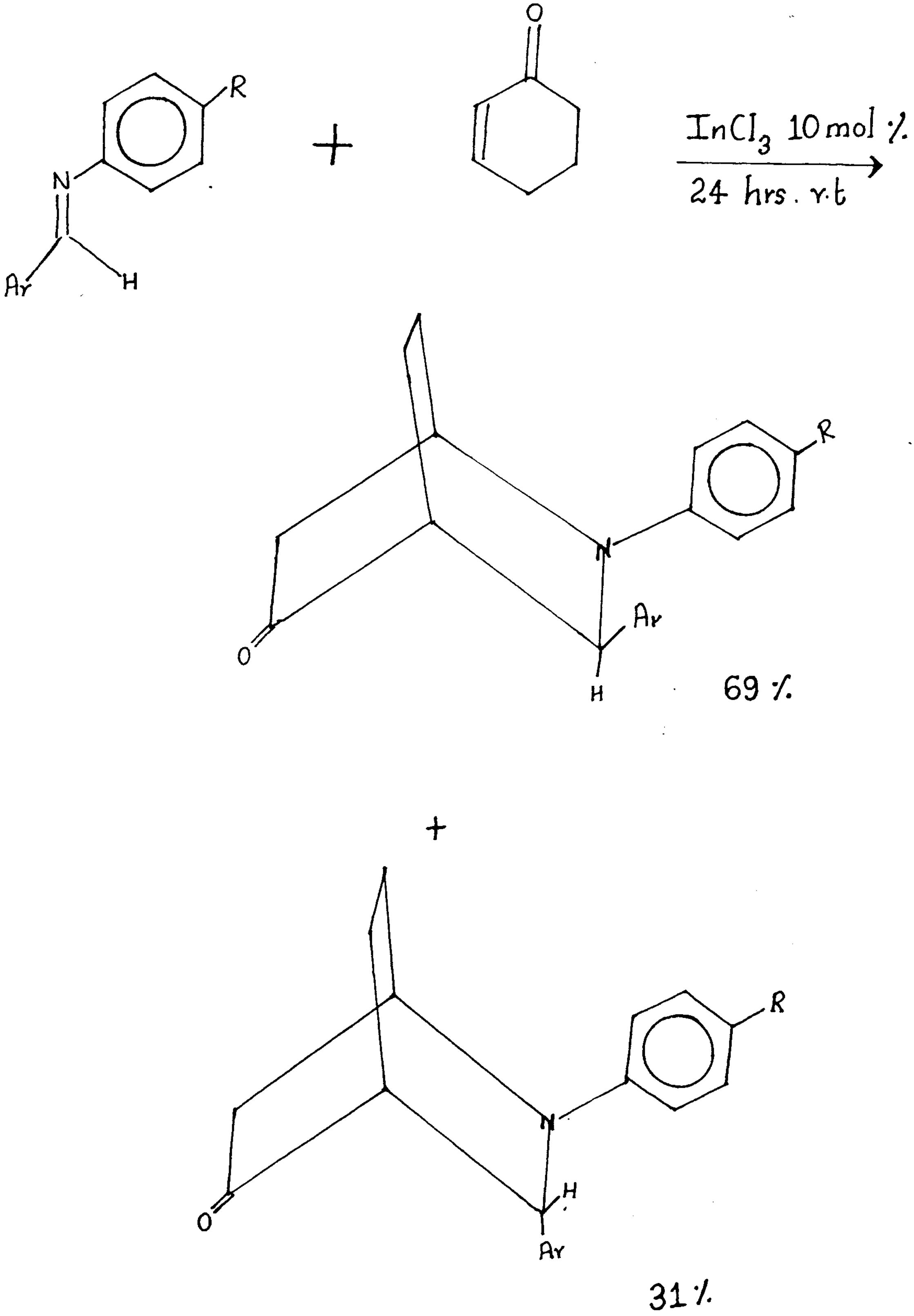
Loh with co-workers reported that Indium tri chloride catalyses Mukaiyama Aldol reactions and Diels Alder reactions in water owing to its high co-ordination number and a fast co-ordination -dissociation equilibrium in aqueous solutions.

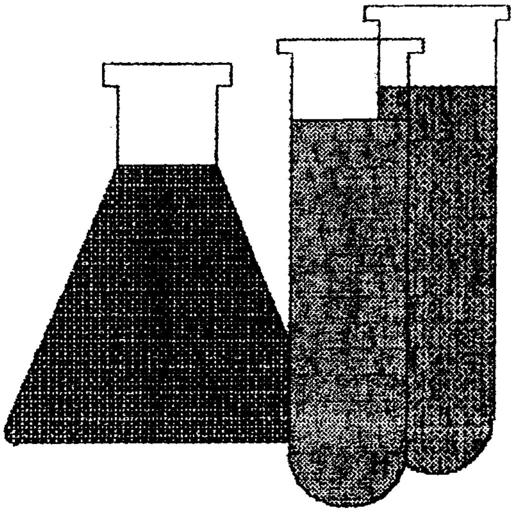




Recently *Babu and Perumal* have reported that Indium tri chloride catalyses imino Diels-Alder reactions of Schiff's bases derived from Benzaldehyde and aromatic amines with cyclopentadiene and 2-cyclo hexenone.




R
N
Ar
H
+
O
$InCl_3$ 10 mol %
24 hrs. r.t
R
N
Ar
O
H
69 %
+
R
N
H
O
Ar
31 %



MATERIALS AND METHODS

3 MATERIALS AND METHODS

Three indole derivatives have been successfully synthesized in the present study.

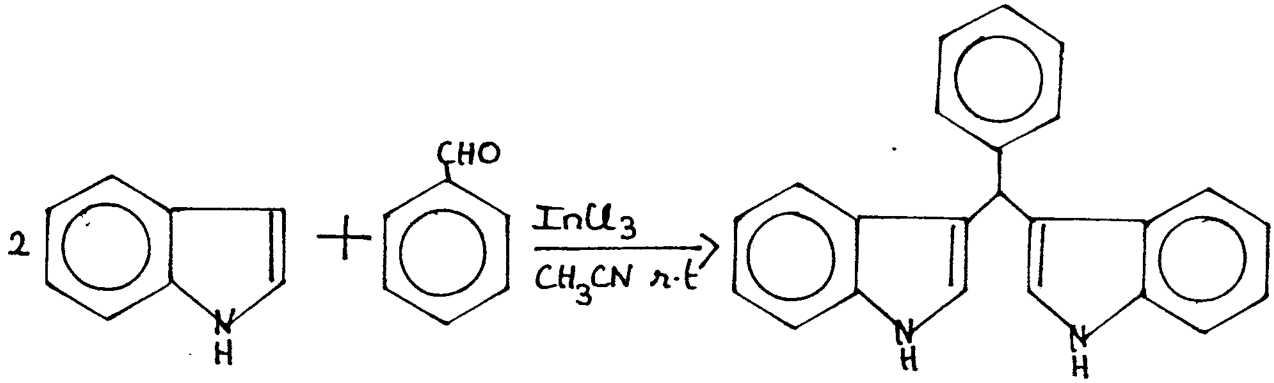
3.1 Scope and Scheme of the Reaction:-

Scope

The synthesis involved the electrophilic substitution reactions of indoles with aromatic aldehydes in the presence of Indium tri chloride as catalyst. In all of the above reactions acetonitrile was used as the solvent. The reactions were carried out at room temperature.

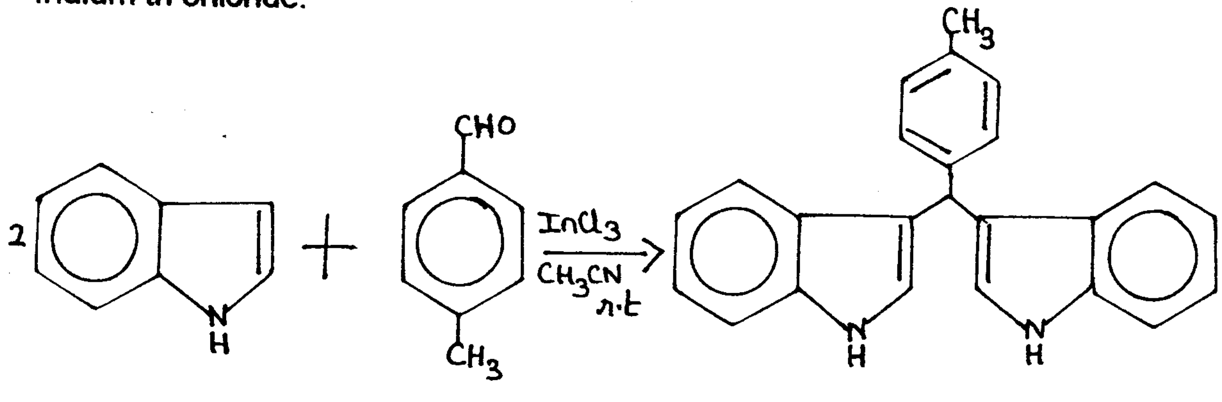
Scheme I

Reaction between Indole and Benzaldehyde in the presence of Indium tri chloride.



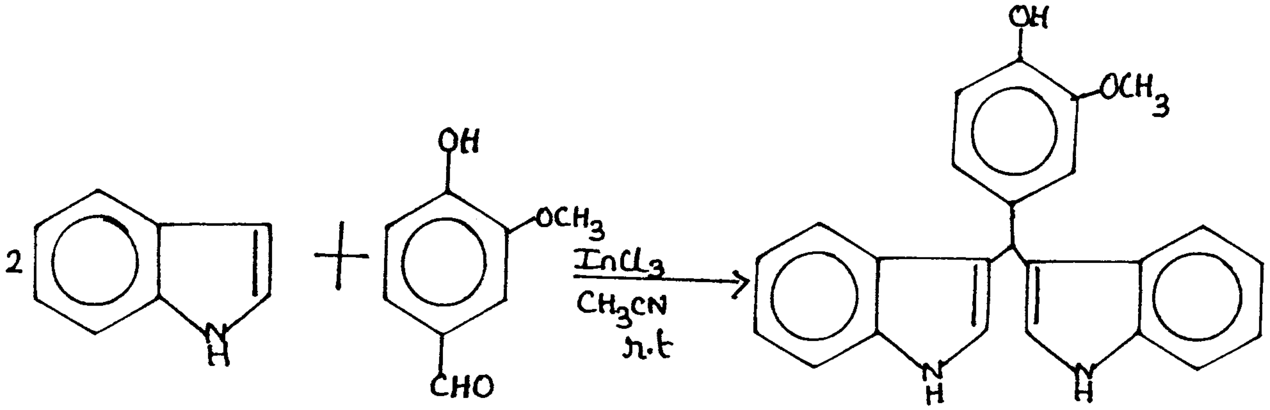
Scheme II

Reaction between Indole and Tolualdehyde in the presence of Indium tri chloride.



Scheme III

Reaction between Indole and Vanillin in the presence of Indium tri chloride.



