New Lewis Acid Catalysts For Biginelli Reaction of Benzaldehyde with Thiourea

Project report submitted to

Mahatma Gandhi University, Kottayam

In partial fulfillment of the requirement for the award of the Bachelor's degree of

B.Sc. CHEMISTRY

BY

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(Reg. no: **200021026016**)

Under the supervision of

Dr. Litty Sebastian

DEPARTMENT OF CHEMISTRY

BHARATA MATA COLLEGE, THRIKKAKARA

(Affiliated to Mahatma Gandhi University, Kottayam)

2020-2023

DEPARTMENT OF CHEMISTRY

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(Affiliated to Mahatma Gandhi University, Kottayam)

CERTIFICATE

This is to certify that the project report entitled "**NEW LEWIS ACID CATALYSTS FOR BIGINELLI REACTION OF BENZALDEHYDE WITH THIOUREA**" is a bonafide work carried out by **Bhavana Suresh,** B.Sc. Chemistry student, under my supervision and guidance and that no part of this has been presented earlier for the award of any other diploma or other similar titles of recognition.

Forwarded by

Dr. Sindhu Joseph
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Project Guide

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Assistant Professor
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Place:

Date:

DECLARATION

I, Bhavana Suresh, declare that the project report entitled "**New Lewis Acid Catalysts For Biginelli Reaction of Benzaldehyde with Thiourea**", is an authentic record of original work carried out during my course of study, under the supervision of Dr. Litty Sebastian, Department of Chemistry, Bharata Mata College, Thrikkakara and no part of this has been previously formed on the basis for the award of any assistantship of any other institution.

Place: Thrikkakara

Date:

ACKNOWLEDGMENT

Praise and gratitude are first and foremost due to God, the Almighty, for his numerous blessings that made the project work possible.

Words are often inadequate to express my sincere gratitude to my guide, Dr. Litty Sebastian, for her frequent guidance and encouragement throughout the course of this project. Without her solicitude, I would not have been able to make such a study.

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Bhavana Suresh

CONTENTS

CHAPTER 1

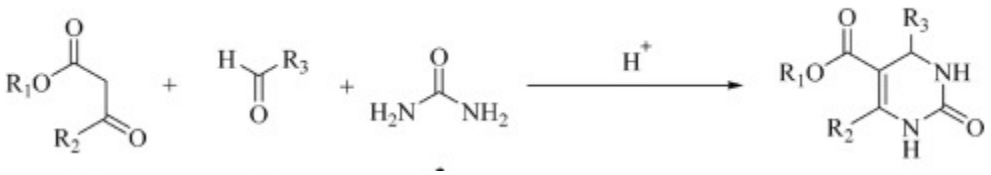
1.1 INTRODUCTION

The most significant heterocyclic ring systems that contribute significantly to the synthesis of DNA and RNA are dihydropyrimidines. They were produced artificially by means of multi-component reactions like the Biginelli reaction and Hantzsch dihydropyridine. These Biginelli type dihydropyrimidones have drawn a lot of attention in recent years because of the intriguing pharmacological characteristics connected to their heterocyclic structure.

1.2 BIGINELLI REACTION

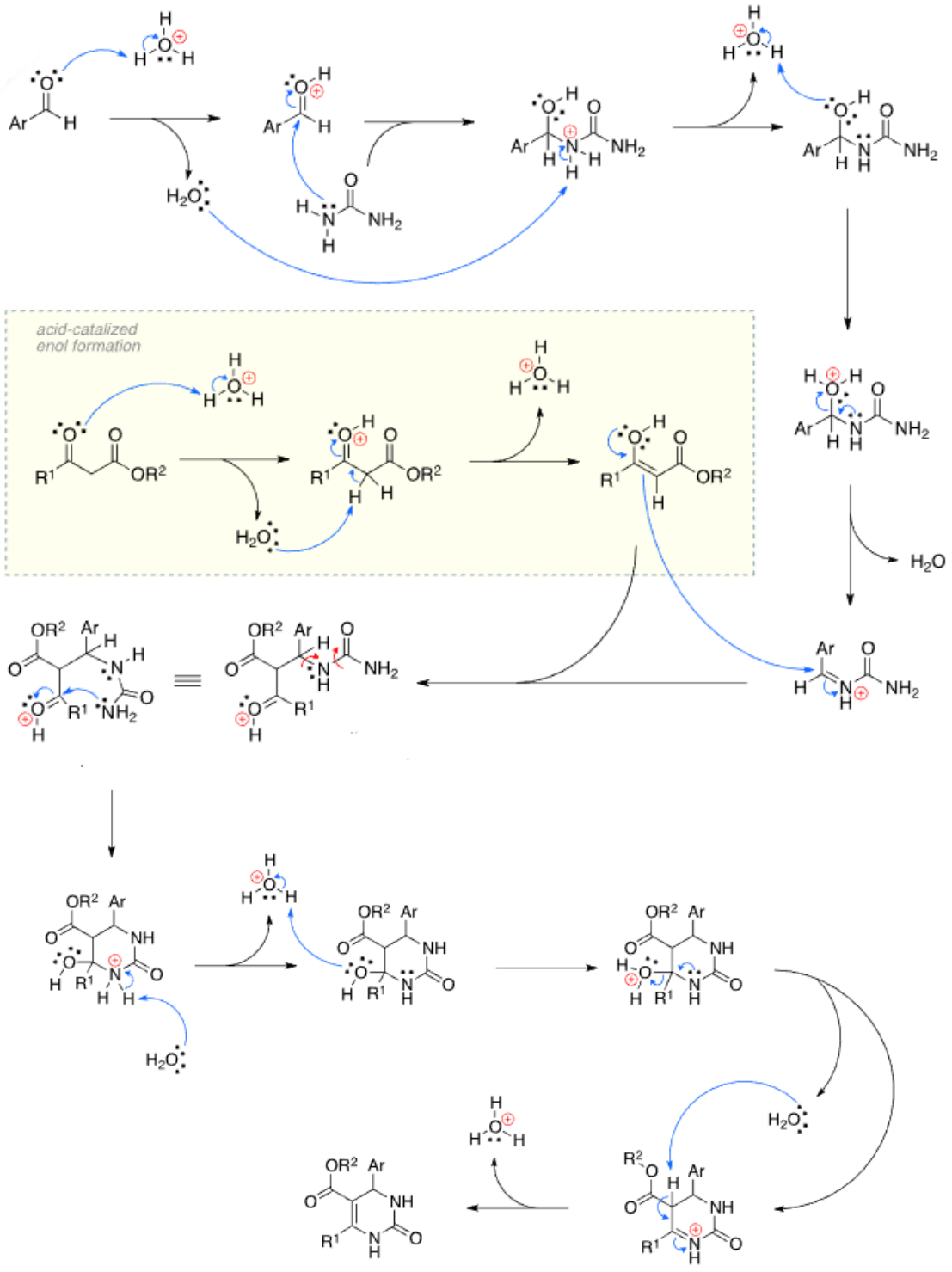
To produce dihydropyrimidones, a multicomponent chemical reaction known as the Biginelli reaction is used. An aldehyde, a ketoester, and urea/thiourea are involved in this reaction, which is facilitated by an acid. The reaction was discovered by Pietro Biginelli in 1891.

The Scheme of the reaction is given below:



1.3 MECHANISM

The aldehyde is first protonated by the acid, and then the amine from urea attacks it to complete the reaction. A protonated alcohol is produced as a result of the subsequent proton transfer steps, and it departs as water to create an intermediate N acyliminium ion. The enol form of the keto ester then engages in an attack on the intermediated. A cyclic intermediate is created when the carbonyl and the other amine group react. The final pyrimidone product is made up of proton transfer stages, water release, and deprotonation. The following illustrates the mechanism:


acid-catalized
enol formation

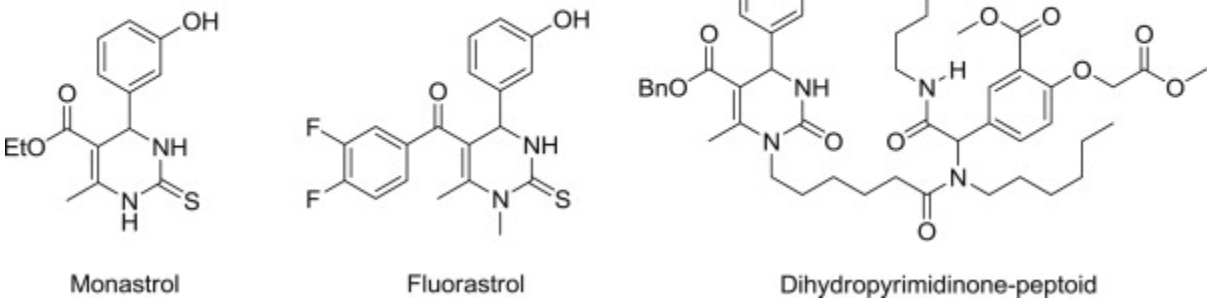
1.4 PHARMACEUTICAL ACTIVITY OF DIHYDROPYRAMIDINONES

I. Anticancer activity

Monastrol has been the subject of the most research on biginelli adducts, which have the potential to treat malignancies. In 1999, a study was published that examined the impact of monastrolin on cancer cells for the first time. Monastrol was discovered to stop mitosis by preventing the kinesin Eg5 protein, which is essential for the development of spindle bipolarity, from moving. Since then, the development of fresh anticancer drugs has been motivated by monastrol.