3.2 Reagents Used

(I) Indole

(ii) Acetonitrile

(iii) Indium tri chloride

(iv) Benzaldehyde

(v) Tolualdehyde

(vi) Vanillin

(vii) Chloroform

3.2.1 Purification of Reagents

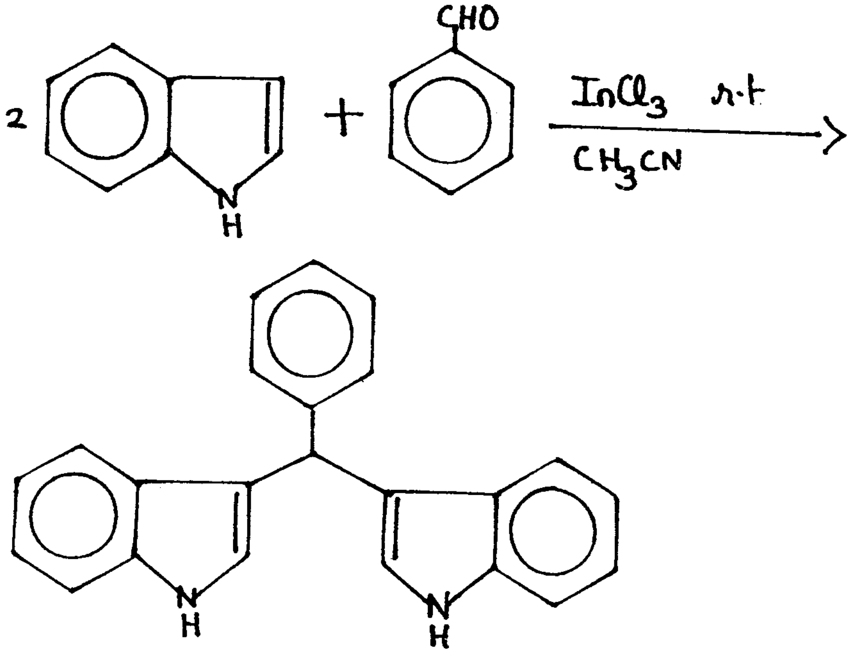
- Indole (Loba) was purified by re-crystallisation from n-hexane

- Acetonitrile (S.D.Fine Chemicals) was distilled over calcium hydride and dried with molecular sieves (4 Å).

- Chloroform (Ranbaxy) for extraction, Benzaldehyde, Tolualdehyde (Ranbaxy) were used as such.

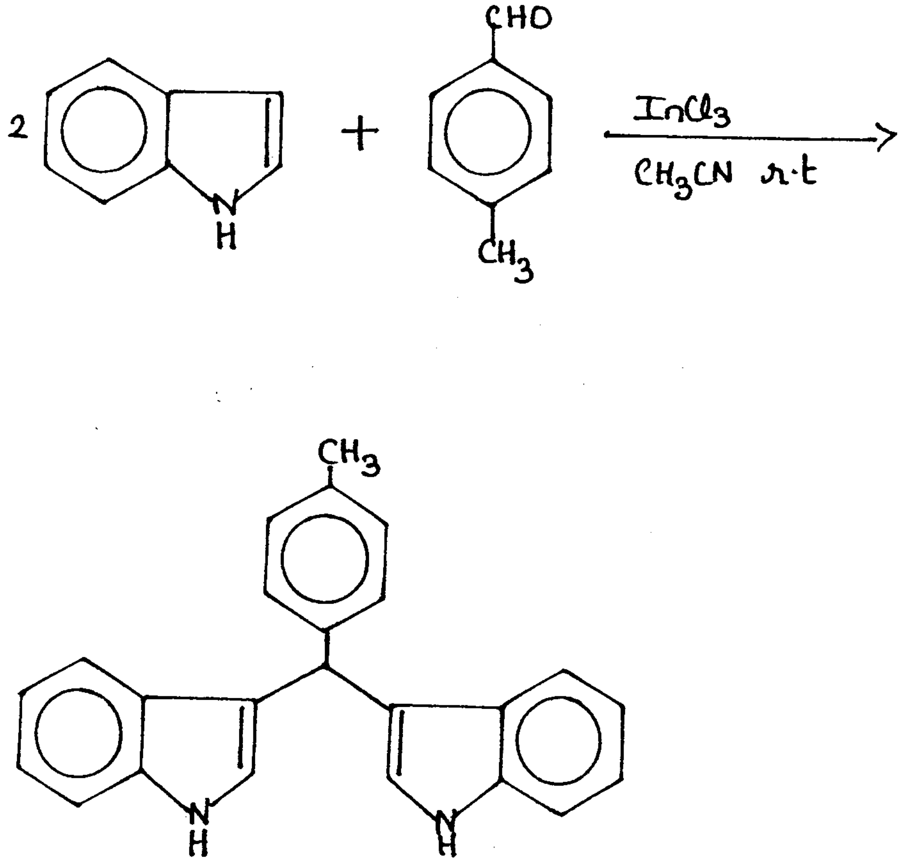
3.2.2 *Synthesis Procedure Adopted :*

3.2.2.1 Procedure for Reaction between Indole and Benzaldehyde



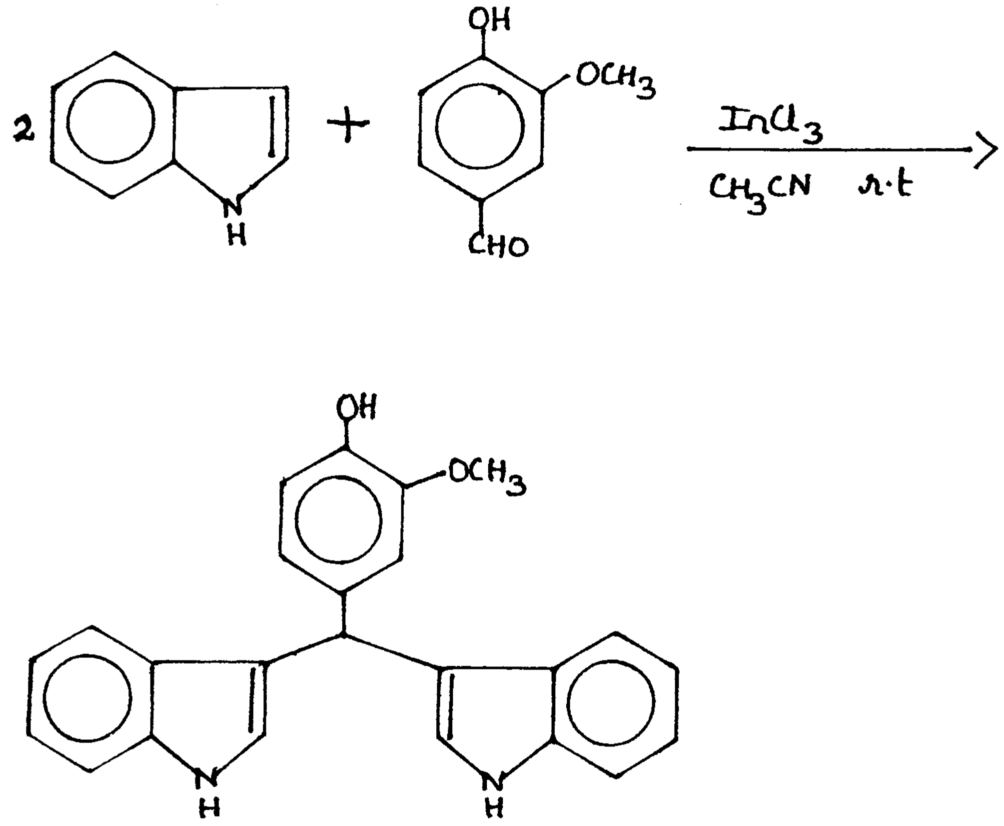
In a 100ml RB flask, Indole (0.2728 g & 2.5 m .moles) and benzaldehyde (0.1326g, 1.25 m moles) were taken and dissolved in acetonitrile (10 ml) and protected by a guard tube. To this reaction mixture Indium tri Chloride (55 mg, 20 mol%) was added and stirred at room temperature for 4-5 hours. The progress of the reaction was checked perodically using thin layer chromatography.(Appendix 1) When the reaction was complete water (10 ml) was added to arrest the reaction and extracted with chloroform (3x20 ml). The combined organic layers were dried using anhydrous sodium sulphate and the solvent evaporated.

3.2.2.2 Procedure for Reaction between Indole and Tolualdehyde



In a 100 ml. RB flask Indole (0.2937 g 2.5 m moles) and tolualdehyde. (0.15015 g, 1.25 m moles) were added and dissolved in acetonitrile (10 ml) and protected by a, guard tube. To this reaction mixture Indium tri-chloride. (55 mg, 20 mol %) was added and stirred at room temperature for 24 hours. The progress of the reaction was checked periodically using thin layer chromatography.(Appendix 1) When the reaction was complete, water (10 ml) was added to arrest the reaction and extracted with chloroform (3x20ml). the combined organic layers were dried using anhydrous sodium sulphate and the solvent evaporated.

3.2.2.3 Procedure for Reaction between Indole and Vanillin



In a 100 ml RB flask (0.468 g, 4 m.moles) Indole and vanillin (0.304 g, 2 m.moles) were taken and dissolved in acetonitrile (10 ml) and protected by a guard tube. To this reaction mixture, Indium tri chloride (88 mg, 20 mol %) was added and stirred at room temperature for 24 hours. The progress of the reaction was checked periodically using thin layer chromatography.(Appendix 1) When the reaction was complete water was added to arrest the reaction and extracted with chloroform (3x20 ml). The combined organic layers were dried using anhydrous sodium sulphate and the solvent evaporated.

3.3 Separation and Purification of products

The column packing was done with silica gel. The height of the column employed was of 50 cms in height and 3 cms in diameter. The residue was eluted with a solvent mixture of n-hexane and ethyl acetate (Appendix 2).

For the product I & II the solvent mixture was used in the ratio 80:20

For the product III the solvent mixture was used in the ratio 70:30.

3.4 Identification of the Synthesized Products

The synthesized products were identified and confirmed by various instrumental analysis as given below.

The melting points were recorded on a `'Mettler FP6'` instrument. It was checked whether the reading corresponded to any of the reactions. It was confirmed to be the melting point of the products.

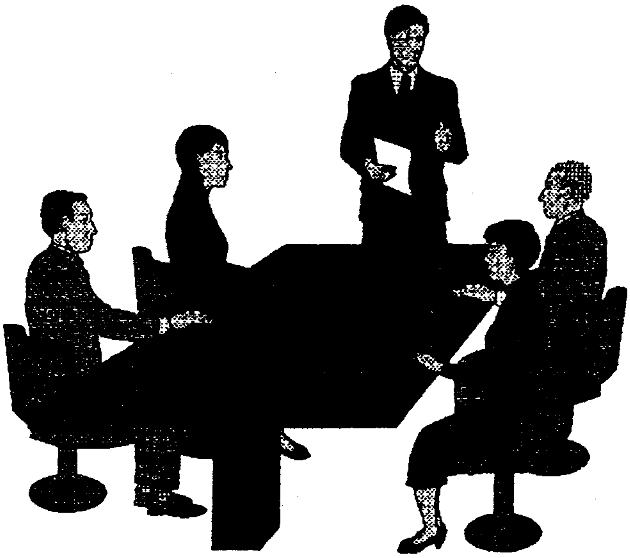
Spectral Analysis

IR spectra were recorded on a 'Nicolet Impact - 400 FTIR 'spector photometer and were reported in wave number (cm^{-1}).

Proton Nuclear Magnetic Reasonance (^{1}HNMR) were recorded on Bruker (300 MH) spectrometer.

Carbon Nuclear magnetic Resonance. CMR spectrophotometer were recorded on 'Bruker (75 MHz)' spectrophotometer.

Mass spectrum was recorded on Varian VG 70-70 H mass spectrometer.