Kinesin Eg5 is a motor enzyme that is responsible for the formation and maintenance of mitotic spindles. The inhibition of this enzyme activity by monastrol leads to the loss of chromosome alignments and bipolar spindle formation. The resulting "monastral phenotype" inspired scientists to name this specific Biginelli compound as monastrol. (*S*)-Monastrol was found to be more potent (15 times higher potency) inhibitor of Eg5 than the (*R*)-enantiomer.

As it can interact with an allosteric site of this enzyme due to the presence of fluorine atoms, Fluorastrol, a monastrol- derived Eg5 inhibitor, proved to be more effective than Monastrol.

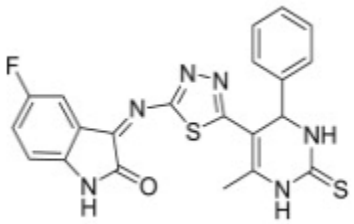


Monastrol Fluorastrol Dihydropyrimidinone-peptoid

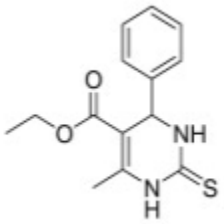
The protein Hsp 70 can also be modulated by Biginelli chemicals. One of the most prevalent Biginelli adducts on Hsp 70 is DHPM peptoid. This protein, which is known to be overexpressed in some cancer cell lines, is in charge of various cellular functions, including the transport and rearrangement of protein complexes.

II. Antifungal activity

Biginelli adducts having notable action against Esterchia coli, Pseudomonas aeruginosa, Klebisella pneumonia, and Staphylococcus aureus were described by Akhaja and colleagues in 2011. All of the investigated microbial strains showed good action against the DHPM-1 structure. According to Singh and colleagues, Biginelli adducts have antifungal activity against three different types of fungus including Aspergillus niger, and Trichoderma hammatum. One of the most effective synthetic compounds against A was DHPM-2. The MIC value of the niger 0.35mg/mL.



DHPM -1

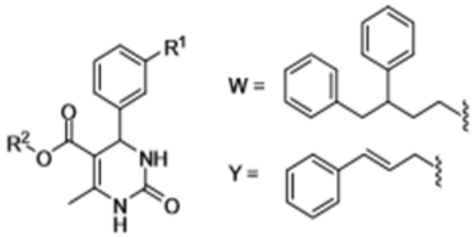


DHPM-2

III. Antioxidant property

Oxygen and nitrogen reactive species (ROS and RNS, respectively) are ubiquitous in nature being a result of electron escape from electron transport chain (present in mitochondria and chloroplast). If the cellular antioxidant system is unable to effectively restore the normal levels, the overproduction of ROS and/or RNS can be harmful to cells and ultimately lead to pathologies.

Biginelli adducts' first report on their antioxidant effects was made in a 2006 study that looked into how well these compounds may protect male adult albino Wistar rats from ROS production and lipid peroxidation.



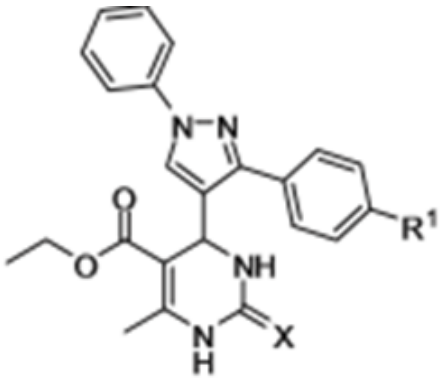
R^1 = H and R^2 = W DHPM-3
R^1 = NO_2 and R^2 = W DHPM-4

When given at 200 µM, the Biginelli adducts DHPM-3 and DHPM-4 returned the lipid hydroperoxide to normal levels in the liver cells. These findings suggest that an aromatic ring need not contain a nitro group in order to avoid lipid peroxidation.

IV.Antibacterial Activity

The minimum inhibitory concentrations (MICs) of the Biginelli compounds with a 1,3-diarylpyrazole moiety (DHPM5-8) against Mycobacterium tuberculosis H37Rv (MTB H37Rv) were 20 ng mL^{-1}, 20 ng mL^{-1}, 250 ng mL^{-1}, and 125 ng mL^{-1}, respectively. The impact of these substances on healthy African green monkey kidney cells (VERO line) was evaluated, and it was discovered that both Biginelli adducts are extremely selective to MTB H37Rv (selectivity index >500).

The reference medicines ethambutol (MIC = 7.6M) and ciprofloxacin (MIC = 9.4 M) were found to be as potent as or more potent than the other 16 Biginelli adducts against MTBH37Rv. 3.4 to 76.2 M was the range of the MIC values for the various substances.

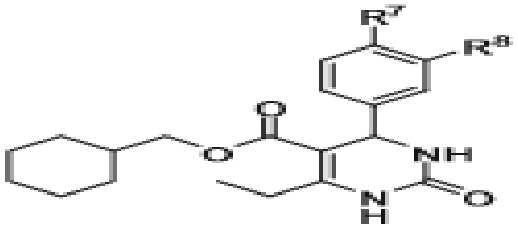


X = O and R^1 = F DHPM-5
X = O and R^1 = NO_2 DHPM-6
X = O and R^1 = Cl DHPM-7
X = S and R^1 = Cl DHPM-8

t

V. Antiviral Activity

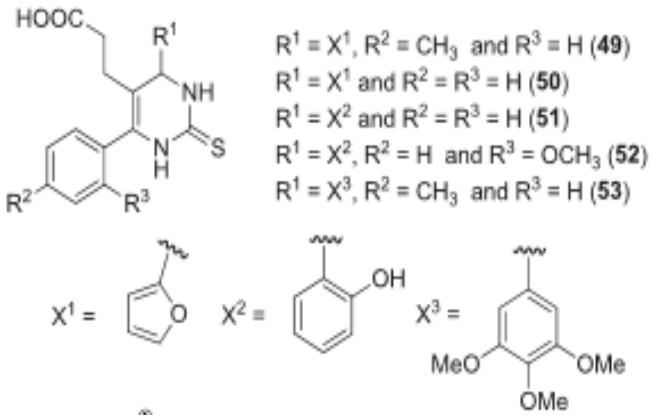
Some Biginelli adducts have the potential to be used as tools to stop reproduction of HIV-1virus, as demonstrated by Kim and colleagues. Notably, when used at dosages lower than 90 nm, compounds 77-82 enantiomer reduced HIV-1 proliferation in SEMx174-LTR-GFP cells (clone CG8) by 50%. The EC50 result for the reference medication nevirapine was 150 nm under the identical experimental circumstances. The antiviral activity of the (S)- enantiomer was found to be stronger than that of the equivalent (R)- enantiomer. That (S)-77 is at minimum 26 times more effective than (R)-77 has been demonstrated.



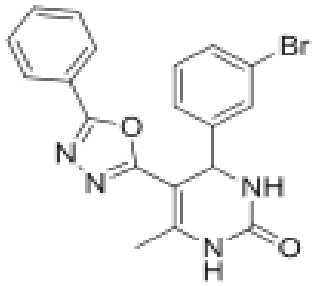
R^7 = H and R^8 = OH (77)
R^7 = OH and R^8 = H (78)
R^7 = NHAc and R^8 = H (79)
R^7 = CN and R^8 = H (80)
R^7 = F and R^8 = H (81)
R^7 = Cl and R^8 = H (82)

VI. Anti Inflammatory Activty

Biginelli adducts have drawn a lot of interest because of their potential as anti-inflammatory drugs. When compared to diclofenac, a reference medicine, the propanoic acid derivatives thio adducts (49-53) were shown to be the most promising anti-inflammatory compounds based on the length of action and percentage of inflammation suppression on Albino rats paw edema.



By decreasing the carrageenan-induced rat paw edema by 75% after 3 hours of therapy, the Biginelli derivative 54, which has a 1,3,4oxadiazol-2-yl moiety, inhibits the inflammatory process. This impact is comparable to that of diclofenac.



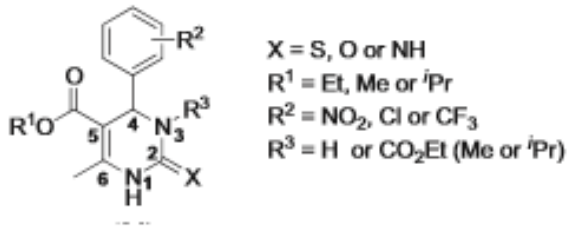
(**54**)

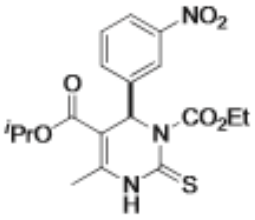
VII. Calcium Channel Inhibitors

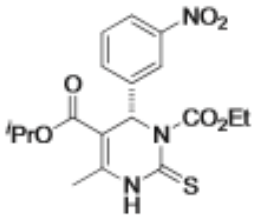
Due to their capacity to suppress calcium channel activity, dihydropyridines like nifedipine were first introduced to the market in 1975 for the treatment of cardiovascular disorders (hypertension, cardiac arrhythmias, and angina). Following the discovery of this medication, various Biginelli adducts were created to test its ability to inhibit calcium channels. In 1990, a study on structure- activity relationship using Biginelli adducts was published in regard to the capacity to target calcium channels. Comparing thio-adducts to oxo- and aza-analogues, it was found that Biginelli compounds were the most powerful.

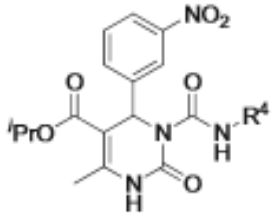
According to in vitro analogue studies, the adduct with a nitro group at the aromatic ring's ortho position was a more potent antihypertensive molecule than the one with CF_3 or Cl as a substituent. Interestingly, compared to the effects of the Biginelli adducts having an ethyl ester or methyl ester group at the same carbon, respectively, the presence of an isopropyl ester group at C5 increased the potency by 10 and 60 times. Although substances with substituents at N3 are effective calcium channel blockers in vitro, metabolization causes these substances to lose their antihypertensive effects in in vivo tests.

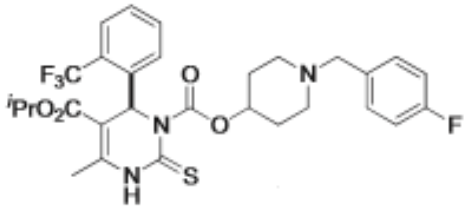
Compounds showing calcium channel inhibition:

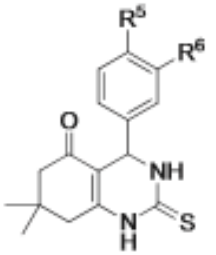


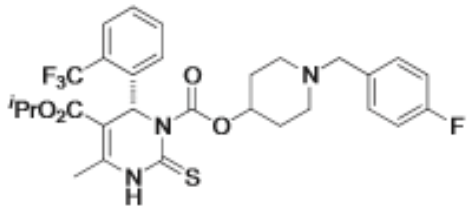


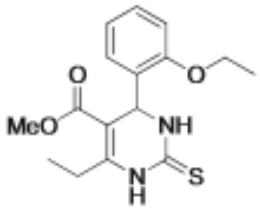


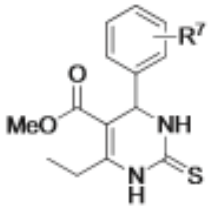


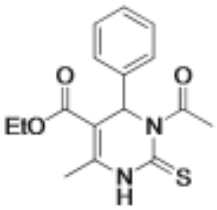








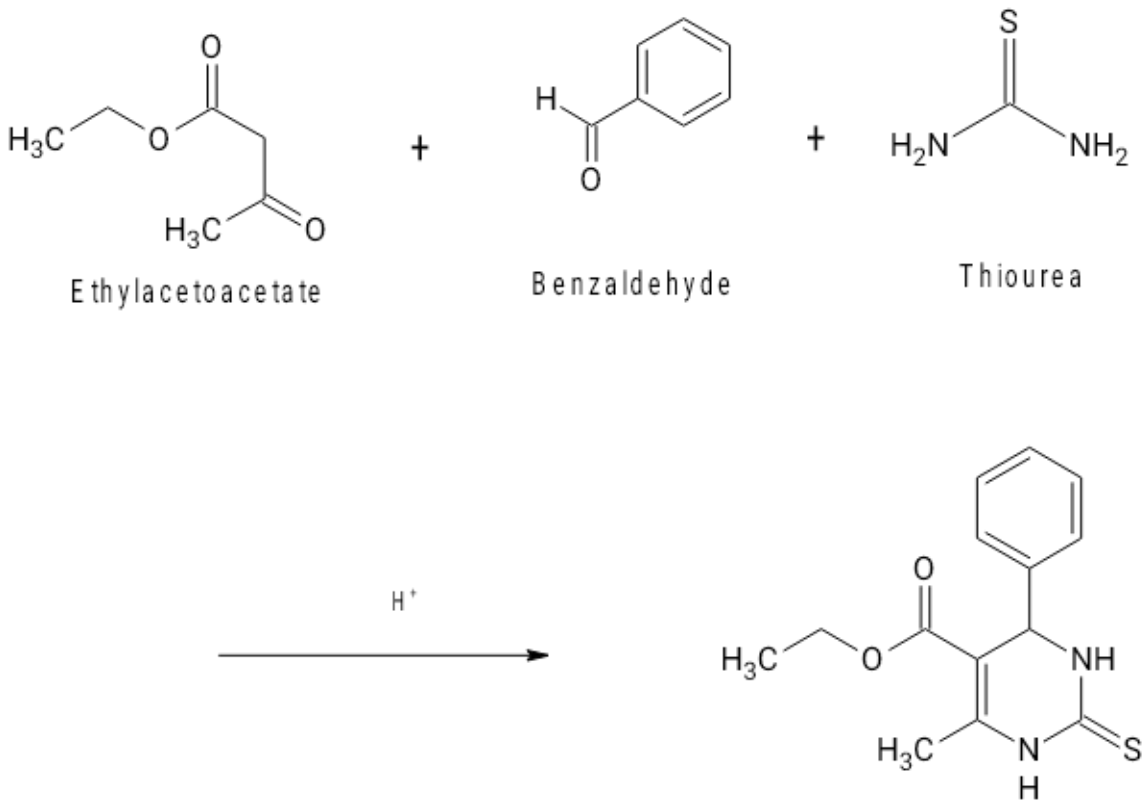




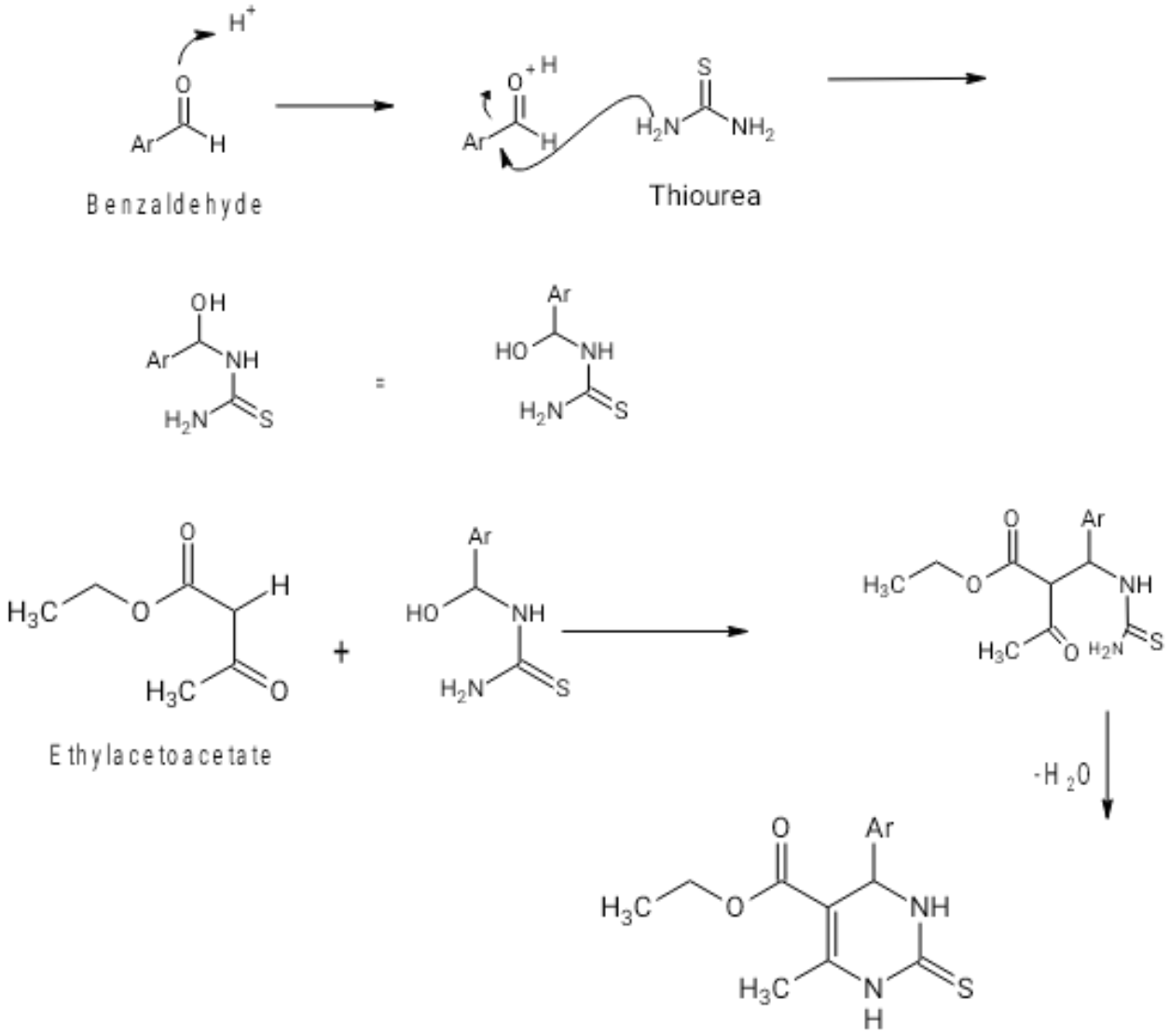
1.5 SCOPE AND OBJECTIVE OF THE PROJECT

Though, the synthesis of the Biginelli reaction using urea as a component has been well studied, the one using thiourea is not very well investigated. The aim of the present study was to investigate whether Lewis acid catalyst can be used for catalyzing the reaction. Five different Lewis acid catalysts were investigated for the purpose. They include $AlCl_3$ and AlF_3 and transition metal chlorides like $FeCl_3$,$MnCl_2$ and $ZnCl_2$.