RESULTS AND DISCUSSION

4 RESULTS AND DISCUSSION

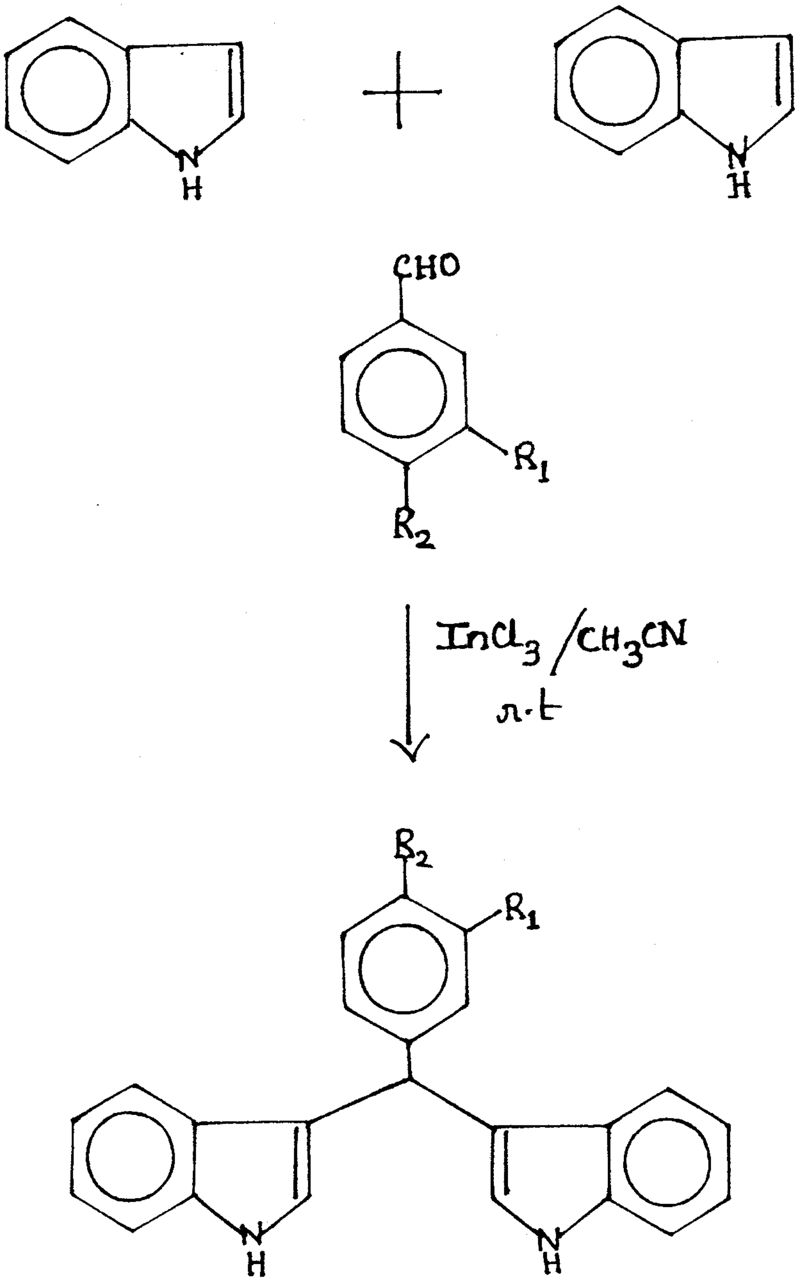
The acid catalysed reactions of electron rich heterocyclic compounds with p-dimethyl amino benzaldehyde have been known as the Ehrlich test for π - electron excessive heterocycles such as pyrroles and Indoles. The analagous reaction of Indoles with other aromatic and aliphatic aldhydes and ketones produced azafulvenium salts which accounted for the colour developed. The azafulvenium salts can undergo futher addition with the second molecule of Indoles to form bis indolyl-methanes. The acids utilized in the type of reactions were protic acids as well as Lewis acids like Aluminium chloride.

Indium trichloride has high coordination and dissociation tendency. Hence we investigated its catalytic activity for the electrophilic substitution of Indoles. Indium trichloride catalyst provided a facile entry to the electrophilic substitution of Indoles with aromatic aldehydes such as

1. Benzaldehyde
2. Tolualdehyde
3. Vanillin

The electrophilic substitution reactions were catalysed by 20 mole percentage of Indium tri chloride and the solvent medium was acetonitrile.

GENERAL REACTION :-



The reaction afforded the products with good yield after chromatographic separation using n-hexane and ethyl acetate of appropriate ratio. (80:20 for reaction with benzaldehyde , tolualdehyde and 70:30 for the reaction with Vanillin). The colour of the compounds were due to the absorption in the visible region. The compounds were amorphous crystals, pink in colour.

4.1 The results obtained in the above reaction with various substituents are summarised and discussed below.

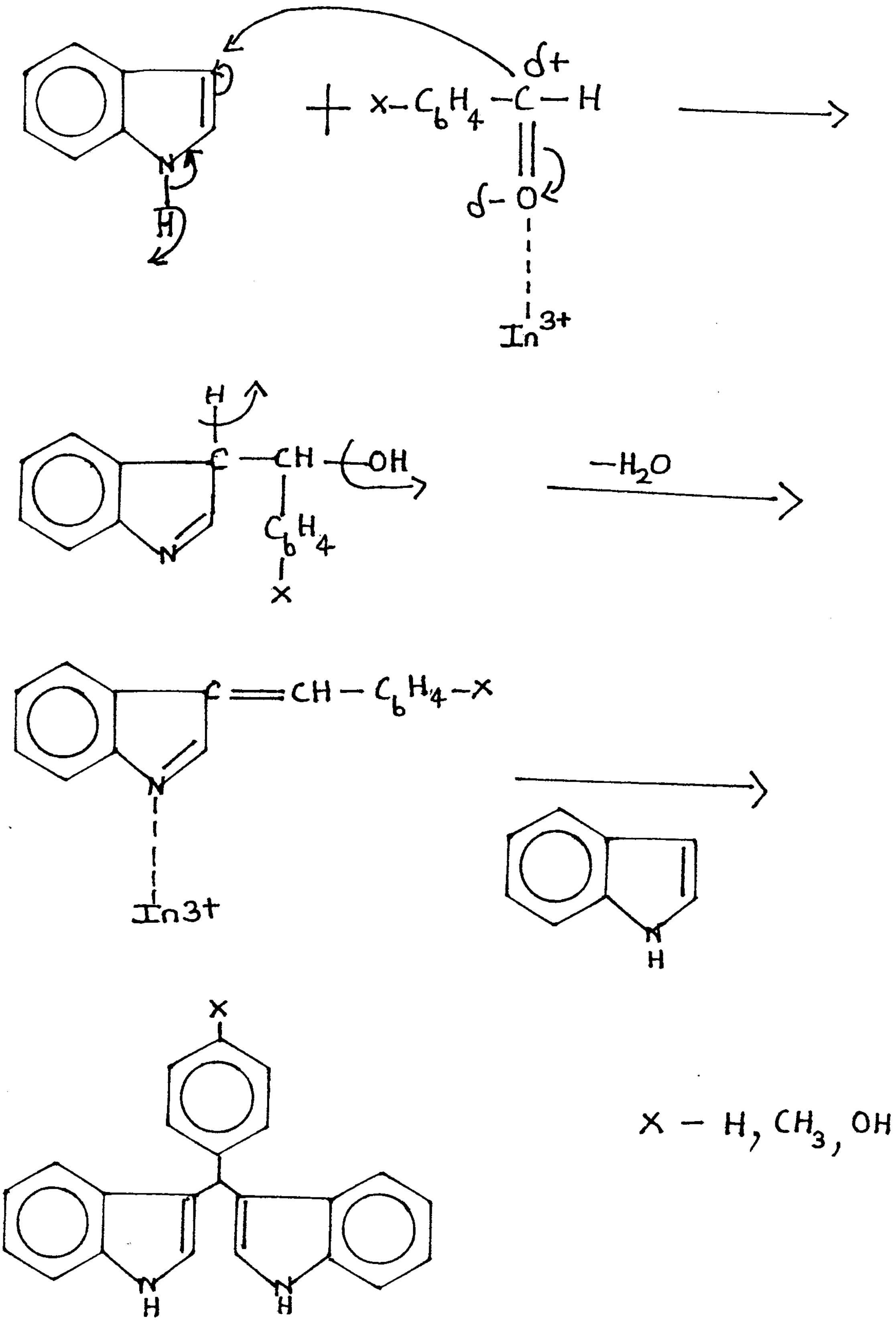
The percentage yield and the melting point of the products are listed in Table I.

4.1.1 Mechanism proposed for the reaction

The following mechanism is proposed to account for Indium tri chloride catalysed electrophilic substitution reactions of Indole with aromatic aldehydes.

An aldehyde is activated first by Indium trichloride and attacked at C-3 of Indole as an electrophile. After loss of water an intermediate is generated. This intermediate is further activated by Indium trichloride and serve as an electrophile to attack a second molecule of Indole to form the product.

Mechanism :



X – H, CH_3, OH

4.2 SPECTRAL CHARACTERISATION

The spectral confirmation was done using IR, PMR, CMR and Mass spectral studies.

4.2.1 IR Spectrum

The IR spectrum of the synthesized products portray characteristic bands of the funtional groups present.

- The broad band of 3416 cm^{-1}, 3412 cm^{-1}, 3407cm^{-1} of Product I (GB sam-I), Product II (GB sam-2), Product III (GB sam-3) respectively, reveal the presence of NH group.
- The presence of CH_3 group in Product II (GB sam-2) is well reflected from the band at 2919.37 cm^{-1}.
- The bands in the Finger Print region ranging from 579 to 1634 cm^{-1} are characteristic and a strong evidence for aromatic nuclei in the proposed structures of products I, II, and III(Fig i,ii,iii)

- The presence of OH functional group is confirmed from the strong band at 3500 cm^{-1}(off set) of the Product III (GB sam-3).

The IR spectrum of GB sam-1, 2, 3 obtained was superposed with that of the respective standard compounds.

The Finger print regions of the synthesized products was found to coincide with that of standards there by confirming the starctures as proposed. The details are depicted in Table II.

4.2.2 Proton NMR Spectrum

The 300 MHz $\overset{1}{H}$NMR spectrum of (Fig i, ii, iii) of the products I,II, & III respectively were recorded to confirm the proposed structure.

4.2.2.1 For the product - I

- The spectrum obtained for product I (GB 21) shows 3 peaks in the ratio 15:2:1.
- An unsymmetrical multiplet at δ 7.02 to 7.4 integrating to 15 protons, corresponding to protons of the rings A, D, E and NH protons.
- A singlet at δ 6.5 integrating to 2 protons corresponding to the protons of 2, 2' carbon atoms.
- A singlet at δ 5.9 integrating to 1 proton is attributed to the $3\overset{o}{C}$ proton.

The chemical shifts, signal multiplicity, integral proton ratio and their assignments in $\overset{1}{H}$NMR are given in the Table III.

4.2.2.2 For the Product II

- The proton NMR of product II (GB 11) shows the presence of peaks in the ratio 14:3:2:1.

- An unsymmetrical multiplet at δ 7.02 - 7.45 integrating to 14 protons, corresponding to protons of the rings A, D, E and NH protons.

- A singlet at δ 5.87 integrating to 1 proton is attributed to the 3C proton.

- A singlet at δ 2.37 integrating to 3 protons is that of methyl protons.

The chemical shifts, signal multiplicity Integral proton ratio and their assignments in ^{1}HNMR are given in Table IV.

4.2.2.3 For the product III

- The proton NMR of product III (GB 71) shows the presence of 4 peaks in the ratio of 13:3:2:1.

- An unsymmetrical multiplet at δ 6.87-7.39 integrating to 13 protons, corresponding to protons of the ring A, D, E and protons of 2, 2' carbon atoms.

- A singlet at δ 7.9 integrating to 2 protons corresponding to the NH protons.

- A singlet at δ 5.8 integrating to 1 proton is attributed to the 3C proton.

- A singlet at δ 3.73 integrating to 3 protons of the methoxy group.

- A singlet at δ 9.8 shows the presence of OH group (H).

The chemical shifts, signal multiplicity, integral proton ratio and their assignments in ^{1}HNMR spectrum are given in the Table V.

CMR Spectrum

CMR spectral studies further confirms the proposed structures of the products I, II and III.

- In all the spectra GB21,GB11 and GB71 of the three products I, II, III respectively, the peaks at δ values ranging from 119-128 ppm are characteristic of the CH doublets.

- The low intense singlet peaks at δ 141, 138 and 135 ppm respectively are characteristic of quarternary carbon atoms in the products I, II, III.

- The triplet peak at δ 75-80 ppm is that of the solvent $CDCl_3$

- The singlet peak at δ value 39 & 21 ppm in the CMR spectrum GB11 of product II corresponds to aliphatic carbon atom i.e C10 and CH_3 group.