The scheme of the reaction is as follows:



Mechanism of the reaction is given below:



CHAPTER 2

2.1 MATERIALS AND METHODS

2.2 EXPERIMENT

2.2.1 Materials required

- 200 ML Erlenmeyer flask
- Condenser
- Bunsen burner
- Measuring jar
- Beaker
- Glass rod

2.2.2 Chemicals required

- Thiourea
- Benzaldehyde
- Ethyl acetoacetate
- Catalysts used were:
    - Hydrochloric Acid
    - Zinc Chloride
    - Aluminium Chloride
    - Aluminium Flouride
    - Ferric Chloride
    - Manganese Chloride

2.2.3 Procedure

I. SYNTHESIS OF DIHYDROPYMIDNONES.

In a 200 mL Erlenmeyer flask, 2.0 mmol of benzaldehyde, 2.0 mmol of ethyl acetoacetate, and 3.00 mmol of thiourea are mixed. The catalysts are then added to the Erlenmeyer Flask (0.42 mmol). The mixture is warmed and mixed until solidification occurs at 80^0C over a water bath. (time differ for different catalysts). The solid Biginelli product is processed by grinding it into a fine powder, collecting it under a vacuum, rinsing it with ethyl acetoacetate and drying it to generally produce an average yield of 65%, to 90%. The completion of the product formation was monitored by TLC and was characterized by NMR and IR. The amount of the reagent and the catalyst used is summarized in this table:

Sl.no	Reagent & Catalyst	Amount
1.	Benzaldehyde	4ml
2.	Thiourea	4.56 g
3.	Ethyl acetoacetate	5 ml
4.	HCl	0.01531 g
5.	$ZnCl_2$	1.144 g
6.	AlF_3	0.704 g
7.	$AlCl_3$	1.12 g
8.	$FeCl_3$	1.363 g
9.	$MnCl_2$	1.662 g

2.2.4 Characterization Techniques

I. THIN LAYER CHROMATOGRAPHY

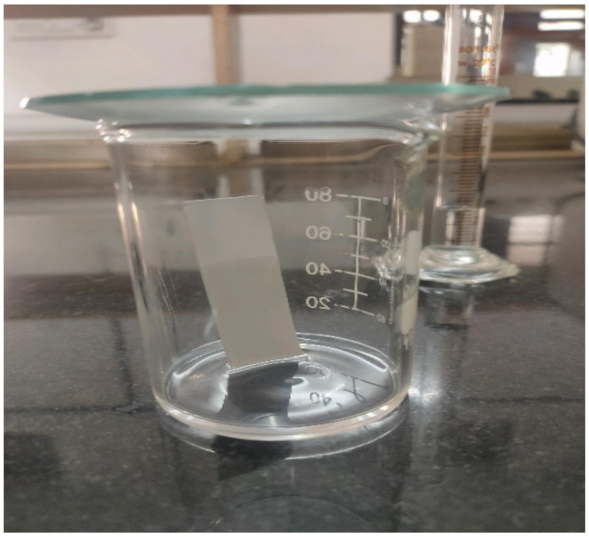
The analytical method of thin layer chromatography is used to recognize and separate the constituents of a mixture. The separation of two or more components from a mixture by passing a mobile phase through a stationary phase is the foundation of the TLC process. It is additionally used for determining a compound's purity within a combination. The method is highly selective. By comparing and aiding in the identification of substances by thin layer chromatography, the retention factor (Rf) is used. The distance travelled by a compound divided by the distance travelled by the solvent front, both measured from the origin, gives the compound's Rf value. Rf value is characteristic of each component and can be used to check the purity of compound formed.

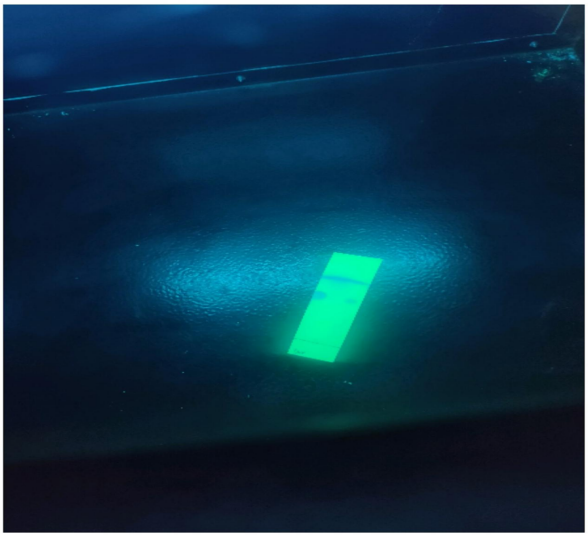
PROCEDURE

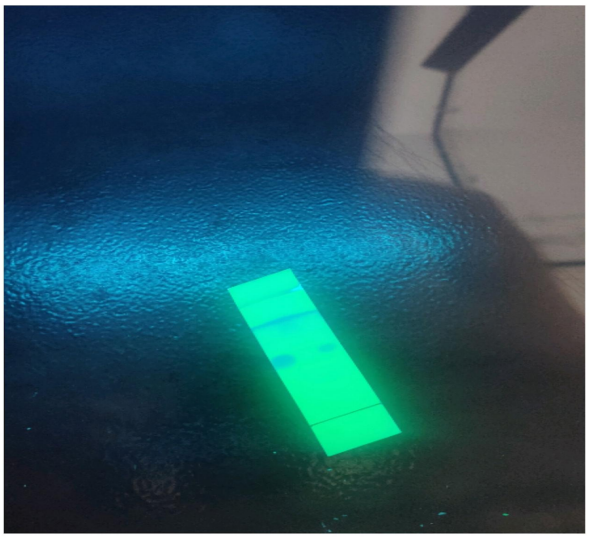
The TLC plate was cut to our convenience. A line was drawn near the bottom of TLC with a pencil. If one uses pen, there is a chance of ink smudge. The sample was dissolved in methanol.

The solvent used for TLC was a mixture of ethyl acetate and hexane in the ratio 9:1. The solvent was added to into TLC chamber. The solvent here used is 4.5 ml ethyl acetate and 0.5 ml hexane (9:1 ratio).

Using a capillary tube, the prepared sample was spotted in in TLC plate and the TLC plate was placed in the chamber. The plate should be submerged to a depth where the sample spots are significantly higher than the mobile phase. The solvent will ascend through capillary action, sample will separate into fractions. After the development of spots, the plates were taken out and spots was observed under UV light.








ENTIO METER

II. INFRARED SPECTROSCOPY

Infrared Spectroscopy or IR Spectroscopy, as the name implies, deals with light particles. Infrared rays are at the far end of the spectrum of light because of their frequency, which is significantly lower than that of visible light. Understanding how one molecule interacts with infrared light or reacts under the influence of infrared light is the focus of infrared spectroscopy.

In order to see how molecules interact and what they really do, IR spectroscopy is frequently utilized in the domains of inorganic as well as organic chemistry. These particles, which are ordinarily invisible to the human eye, may be seen using infrared light.

An IR spectrum is a graph where the Y-axis represents the amount of absorbed infrared light and the X-axis represents the wavelength or frequency. If they indeed correlate to vibrations that are present in the bonds of that particular molecule, this is then employed in IR Spectroscopy to ascertain precisely how that molecule absorbs the infrared light.

Infrared light has a frequency that is identical to the bond frequency found inside these molecules. This also has a lot of highly useful uses in modern life and helps a lot of industrial operations.

Based on how they relate to the visible spectrum, the infrared spectrum may be roughly classified into three regions: near, mid, and distant. The 0.8-2.5 m wavelengths or 14000-4000 cm-1, in the high energy and near IR area can cause harmonic or overtone vibration. On the other hand, the mid-IR region, which has a wavelength of 2.5–25 m, or 400–400 cm-1, may be used to analyse basic vibrations as well as related rotational vibrational structure. The microwave zone is exactly close to the far IR region, which has wavelengths between 25 and 1000 m (or 400 and 10 cm-1). This is helpful for rotational spectroscopy since it is low energy.

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for the infrared spectrum's areas than those described above. In other words, bands in the range from 4000 cm^{-1} to 1300 cm^{-1} are useful for determining the functional group of a mystery molecule. And just like a fingerprint, the region between 1300 cm^{-1} and 400 cm^{-1}—also known as the fingerprint region—contains bands that are exclusive to each molecule. These bands are helpful for comparing the spectra of various compounds with one another.

In the present study, the FTIR spectrum of the sample was taken using Thermo Scientific Nicolet iS 5 FTIR Spectrometer available in the Department of Chemistry, Bharata Mata College, Thrikkakara.

III. NMR SPECTROSCOPY

Nuclear magnetic resonance (NMR) spectroscopy is a crucial analytical technique for organic chemists. The study being carried out in the organic lab has greatly benefited from the NMR. It can reveal details about the content and purity of the sample as well as the structure of the molecule. Proton (1H) NMR is one of the NMR techniques that organic chemists use the most frequently. By watching how a molecule's protons react to the surrounding chemical environment, one can infer the structure of the molecule.

It depends on evidence indicating that all nuclei have electric charges and that the majority of atoms' nuclei have spin. The base of NMR spectroscopy is the ability of electromagnetic radiation to absorb energy between the radiofrequency range of 3 kHz and 300 GHz. A magnetic field is formed by the electrical charge and spin of atom nuclei. When an external magnetic field is present, atomic nuclei will either align themselves in the direction of the external magnetic field or in the opposite path.

When there is an external magnetic field present, energy travels from the ground state to the excited state.

An electron generates a radio wave with the same frequency when it shifts from an excited state to the ground state since this shift happens at a wavelength that coincides with radio frequencies. This radio frequency allows entry to the NMR spectrum. The radiofrequency that is being radiated is directly associated with the magnitude of the applied external magnetic field.

The NMR of the sample was measured in NIT, Calicut using the machine Jeol 500 MHz.