- In the CMR spectrum GB21 and GB71 of the products I and III the peak at δ 40 ppm corresponds to aliphatic carbon atom C.10

- The peak at δ 55 ppm in the CMR spectrum GB71 of product III is that of deutriated - OCH$_3$ group. The effect of OH substitution also portrays from much less intense singlet peak at δ 135 in GB71 of product III displaying the quarternary carbon.
- The absence of peaks beyond δ 160ppm is a positive evidence for the absence of carbonyl groups in the proposed structures. [TABLE VI]

4.2.3 Mass Spectrum

Mass spectrum of GB21 of product I also confirms the proposed structure of the product I.

- The molecular ion peak at m/e 322 corresponds to the calculated molecular weight of the product I.
- The other 4 peaks in the spectrum represents the fragment I ions of product I.

Thus the following structures for the products I, II, III i.e in figures (I), (ii) and (iii) are proposed on the basis of IR spectra, ^{1}HNMR spectra, CMR and Mass a. The double bond equivalence as calculated from the molecular formula of bis-indoles also confirms the structures.

4.3 A brief comparison between the catalytic activity of Lanthanide triflates and that of Indium tri chloride

From the previous studies it was found that Lanthanide triflates acted as Lewis acids in chloroform or methanol/ water or ethanol/ water solvent systems to catalyse the reactions of Indoles with aromatic aldehydes or ketones. Ethanol/ water system was found to be the best in terms of yield. Lanthanide triflates were used as Lewis acids in aqueous solutions. [DEPU CHEN, et al (1996)]

Whereas in the present study Indium tri chloride was used as a Lewis acid in amorphous form; when compared to Lanthanide triflates, Indium tri chloride was found to give better yeild. The most suitable solvent system was that of acetonitrile.

The above fact was clearly depicted in the Tables VII & VIII. Among the Lanthanide triflates Dysprosium triflates gave best result for the reaction between Indole and Benzaldehyde.Whereas from the present study Indium tri chloride was proved to be even better than Dysprosium triflate.

This is shown clearly in Graph 1

TABLE I

MELTING POINTS AND YIELD OF PRODUCTS

PRODUCT	R_1	R_2	% YIELD	M.pt °C
I	H	H	96	125-127
II	H	CH_3	97	132-134
III	OCH_3	OH	89	99-101

TABLE II

IR SPECTRAL DETAILS FOR ALL THE PRODUCTS

FIGURE	DIP REGION(CM^{-1})	FUNCTIONAL GROUP
GB SAM[I]	3416	−NH
	594-1634	AROMATIC NUCLEI
GM SAM[II]	3412	−NH
	579-1634	AROMATIC NUCLEI
	2919	$-CH_3$
GB SAM[III]	3407	−NH
	584-1628	AROMATIC NUCLEI
	3500 (OFFSET)	−OH

TABLE III

H^{1}NMR SPECTRAL DETAILS FOR THE PRODUCT I

Chemical Shift δ ppm	Signal Multiplicity	Integrated Proton Ratio	Assignment of Protons
7.02 - 7.44	Unsym [m]	15	4,5,6,7,4',5',6',7'
			1,1',12,12'
			13, 13', 14
6.5	[s]	2	2, 2'
5.9	[s]	1	10

[s] - Singlet

Unsym [m] - Unsymmetrical multiplet

TABLE IV

^{1}HNMR SPECTRAL DETAILS FOR THE PRODUCT II

Chemical Shift δ ppm	Signal Multiplicity	Integrated Proton Ratio	Assignment of Protons
7.02 - 7.45	Unsym [m]	14	4,5,6,7,4',5',6',7'
			1,1',12,12'
			13, 13',
6.5	[s]	2	2, 2'
5.87	[s]	1	10
2.37	[s]	3	14

[s] - Singlet

Unsym [m] - Unsymmetrical multiplet

TABLE V

^{1}HNMR SPECTRAL DETAILS FOR THE PRODUCT III

Chemical Shift δ ppm	Signal Multiplicity	Integrated Proton Ratio	Assignment of Protons
6.87 - 7.39	Unsym [m]	13	4,5,6,7,4',5',6',7'
			2,2',12,13,13'
7.9	[s]	2	1,1'
5.8	[s]	1	10
3.73	[s]	3	12'
9.81	[s] offset	1	14

[s] - Singlet

Unsym [m] - Unsymmetrical multiplet

TABLE VI

CMR SPECTRAL DETAILS FOR ALL THE PRODUCTS

Chemical Shift δ ppm	Signal Multiplicity	Assignment of Carbon
For product I,II & III		
119-128	[d]	CH
135-141	[s]	$4^{\circ}C$
39-40	[s]	C_{10}
For Product II		
21	[s]	CH_3
For Product III		
55	[s]	OCH_3

[d] - doublet

[s] - singlet

TABLE VII

Effect of Different Lanthanide Triflates on the Reaction of Indole with Benzaldehyde

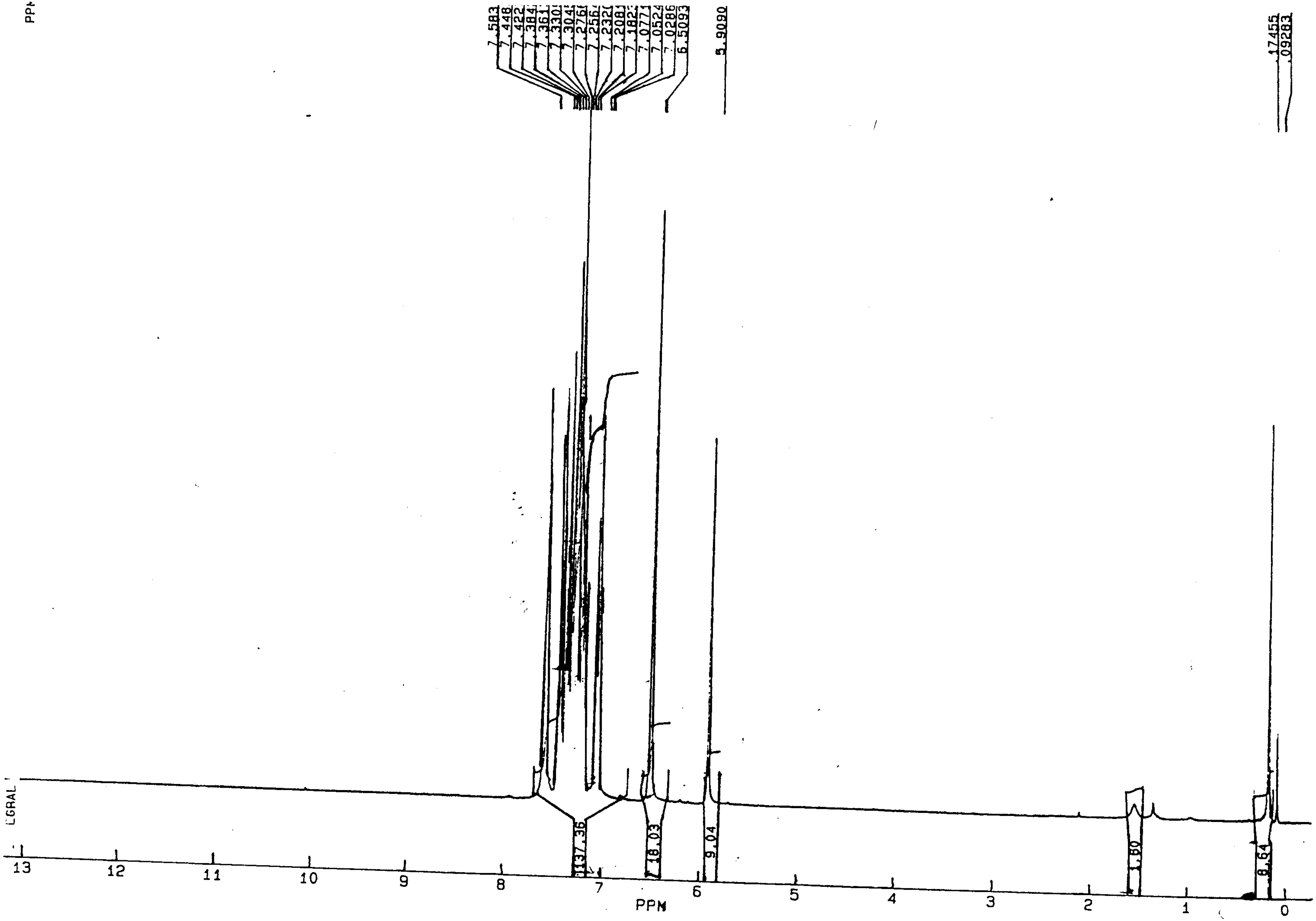
$Ln(OTf)_3$	La	Pr	Nd	Gd	Dy	Er	Yb
Yield %	87	87	66	64	93	78	86

[DEPU CHEN et al 1996]

TABLE VIII

Effect of Indium trichloride on the Reactions of Indole with Aromatic aldehydes

Aldehyde	Benzaldehyde	Tolualdehyde	Vanillin
Yield %	96	97	89



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7.028
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137.36
18.03
9.04
1.80
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7
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PPM

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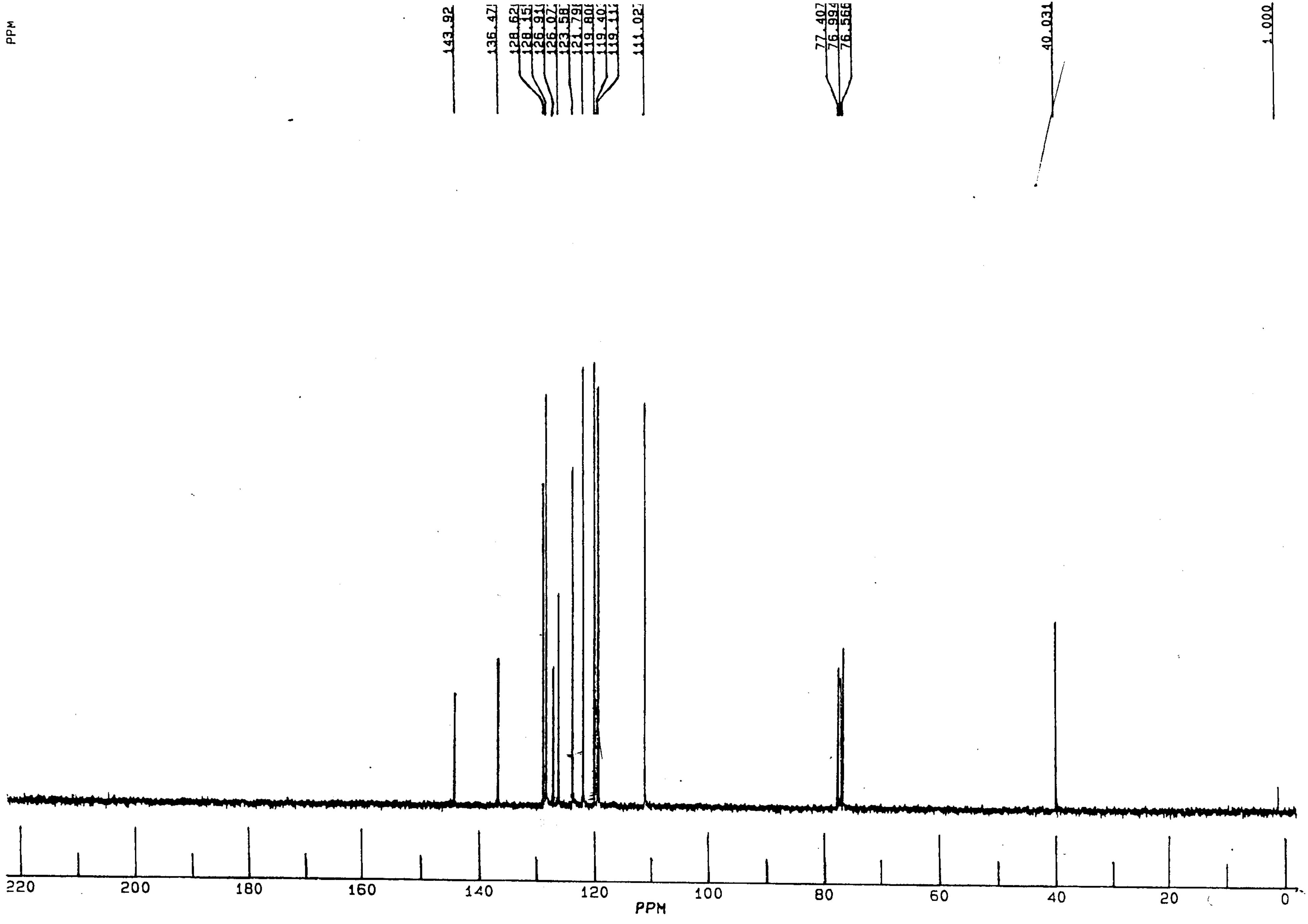
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60
40
20
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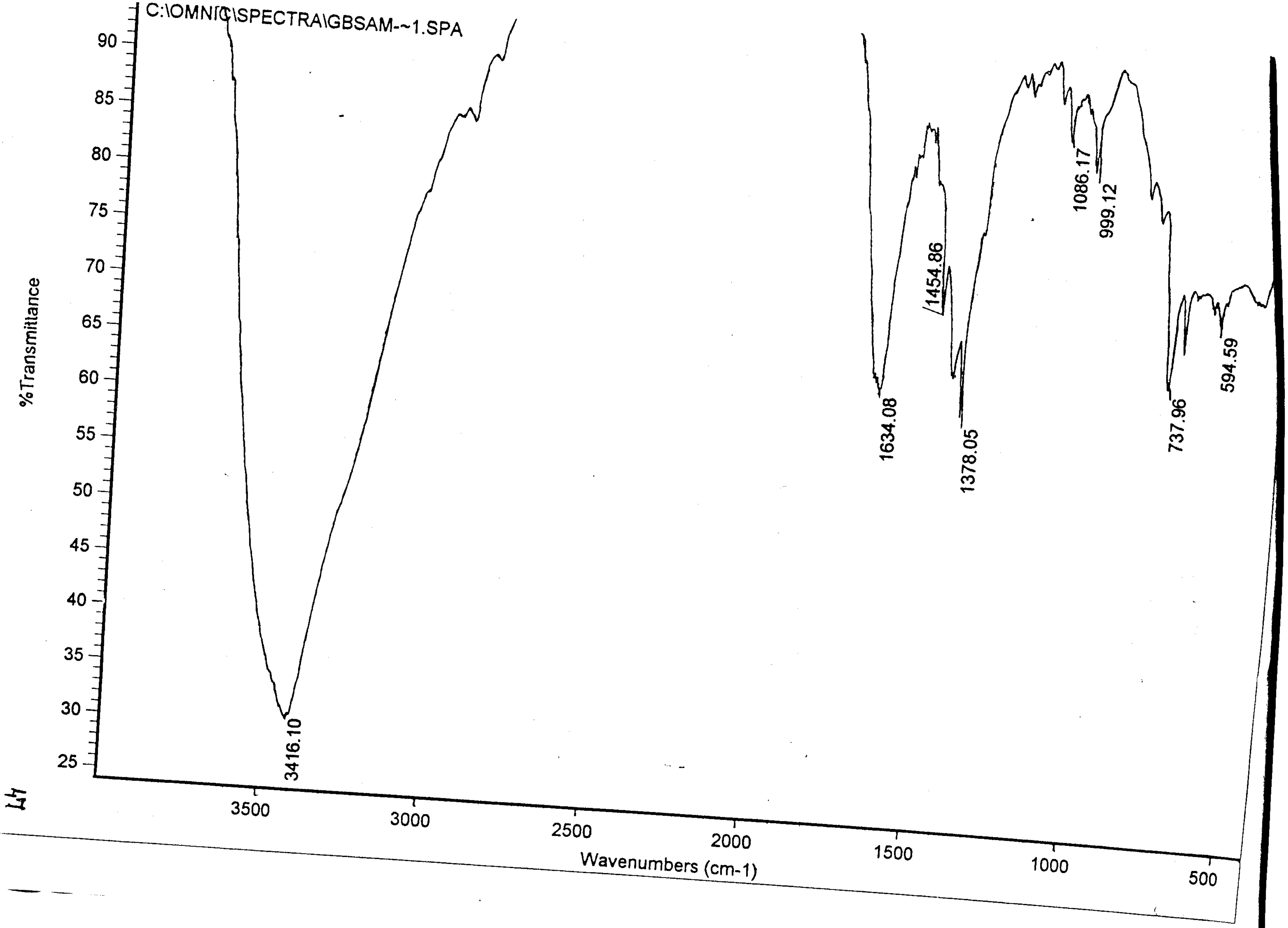
PPM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2000
1500
1000
500
Wavenumbers (cm-1)

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07-24-1997

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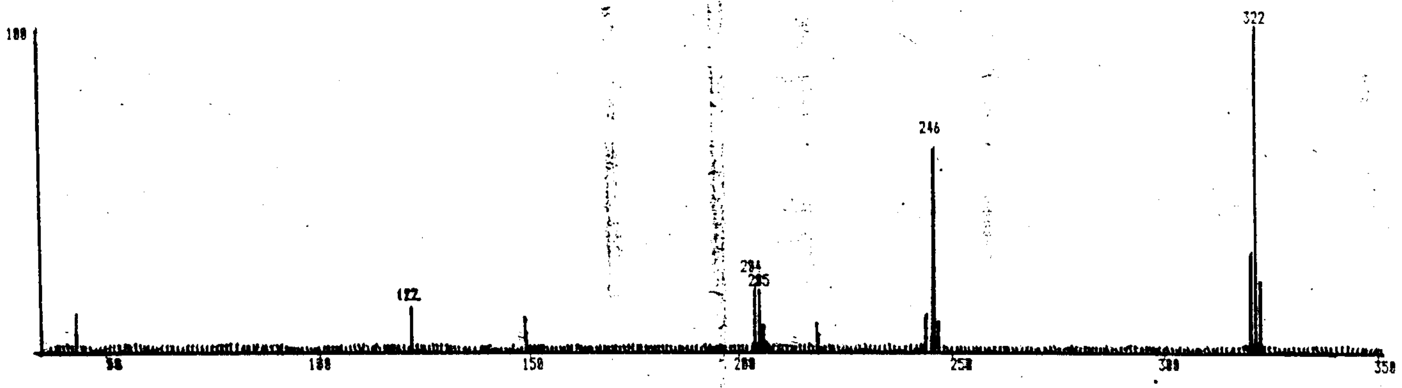