CHAPTER 3

3.1 RESULT AND DISCUSSION

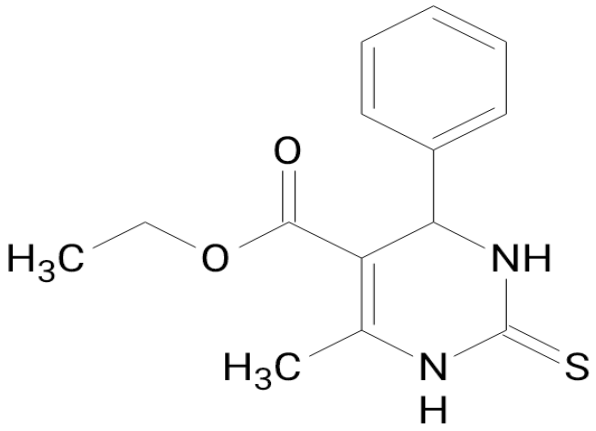
- In this study, the effect of six Lewis acids were used as a catalyst for the Biginelli reaction of Benzaldehyde, Ethyl acetoacetate and thiourea. The list shows the quantity produced by each catalyst.

Sl No.	Catalyst Used	Time taken by the catalyst	% Yield of the complex
1	$ZnCl_2$	3hr 35 min	54%
2	$MnCl_2$	4hr 5min	56%
3	$AlCl_3$	45min	55%
4	AlF_3	4hr 20min	43%
5	$FeCl_3$	1hr 35min	79%
6	HCl	30 min	58%

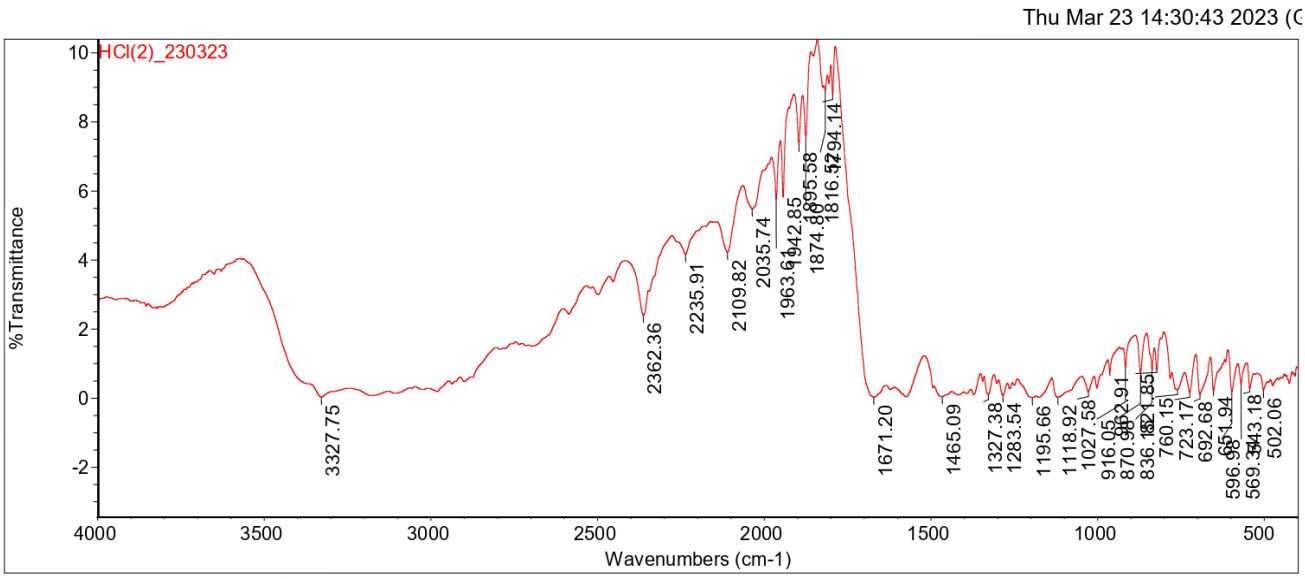
$AlCl_3$ found to be a good catalyst, almost at par with HCl. AlF_3 was not as efficient as $AlCl_3$. Of the three-transition metal catalyst tried, $FeCl_3$ was found to be more efficient than $ZnCl_2$ and $MnCl_2$.

IR SPECTRUM

The IR spectrum revealed the formation of the dihydropyramidine ring. The IR spectrum of the compounds are attached here. The compound shows the characteristic two N-H stretching ar 3328 and 3176 cm^{-1}. The band appearing at 1670 cm^{-1} is due to carbonyl stretching(C=O) of the ethyl acetoacetate moiety. The peak at 1620 cm^{-1} could be N-H bending vibration. The peak at 1327 cm^{-1} could be due to C=S stretching. The sharp bands in the 750~790 and 1520~1540 cm^{-1} regions are due to aromatic C-H and C=C stretching, respectively. The band observed at 1165~1175 cm^{-1} is due to C-N stretching.



- **HCl**



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Thu Mar 23 14:29:46 2023 (GMT+05:30)
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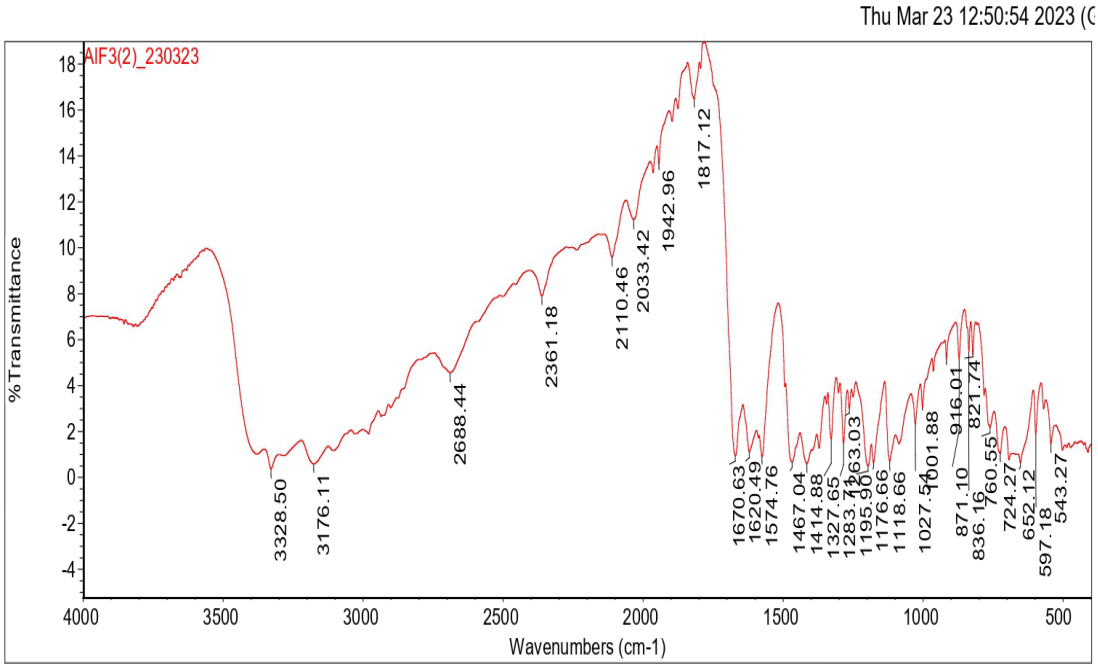
Region: 4000.00 400.00
Absolute threshold: 10.332
Sensitivity: 50
Peak list:

Position:	502.06	Intensity:	0.216
Position:	543.18	Intensity:	0.264
Position:	569.34	Intensity:	0.421
Position:	596.98	Intensity:	0.175
Position:	651.94	Intensity:	0.194
Position:	692.68	Intensity:	0.102
Position:	723.17	Intensity:	0.161
Position:	760.15	Intensity:	0.237
Position:	821.85	Intensity:	0.798
Position:	836.15	Intensity:	0.790
Position:	870.98	Intensity:	0.738
Position:	916.05	Intensity:	0.883
Position:	962.91	Intensity:	0.732
Position:	1027.58	Intensity:	0.178
Position:	1118.92	Intensity:	0.0156
Position:	1195.66	Intensity:	0.0091
Position:	1283.54	Intensity:	0.0723
Position:	1327.38	Intensity:	0.0971
Position:	1465.09	Intensity:	0.0374
Position:	1671.20	Intensity:	0.0248
Position:	1794.14	Intensity:	8.764
Position:	1816.52	Intensity:	8.908
Position:	1874.80	Intensity:	7.558
Position:	1895.58	Intensity:	7.366
Position:	1942.85	Intensity:	5.826
Position:	1963.61	Intensity:	5.764
Position:	2035.74	Intensity:	5.475
Position:	2109.82	Intensity:	4.222
Position:	2235.91	Intensity:	4.188
Position:	2362.36	Intensity:	2.396
Position:	3327.75	Intensity:	0.0268