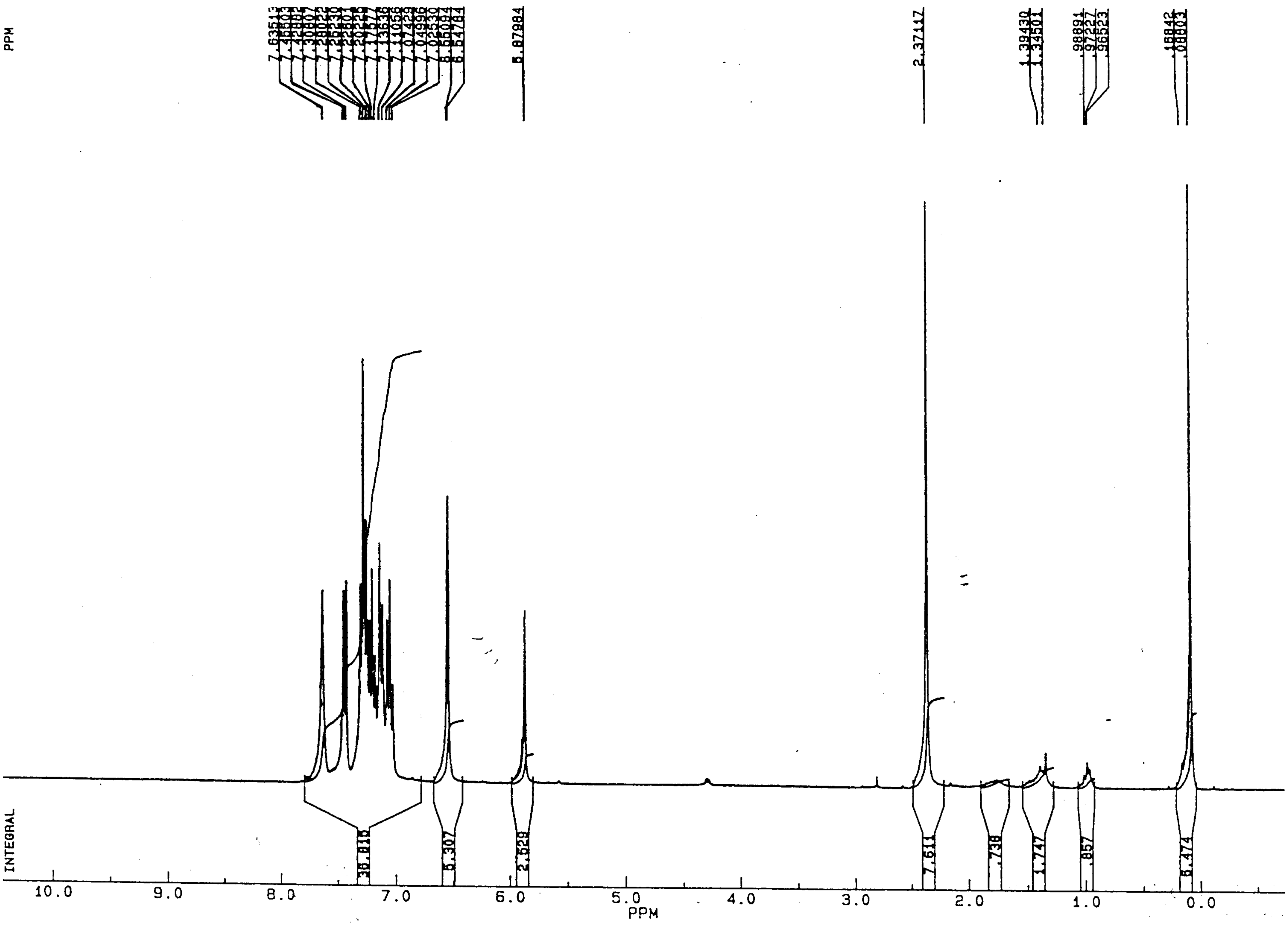
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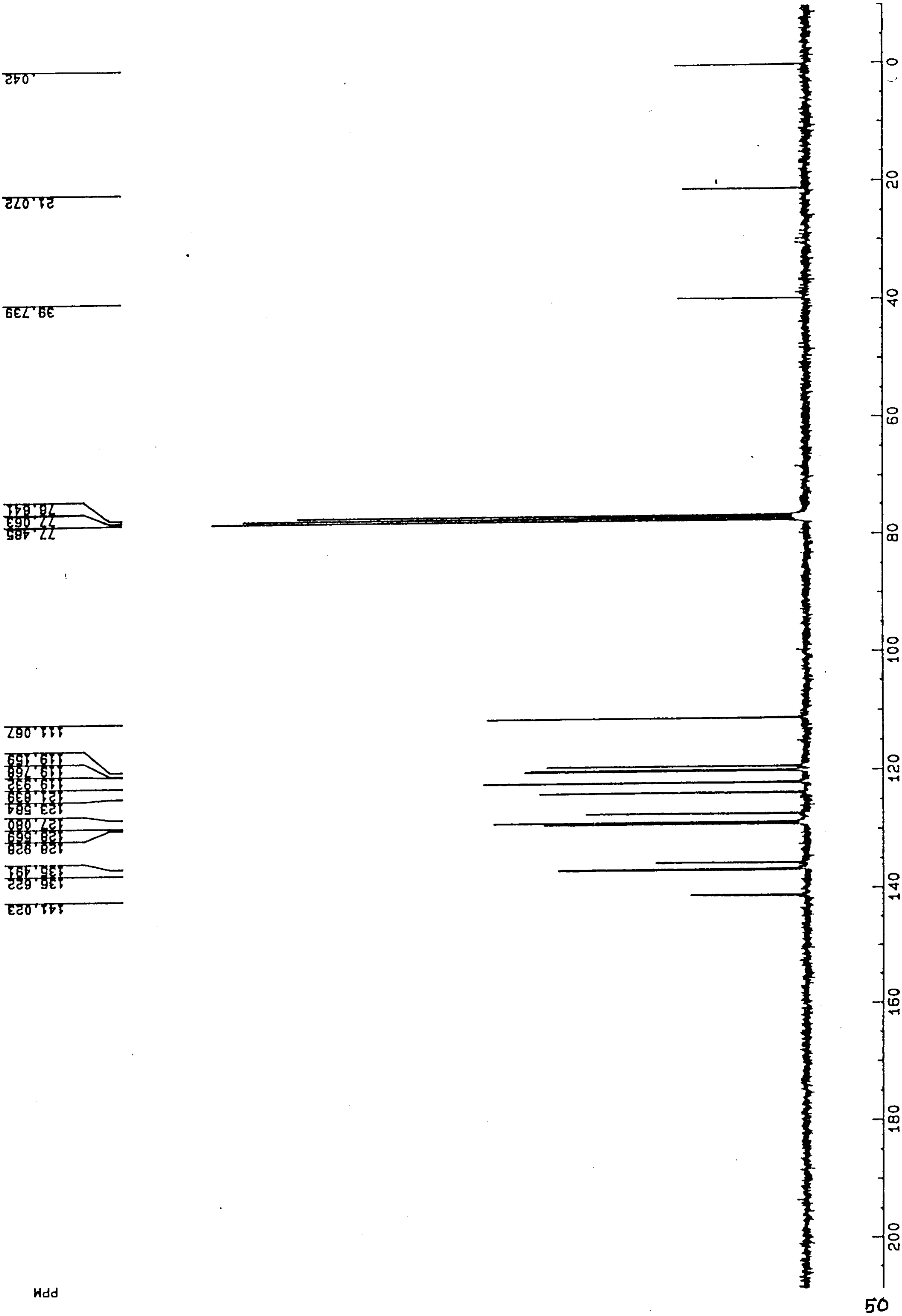
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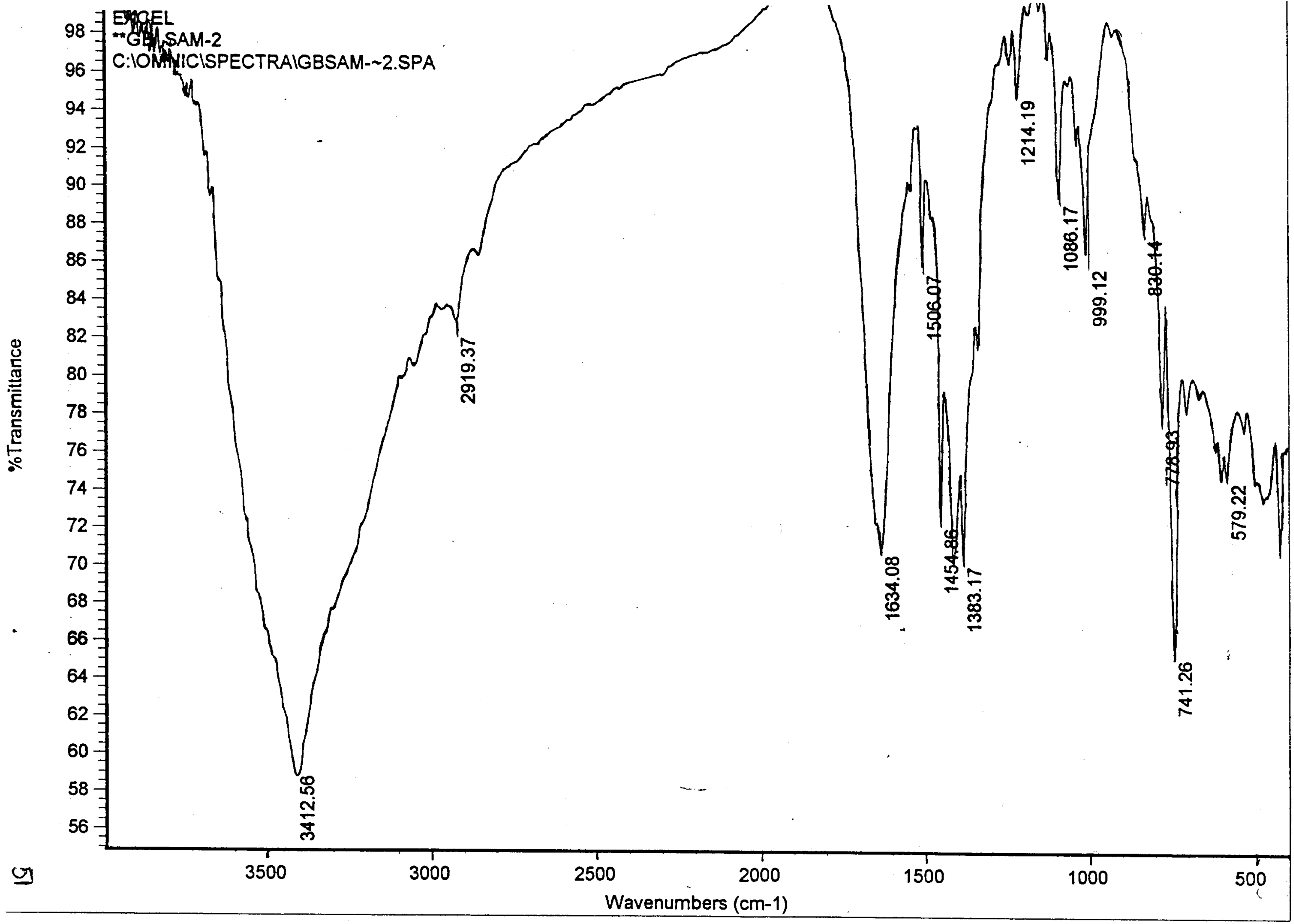
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56
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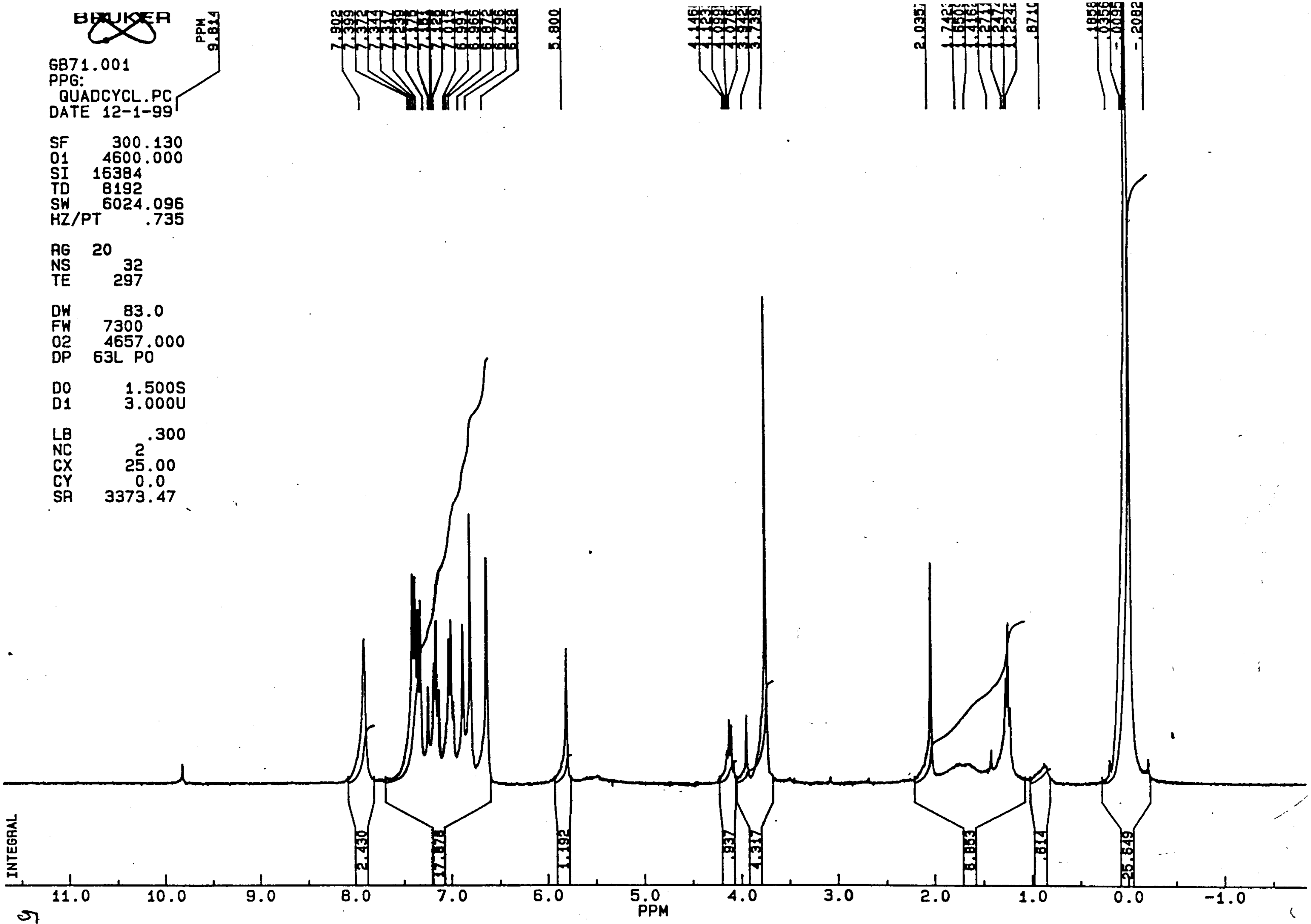
Wavenumbers (cm-1)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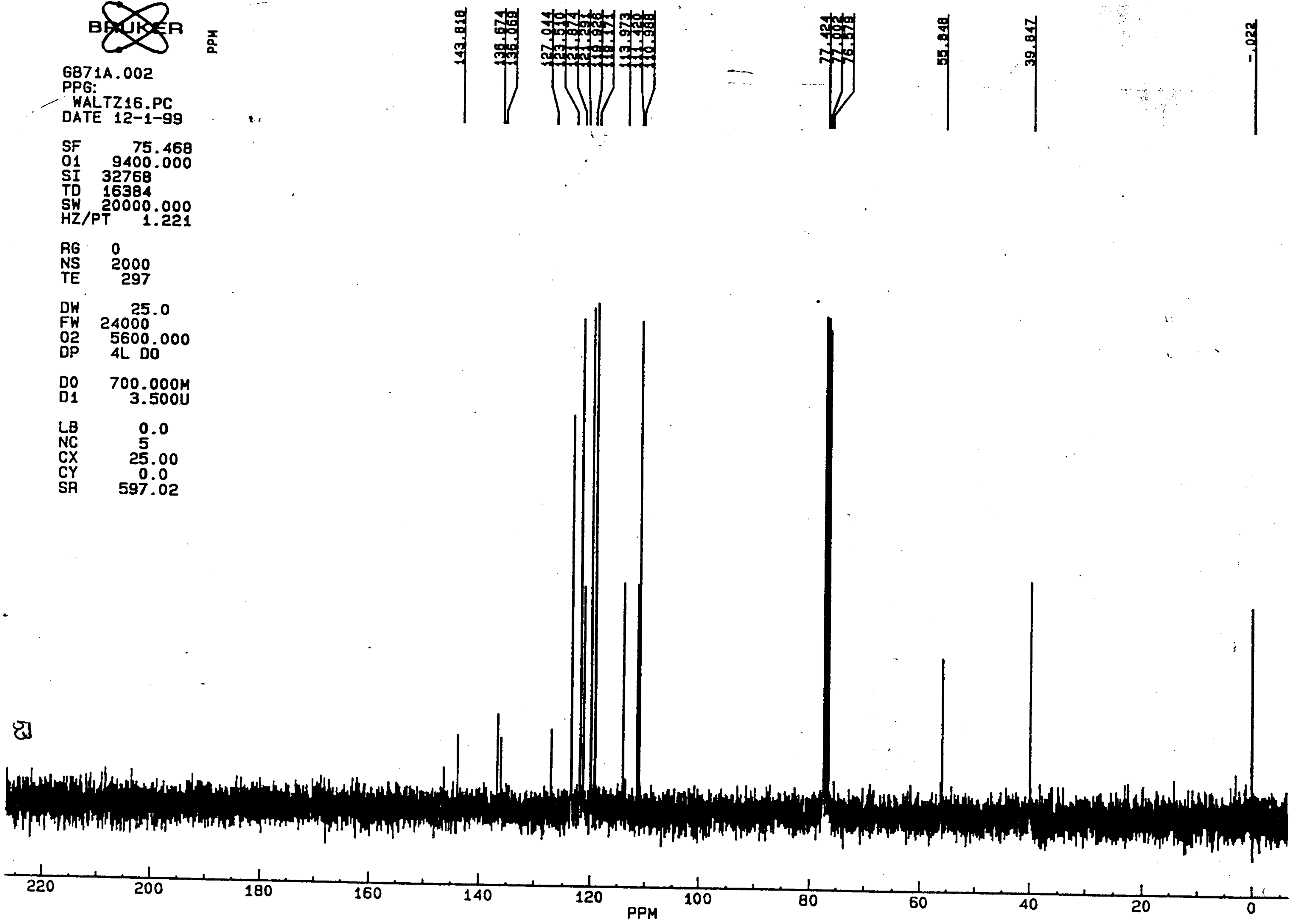

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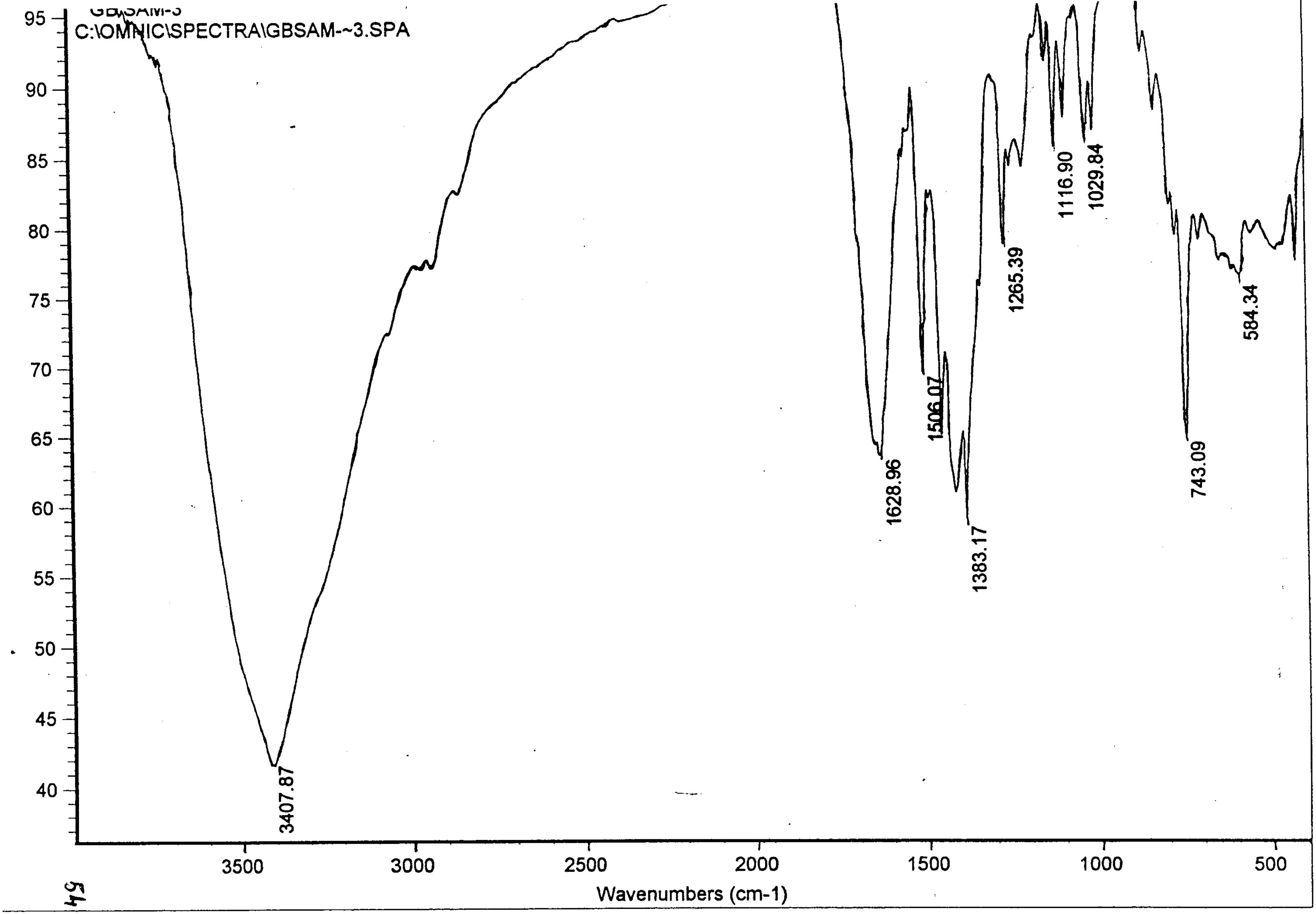
53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1265.39
1116.90
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2500
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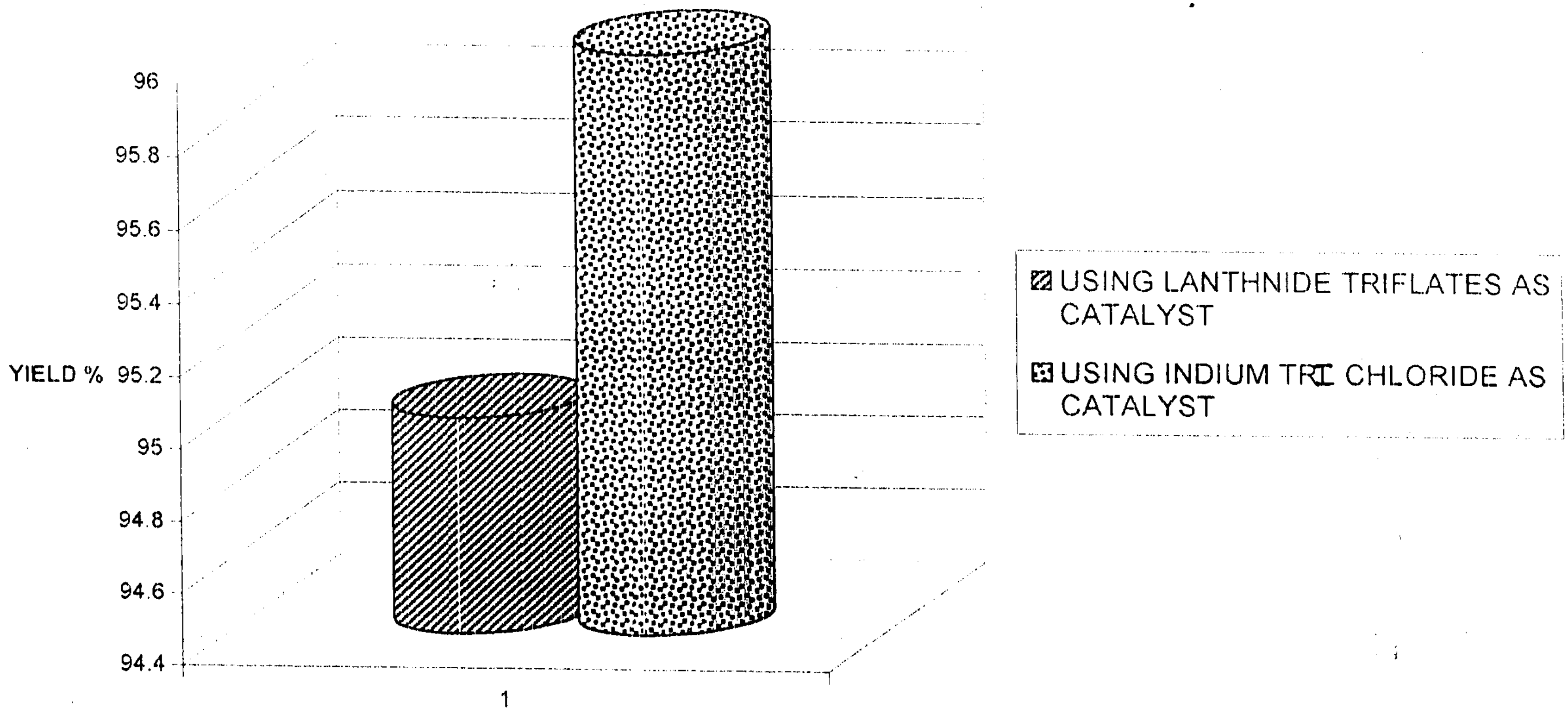
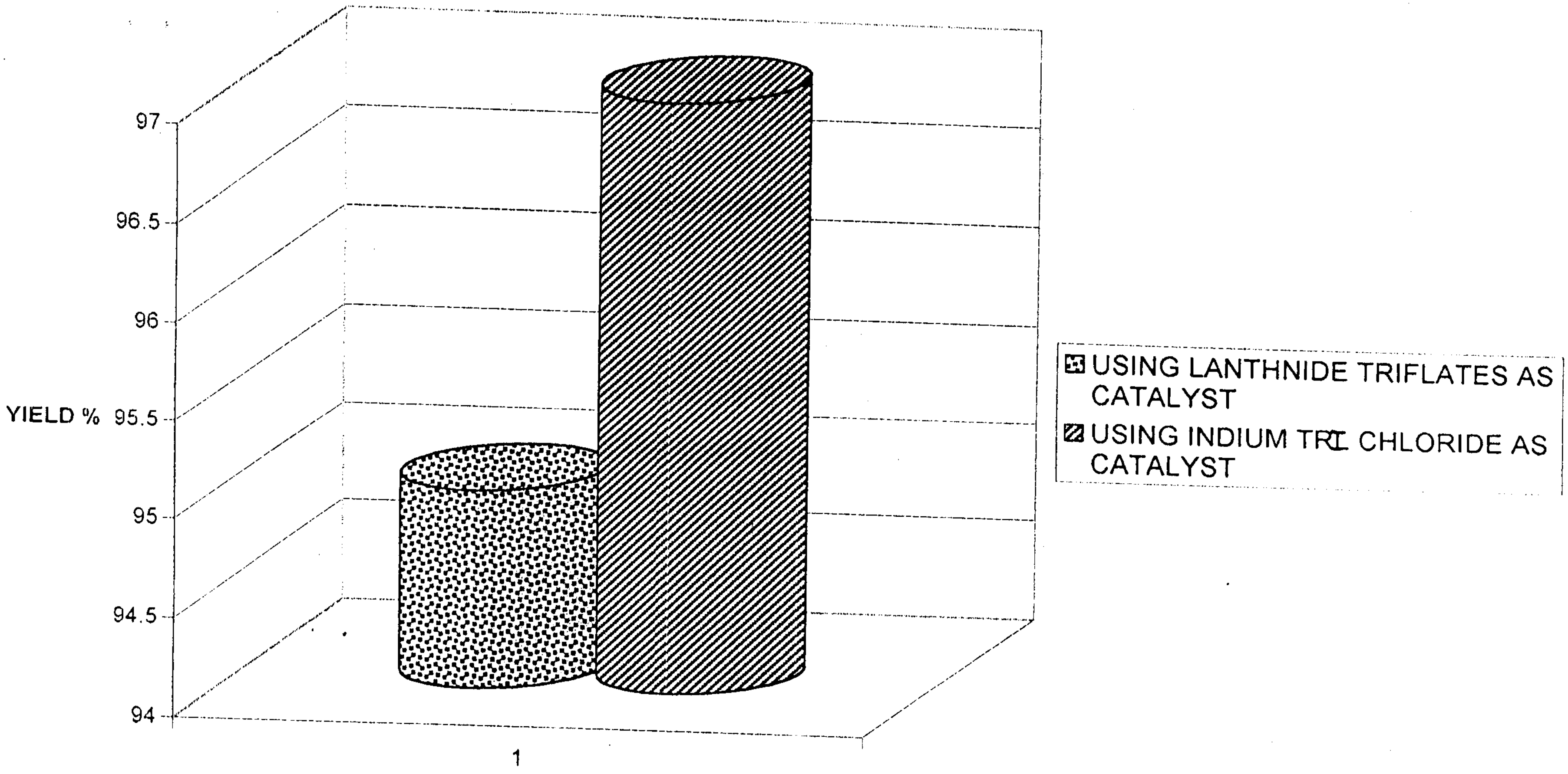
1000
500
Wavenumbers (cm-1)