- **AlF_3**

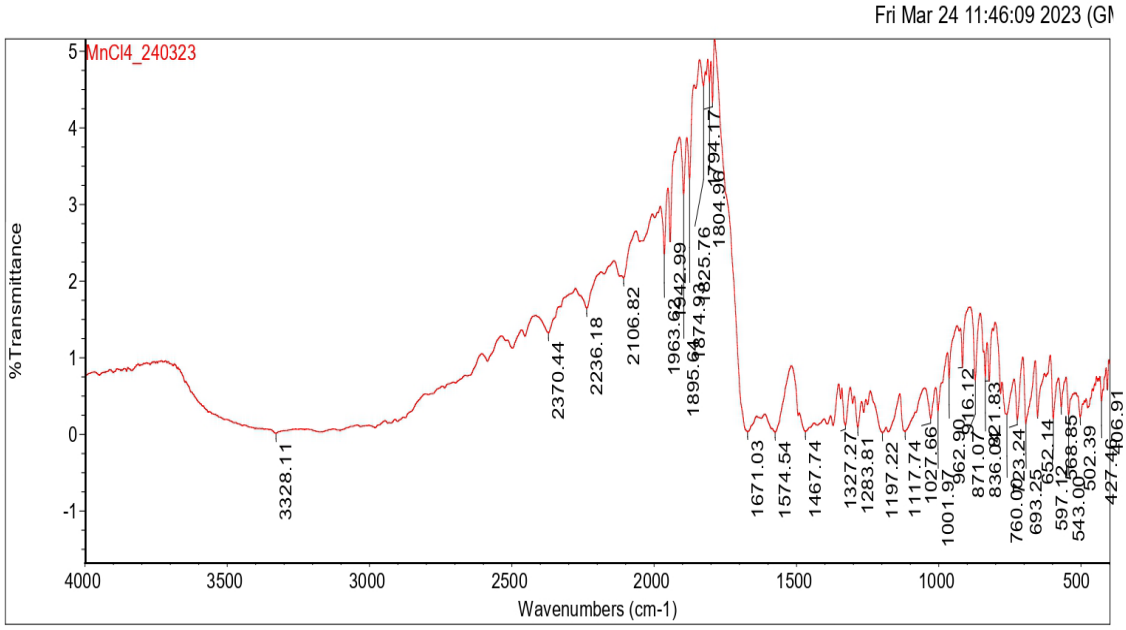


Collection time: Thu Mar 23 12:49:44 2023 (GMT+0

Thu Mar 23 12:50:37 2023 (GMT+05:30)
FIND PEAKS:
Spectrum: AlF3(2)_230323
Region: 4000.00 400.00
Absolute threshold: 18.865
Sensitivity: 50
Peak list:

Position:	543.27	Intensity:	1.434
Position:	597.18	Intensity:	1.871
Position:	652.12	Intensity:	0.615
Position:	724.27	Intensity:	1.019
Position:	760.55	Intensity:	2.165
Position:	821.74	Intensity:	5.316
Position:	836.16	Intensity:	5.454
Position:	871.10	Intensity:	5.150
Position:	916.01	Intensity:	5.131
Position:	1001.88	Intensity:	3.027
Position:	1027.54	Intensity:	2.307
Position:	1118.66	Intensity:	0.878
Position:	1176.66	Intensity:	0.615
Position:	1195.90	Intensity:	0.485
Position:	1263.03	Intensity:	2.999
Position:	1283.71	Intensity:	1.475
Position:	1327.65	Intensity:	1.857
Position:	1414.88	Intensity:	0.586
Position:	1467.04	Intensity:	0.854
Position:	1574.76	Intensity:	0.877
Position:	1620.49	Intensity:	1.097
Position:	1670.63	Intensity:	0.933
Position:	1817.12	Intensity:	16.453
Position:	1942.96	Intensity:	13.636
Position:	2033.42	Intensity:	11.219
Position:	2110.46	Intensity:	9.576
Position:	2361.18	Intensity:	7.897
Position:	2688.44	Intensity:	4.545
Position:	3176.11	Intensity:	0.570
Position:	3328.50	Intensity:	0.348

- **$MnCl_2$**



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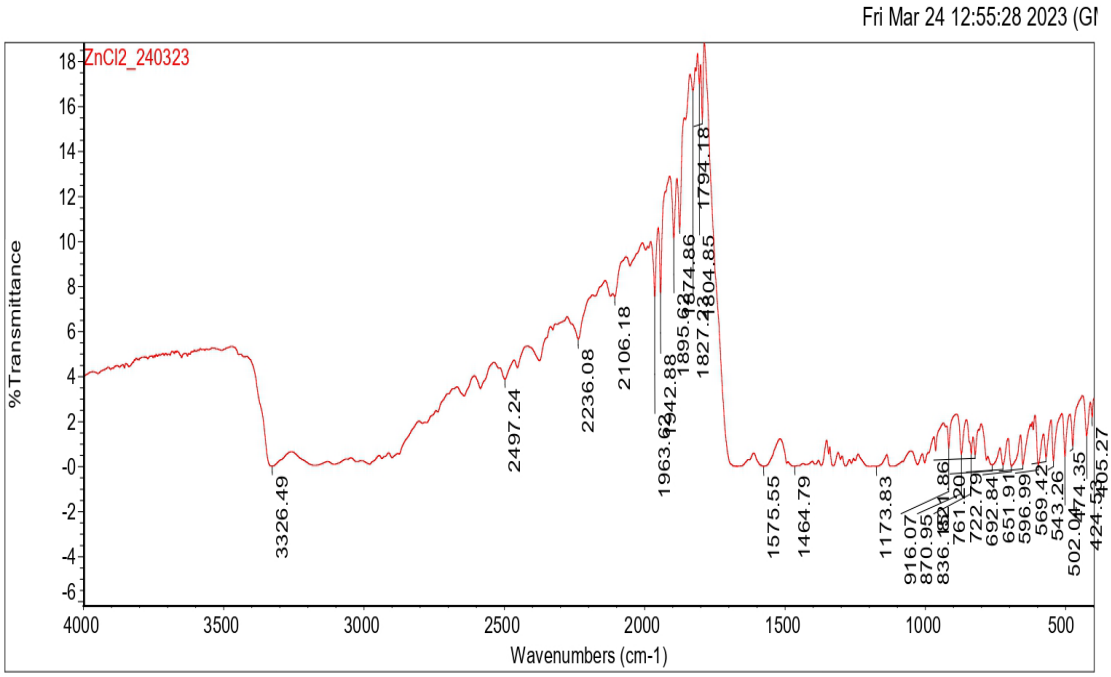
FIND PEAKS:
Spectrum: MnCl4_240323
Region: 4000.00 400.00
Absolute threshold: 5.139
Sensitivity: 50
Peak list:

Position:	406.91	Intensity:	0.986
Position:	427.46	Intensity:	0.431
Position:	502.39	Intensity:	0.219
Position:	543.00	Intensity:	0.260
Position:	568.85	Intensity:	0.352
Position:	597.12	Intensity:	0.204
Position:	652.14	Intensity:	0.226
Position:	693.25	Intensity:	0.137
Position:	723.24	Intensity:	0.191
Position:	760.00	Intensity:	0.256
Position:	821.83	Intensity:	0.696
Position:	836.08	Intensity:	0.750
Position:	871.07	Intensity:	0.705
Position:	916.12	Intensity:	0.876
Position:	962.90	Intensity:	0.731
Position:	1001.97	Intensity:	0.363
Position:	1027.66	Intensity:	0.205
Position:	1117.74	Intensity:	0.0345
Position:	1197.22	Intensity:	0.0296
Position:	1283.81	Intensity:	0.0904
Position:	1327.27	Intensity:	0.115
Position:	1467.74	Intensity:	0.0345
Position:	1574.54	Intensity:	0.0248
Position:	1671.03	Intensity:	0.0302
Position:	1794.17	Intensity:	4.329
Position:	1804.96	Intensity:	4.395
Position:	1825.76	Intensity:	4.945
Position:	1874.98	Intensity:	3.331
Position:	1895.64	Intensity:	3.128
Position:	1942.99	Intensity:	2.910
Position:	1963.62	Intensity:	2.359
Position:	2106.82	Intensity:	2.038
Position:	2236.18	Intensity:	1.644
Position:	2370.44	Intensity:	1.323
Position:	3328.11	Intensity:	0.0106

- **$ZnCl_2$**



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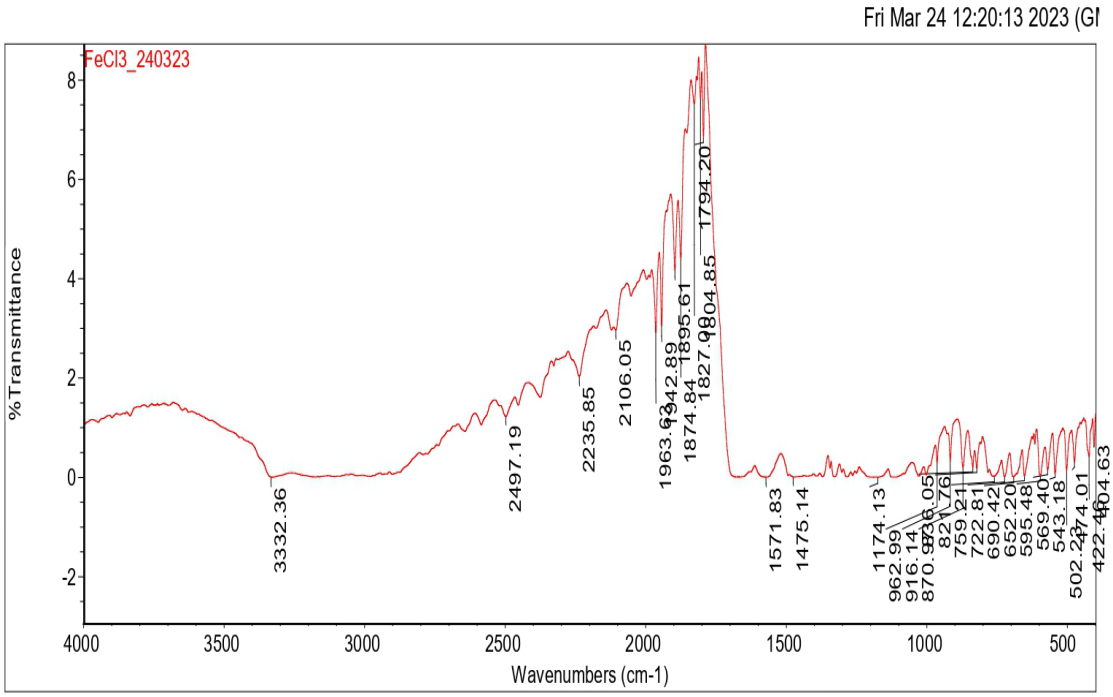
Fri Mar 24 12:55:23 2023 (GMT+05:30)
FIND PEAKS:
Spectrum: ZnCl2_240323
Region: 4000.00 400.00
Absolute threshold: 18.694
Sensitivity: 50
Peak list:

Position:	405.27	Intensity:	2.186
Position:	424.53	Intensity:	1.350
Position:	474.35	Intensity:	0.920
Position:	502.04	Intensity:	0.442
Position:	543.26	Intensity:	0.254
Position:	569.42	Intensity:	0.405
Position:	596.99	Intensity:	0.0826
Position:	651.91	Intensity:	0.0787
Position:	692.84	Intensity:	0.0209
Position:	722.79	Intensity:	0.0756
Position:	761.20	Intensity:	0.0673
Position:	821.86	Intensity:	0.513
Position:	836.15	Intensity:	0.549
Position:	870.95	Intensity:	0.547
Position:	916.07	Intensity:	0.817
Position:	1173.83	Intensity:	-0.0068
Position:	1464.79	Intensity:	0.0028
Position:	1575.55	Intensity:	-0.0047
Position:	1794.18	Intensity:	15.409
Position:	1804.85	Intensity:	16.996
Position:	1827.23	Intensity:	16.710
Position:	1874.86	Intensity:	10.571
Position:	1895.62	Intensity:	10.127
Position:	1942.88	Intensity:	7.713
Position:	1963.62	Intensity:	7.555
Position:	2106.18	Intensity:	7.544
Position:	2236.08	Intensity:	5.657
Position:	2497.24	Intensity:	3.872
Position:	3326.49	Intensity:	0.0088

- **$FeCl_3$**



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FIND PEAKS:
Spectrum: FeCl3_240323
Region: 4000.00 400.00
Absolute threshold: 8.694
Sensitivity: 50
Peak list:

Position:	404.63	Intensity:	0.628
Position:	422.46	Intensity:	0.417
Position:	474.01	Intensity:	0.299
Position:	502.23	Intensity:	0.137
Position:	543.18	Intensity:	0.0866
Position:	569.40	Intensity:	0.143
Position:	595.48	Intensity:	0.0312
Position:	652.20	Intensity:	0.0183
Position:	690.42	Intensity:	0.00092
Position:	722.81	Intensity:	0.0015
Position:	759.21	Intensity:	0.0125
Position:	821.76	Intensity:	0.174
Position:	836.05	Intensity:	0.187
Position:	870.97	Intensity:	0.191
Position:	916.14	Intensity:	0.330
Position:	962.99	Intensity:	0.282
Position:	1174.13	Intensity:	-0.0062
Position:	1475.14	Intensity:	-0.0013
Position:	1571.83	Intensity:	-0.0056
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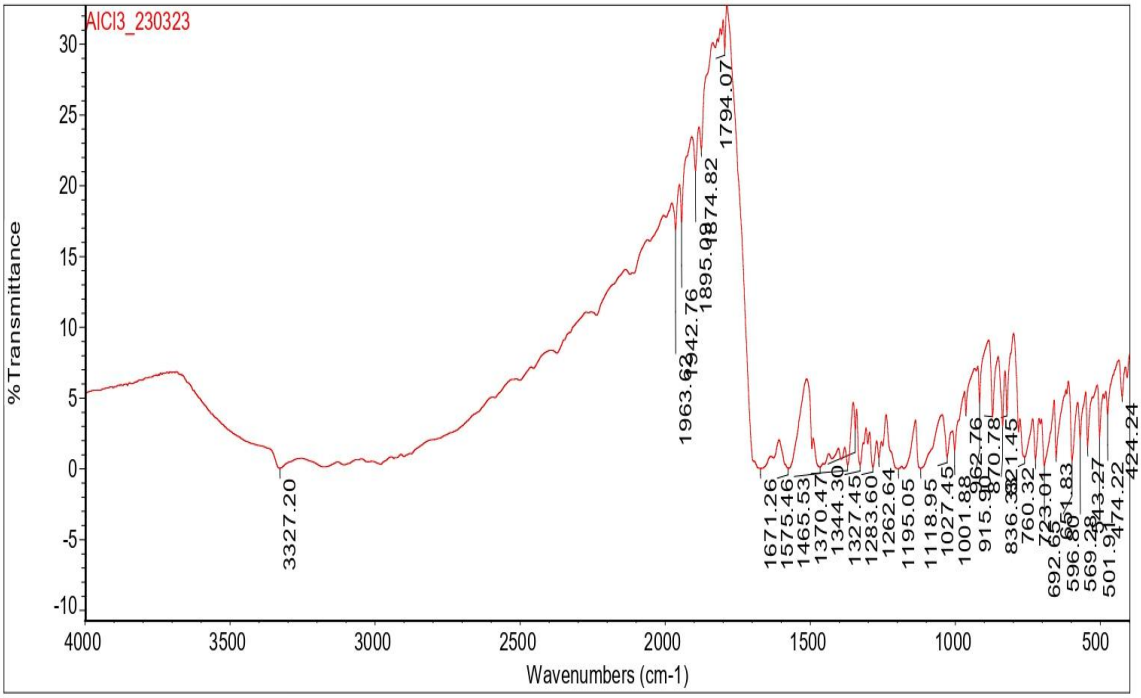
Position:	1804.85	Intensity:	7.629
Position:	1827.00	Intensity:	7.520
Position:	1874.84	Intensity:	4.388
Position:	1895.61	Intensity:	4.156
Position:	1942.89	Intensity:	3.045
Position:	1963.63	Intensity:	2.913
Position:	2106.05	Intensity:	2.956
Position:	2235.85	Intensity:	2.027
Position:	2497.19	Intensity:	1.217
Position:	3332.36	Intensity:	-0.0061

- ***AlCl***$_3$



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Thu Mar 23 14:56:48 2023 (GMT+05:30)
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Spectrum: AlCl3_230323
Region: 4000.00 400.00
Absolute threshold: 32.565
Sensitivity: 50
Peak list:

Position:	424.24	Intensity:	5.079
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Position:	543.27	Intensity:	1.577
Position:	569.28	Intensity:	2.176
Position:	596.80	Intensity:	0.610
Position:	651.83	Intensity:	0.774
Position:	692.65	Intensity:	0.229
Position:	723.01	Intensity:	0.677
Position:	760.32	Intensity:	0.787
Position:	821.45	Intensity:	3.921
Position:	836.33	Intensity:	2.953
Position:	870.78	Intensity:	3.683
Position:	915.90	Intensity:	4.688
Position:	962.76	Intensity:	3.881
Position:	1001.88	Intensity:	1.305
Position:	1027.45	Intensity:	0.815
Position:	1118.95	Intensity:	0.0116
Position:	1195.05	Intensity:	-0.0055
Position:	1262.64	Intensity:	0.771
Position:	1283.60	Intensity:	0.120
Position:	1327.45	Intensity:	0.269
Position:	1344.30	Intensity:	2.773
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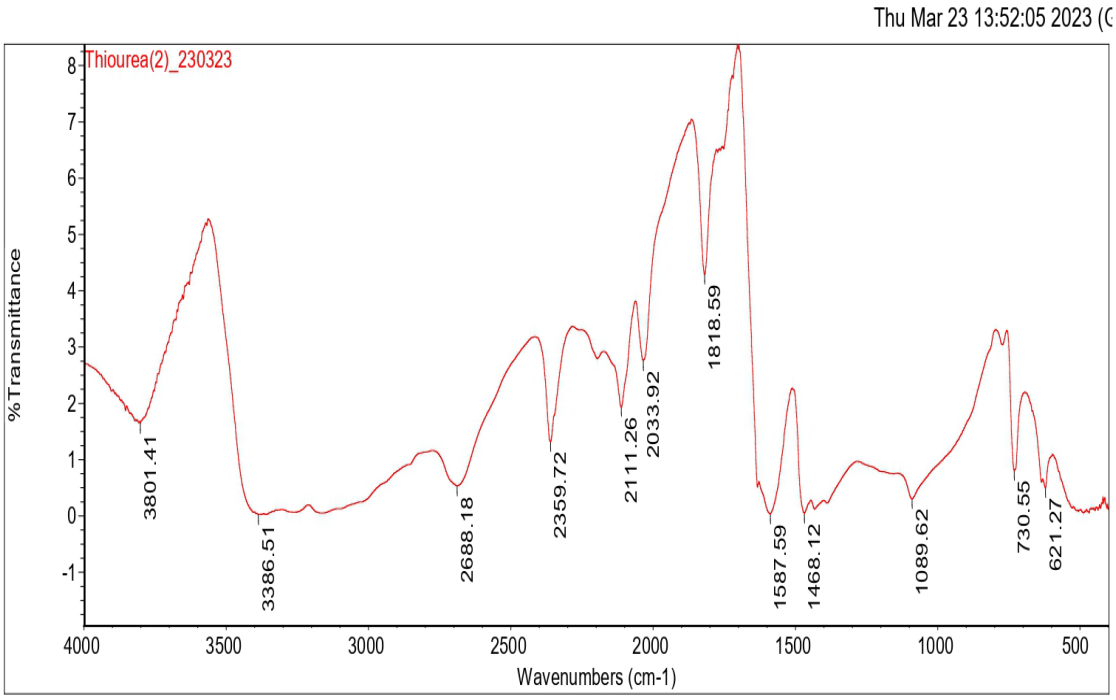
Position:	1465.53	Intensity:	0.0951
Position:	1575.46	Intensity:	0.0142
Position:	1671.26	Intensity:	-0.0048
Position:	1794.07	Intensity:	29.620
Position:	1874.82	Intensity:	22.555
Position:	1895.09	Intensity:	21.015
Position:	1942.76	Intensity:	17.408
Position:	1963.62	Intensity:	16.899
Position:	3327.20	Intensity:	0.0171