GRAPH I FOR PRODUCT - I



GRAPH II FOR PRODUCT II



CONFIRMED STRUCTURES OF BIS INDOLES

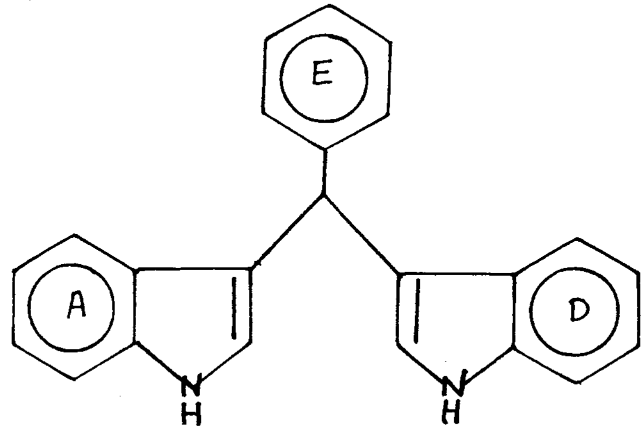


FIG [i]

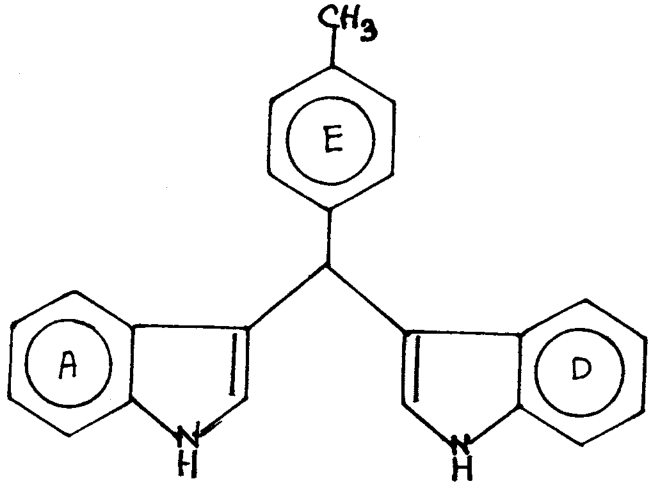


FIG [ii]

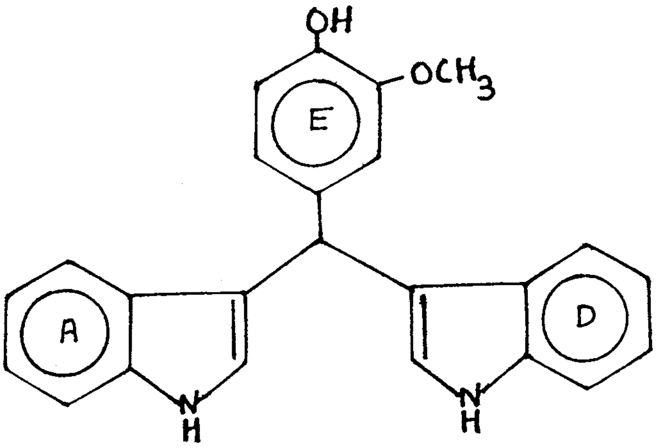


FIG [iii]

SUMMARY AND CONCLUSION

5 SUMMARY AND CONCLUSION

Indole, a π–electron rich heterocycle undergoes electrophilic substitution reaction with aromatic aldehydes producing azafulvenum salts which undergoes further addition with second molecule of Indole to form bis-indolyl methane. This reaction is catalysed by both protic acids as well as Lewis acids for instance $AlCl_3$, Lanthanide triflates etc.

Lanthanide triflates function as stable Lewis acids in aqueous solution catalysing the reaction between Indole and aromatic aldehyde. In the present study we have employed Indium tri chloride as Lewis acid.

The following significant conclusions have been drawn on the basis of present work.

- The electrophilic substitution reactions between Indole and

  a. Benaldehyde
  b. Tolualdehyde
  c. Vanillin have given the products I, II and III respectively.

- Indium trichloride in the amorphous powder from has been found to catalyse the reaction directly.

- These reactions did not take place in the absence of Indium tri chloride.

- The proposed structures (I), (ii) and (iii) for the above products have been confirmed on the basis of IR spectra, ^{1}HNMR spectra, CMR spectra and Mass spectra.

- The proposed mechanism for the above electrophilic substitution reaction is also supporting the above structures.

- Acetonitrile has been found to be the best solvent medium for the reaction.

- A 20 mol percentage of Indium tri chloride has been observed to effectively catalyse the reaction.

- The reactions have been found to take place even at room temperature.

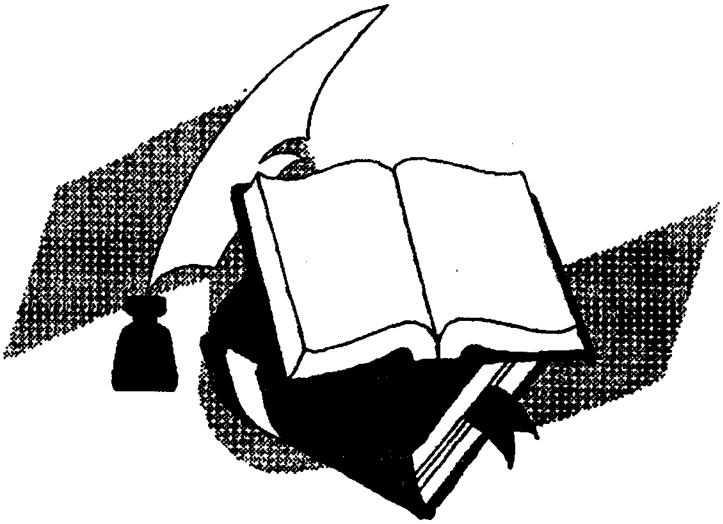
- Excellent yields of the products I (96%), II (97%) and III (89%) have been obtained in the above reaction.

- In presence of Indium tri chloride catalyst, the reaction between Indole and Benzadehyde has been found to require 4-5 hours for completion giving an yield of 96%. But similar reaction using Lanthanide triflates as catalyst had been reported to require a period of 12 hours for completion giving only a maximum yield of 93% with Dysprosium triflates. Hence InCl3 has been found to be more effective Lewis acid catalyst than Lanthanide triflates.

- Indium tri chloride is white amorphous crystal and is decomposed by water.

- Indium tri chloride has been found to be less hazardous, easy to handle and also economical.

In summary $InCl_3$ has been found to effectively catalyse the electrophilic substitution reactions of Indole with aromatic aldehydes.



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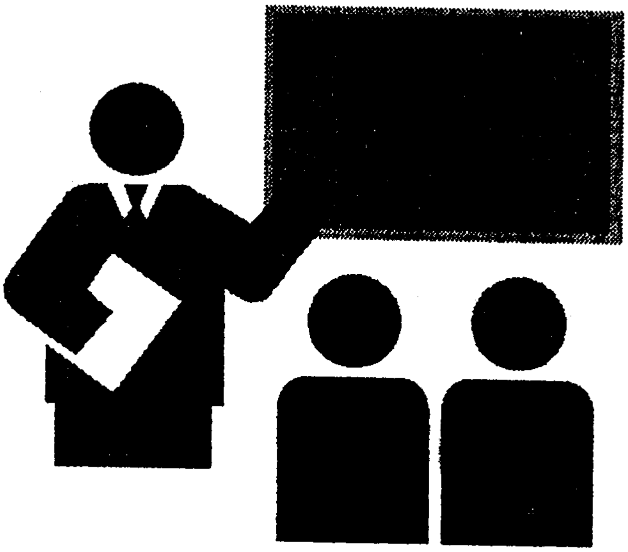

APPENDICES

APPENDIX - I

Procedure for column chromatography

Deciding the solvent system.

Ran `tlcs' to find a solvent system which will give good separation of the components of the mixture. Started with hexane and ethyl acetale mixture. It is in this first step of the procedure that the greatest skill and judgement is required and careful attention should be paid to trial tlcs. With experience, the appropriate column and solvent to choose will become almost instinctive.

Preparation of column

Weighed out the required quantity of silica in a conical flask and made it into a mobile slurry with some of the chosen solvent. Chosen a column which will fill to about 18 cms with the amount of silica being used. To plug the bottom of the column, rolled a piece of cotton wool between the fingers so that it is just wides than the column out let; connected the column to a low vacuum line with the tap closed; drop the cotton woollen ball to the bottom of the column, then opened the tap. This is the most reliable way to insert the plug. Mount the column to a stand and added silica very carefully to the column in small portions via a powder funnel. Between each portion, pressurized the column to pack down the silica and removed excess solvent. Once loaded the sample the remaining steps should be carried out as swiftly as possible and the solvent flow should be continued without interuption if possible, especially during the early stages of elution.

Loading the sample; running them and collecting

Dissolved the sample in the minimum amount of solvent, preferably the same solvent that is used to run the column, (n-hexane & ethyl acetate) kept the tlc sample of the sample mixture to compare with the column fractions

Loaded the solution onto the top of the column, very carefully, using a pipette to drip it around the walls of the column. Caution must be taken not to disturb the layer of sand. The solvent was added from the top and the column was allowed to run. The column fractions were monitored by running tlcs while the column was running.

When all the compounds were collected in separate fractions, they were combined and evaporated on a rotary evaporator and finally the last traces of solvent were removed under high vacuum.

APPENDIX - II

Procedure for Thin Layer Chromatography

Materials for the method

1. Applicator
2. Gauge
3. Spotting guide
4. Glass plate
5. Developing tank with lid
6. Metal drying rack
7. Glass sprayer

Choice of the adsorbent

Silica get has the highest capacity of resolution i.e ability to separate highest amount of the mixture.

Spotting the sample

The sample was applied as a solution in a non-polar solvent such as $CHCl_3$ or C_6H_6. The solvent should be highly volatile.

Mechanism of Application

The sample was applied to bound layers by touching the tips of a filled capillary micropipette to the adsorbent layer in a manner analogous to that used in paper chromatography.

This plate was kept in a solvent chamber containing the solvent mixture of ethylacetate and n-hexane and allowed to rise.

The plate was taken out and detected the spots by keeping in a UV chamber.

The distance travelled by each spot was measured and the Rf values were calculated with which the products were indentified.