- **Thiourea**



Collection time: Thu Mar 23 13:50:47 2023 (GMT+0

Thu Mar 23 13:51:20 2023 (GMT+05:30)
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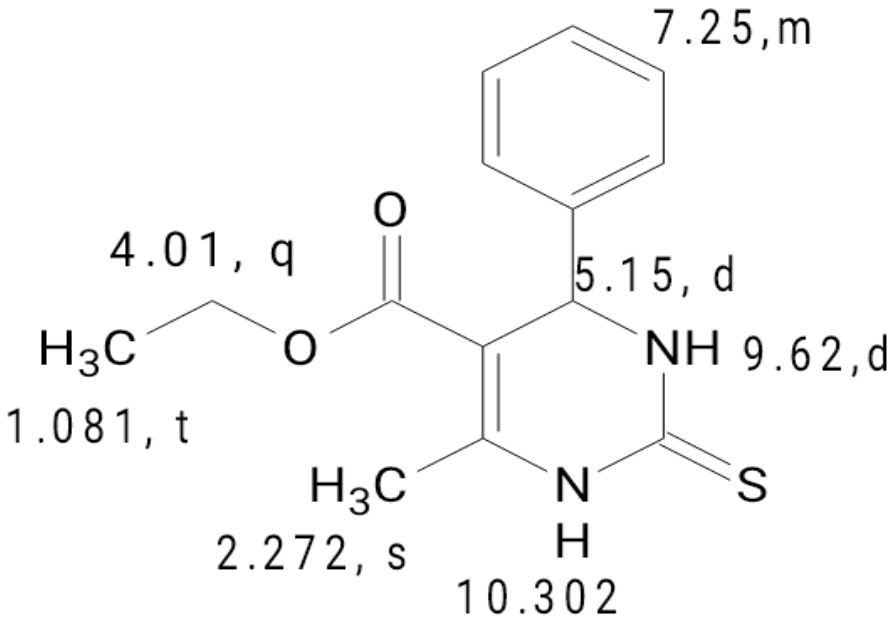
Spectrum: Thiourea(2)_230323
Region: 4000.00 400.00
Absolute threshold: 8.363
Sensitivity: 50
Peak list:

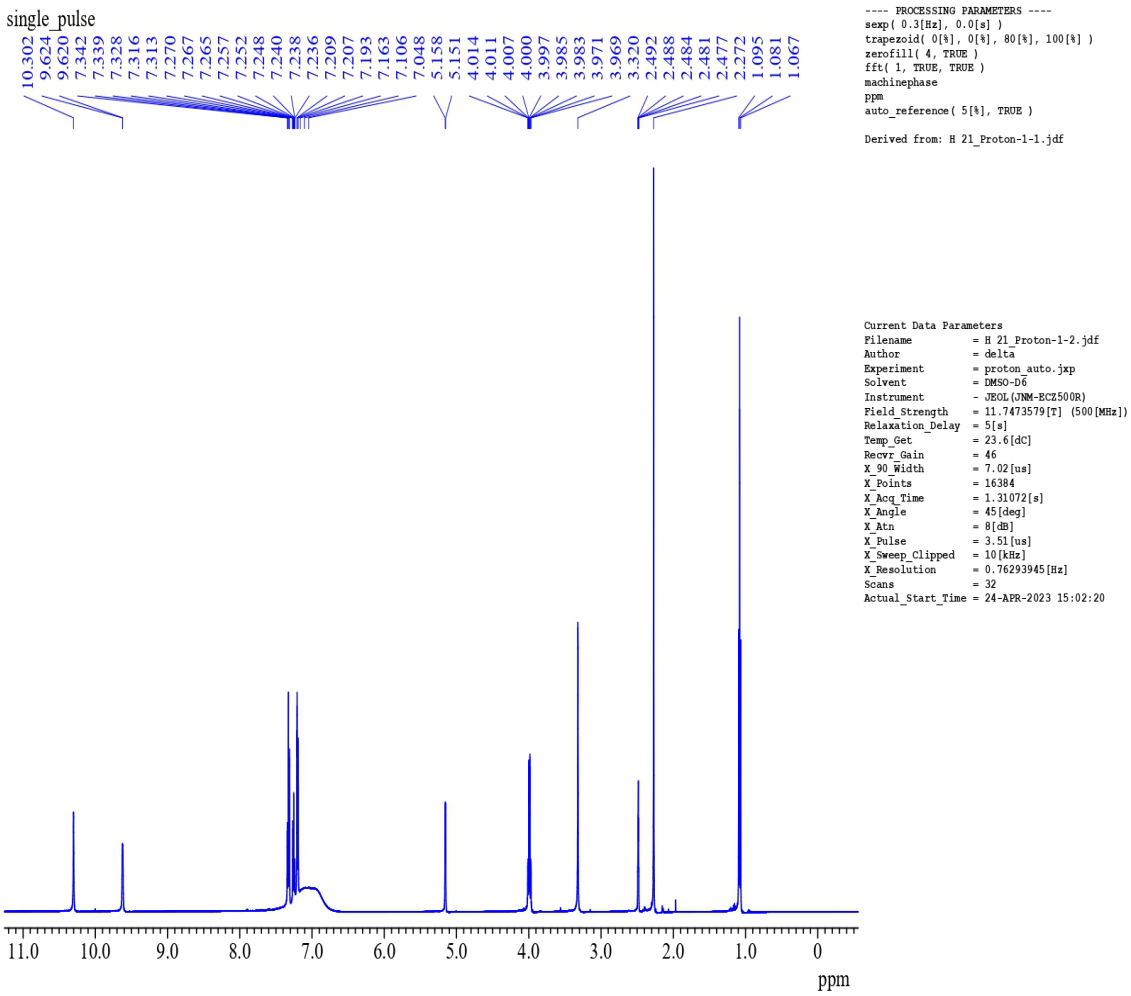
Position:	621.27	Intensity:	0.488
Position:	730.55	Intensity:	0.800
Position:	1089.62	Intensity:	0.296
Position:	1468.12	Intensity:	0.0450
Position:	1587.59	Intensity:	0.0306
Position:	1818.59	Intensity:	4.284
Position:	2033.92	Intensity:	2.757
Position:	2111.26	Intensity:	1.921
Position:	2359.72	Intensity:	1.307
Position:	2688.18	Intensity:	0.529
Position:	3386.51	Intensity:	0.0165
Position:	3801.41	Intensity:	1.644

NMR SPECTRUM

The study's 1H-NMR spectrum, which was captured in DMSO at room temperature, supports the inferences made from the IR spectra. The NMR spectrum confirmed the presence of the formation of the compound. The peaks in the NMR are 1.081 (3H, t), 2.272 (s,3H), 2.484(5nos, 2H), 4.01(q, 2H), 5.158 and 5.151(doublet), 7.25(m,5H), 9.624 and 9.20 (d, 1H) and 10.302. The peaks were identified as:



- **HCl**


single_pulse
10.302
9.624
9.620
7.342
7.339
7.328
7.316
7.313
7.270
7.267
7.265
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7.252
7.248
7.240
7.238
7.236
7.209
7.207
7.193
7.163
7.106
7.048
5.158
5.151
4.014
4.011
4.007
4.000
3.997
3.985
3.983
3.971
3.969
3.320
2.492
2.488
2.484
2.481
2.477
2.272
1.095
1.081
1.067
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sexp(0.3[Hz], 0.0[s])
trapezoid(0[%], 0[%], 80[%], 100[%])
zerofill(4, TRUE)
fft(1, TRUE, TRUE)
machinephase
ppm
auto_reference(5[%], TRUE)
Derived from: H 21_Proton-1-1.jdf
Current Data Parameters
Filename = H 21_Proton-1-2.jdf
Author = delta
Experiment = proton_auto.jxp
Solvent = DMSO-D6
Instrument - JEOL(JNM-ECZ500R)
Field_Strength = 11.7473579[T] (500[MHz])
Relaxation_Delay = 5[s]
Temp_Get = 23.6[dC]
Recvr_Gain = 46
X_90_Width = 7.02[us]
X_Points = 16384
X_Acq_Time = 1.31072[s]
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X_Atn = 8[dB]
X_Pulse = 3.51[us]
X_Sweep_Clipped = 10[kHz]
X_Resolution = 0.76293945[Hz]
Scans = 32
Actual_Start_Time = 24-APR-2023 15:02:20
11.0
10.0
9.0
8.0
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4.0
3.0
2.0
1.0
0
ppm

CHAPTER 4

4.1 CONCLUSION

1. The Biginelli reaction between Benzaldehyde, ethylacetoacetate and thiourea was found to be catalysed by Lewis acids.
2. The reaction was done with five different Lewis acid catalysts.
3. Of all the catalysts, $AlCl_3$ was found to be the best.
4. Of the three transition metal catalyst tried, $FeCl_3$ was found to be more efficient than $ZnCl_2$ and $MnCl_2$.
5. The use of $FeCl_3$ as a catalyst gave the highest yield of the product.
6. IR and NMR data confirm the formation of Biginelli adduct.

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