SYNTHESIS, CHARACTERIZATION & BIOLOGICAL EVALUATION OF SOME NOVEL 1, 3, 4-OXADIAZOLE DERIVATIVES

Dissertation submitted to

THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY

CHENNAI - 600 032

In partial fulfillment of the requirements for the award of the Degree of

MASTER OF PHARMACY

IN

PHARMACEUTICAL CHEMISTRY

Submitted by

Reg No: 261715351

(A.V.ABIRAMI)

Under the guidance of

Mr. V.RAJAMANICKAM M.Pharm.,

DEPARTMENT OF PHARMACEUTICAL CHEMISTRY

ARULMIGU KALASALINGAM COLLEGE OF PHARMACY

ANAND NAGAR, KRISHNANKOIL-626126

Nov 2019

CERTIFICATE

This is to certify that the investigation described in this dissertation entitled "**SYNTHESIS, CHARACTERIZATION & BIOLOGICAL EVALUATION OF SOME NOVEL 1, 3, 4- OXADIAZOLE DERIVATIVES"** submitted by **Reg. No: 261715351 (A.V.ABIRAMI)** for the award of Master of Pharmacy degree comprises of the bonafide work done by her in the Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, Krishnankoil. Their work was supervised by **Mr.V.RAJAMANICKAM, M.Pharm** associate professor, Department of Pharmaceutical chemistry, Arulmigu Kalasalingam College of Pharmacy, Anand Nagar, Krishnankoil.

I recommend this thesis work for acceptance as project for partial fulfillment of the degree of **"MASTER OF PHARMACY IN PHARMACEUTICAL CHEMISTRY"** of the Tamilnadu Dr.M.G.R .Medical University, Chennai.

Place: Krishnankoil

Date:

Dr. N. VENKATESHAN, M.Pharm., Ph.D.,
Principal,
Arulmigu Kalasalingam College of Pharmacy,
Anand Nagar, Krishnankoil- 626126.

CERTIFICATE

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Place: Krishnankoil

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Associate professor,

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Anand Nagar, Krishnankoil - 626126.

EVALUATION CERTIFICATE

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Centre: Arulmigu Kalasalingam College of Pharmacy, Krishnankoil

Date:

Examiners: 1.

2.

DECLARATION

I **A.V.ABIRAMI (Reg No:261715351),** hereby declare that the dissertation work entitled **"SYNTHESIS, CHARACTERIZATION & BIOLOGICAL EVALUATION OF SOME NOVEL 1, 3, 4 - OXADIAZOLE DERIVATIVES"** submitted by me, in partial fulfillment of the requirement for the degree of **MASTER OF PHARMACY in PHARMACEUTICAL CHEMISTRY** to The TamilNadu Dr.M.G.R Medical University, Chennai is the result of my original and dependent research work carried out under the guidance and supervision of **Mr. V. RAJAMANICKAM, M.Pharm.,** during academic year 2018-2019 and this has not formed the basis for the award of any degree/Diploma/Fellowship or similar title to any candidate of any university.

Place: Krishnankoil

Date:

Ms.A.V.ABIRAMI

(Reg No: 261715351)

Department of pharmaceutical chemistry

Arulmigu Kalasalingam College of Pharmacy

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First of all, I thank **God** for planning this project and continue showering his grace and blessings till the end. This project was undertaken with guidance, Co-operation and assistance of distinguished persons cited below who have contributed towards the successful completion of this project work.

I express my deep sense of gratitude to my guide **V.Rajamanickam, M.Pharm.,** who contributed a lot for this project and who pulled out of problems whenever the tight corners are around,Asst associate professor, Arulmigu Kalasalingam College of Pharmacy, KrishnanKoil, for his guidance, valuable suggestions and instinctive support rendered during this project.

I would like to express our thanks to the founder of our institution **Kalvivallal Thiru T. Kalasalingam, B. Com.,** for providing us necessary infrastructure and complete my project successfully.

I express my sincere gratitude to our beloved principal **Dr. N. Venkateshan M.Pharm Ph.D**, Principal and Head, Department of Pharmaceutical Chemistry, Arulmigu Kalasalingam College of Pharmacy, for his valuable advice and providing us the permission and required laboratory facilities for materializing for my project work.

I sincerely thanks to our librarian **Mr.Lakshmanagurusamy** and **Abdhulkadhar** for his all time co-operative for referring library beyond the times am all conditions. I thanks to our, **Mr. Ganeshan** and other lab assistants help in our experiment work. We wish to express our thanks and gratitude to our **staff members** and friends of "**Arulmigu Kalasalingam College of Pharmacy**" for having helped us so generously with their valuable and constructive suggestions to improve the project and provide steady support.

With deep sense of veneration and gratitude I dedicated all my work to my beloved **parents, sister and my friend** who made me genius in field of education and allowed me to do post graduation in pharmacy in adverse condition with love & affection. It would be long list of friends to be thanked, but I am really gratifying to all them, especially **classmates** for standing behind me at all time.

CONTENTS

INTRODUCTION

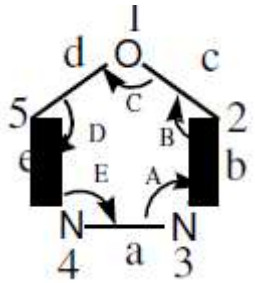
Heterocyclic compounds are also called as heterocycle. These are the class of organic chemical compounds deals with the synthesis, properties and application of heterocycles. These are identified by some or all the atoms in a molecule are joined to ring containing one atom of element other than carbon. In Greek hetero meaning different (non-carbon atom).It resembles cyclic organic compounds that has only carbon atoms in rings E.g.cyclopropane.

Heterocyclic compound include many biochemical material essential for life. E.g. Nucleic acid (consisting of long chains of hetero units with other type of materials).Naturally occurring heterocyclic compound are pigments, vitamins, antibiotics. Synthetic heterocycles are used for drugs, pesticides, dyes & plastics.[1]Classification is based on electronic structure .Usually heterocyclic compound are those having 5 or 6 membered rings & containing hetero atoms of Nitrogen(N),Oxygen(O),Sulfur(S).E.g. pyridine, pyrrole, furan & thiophene. oxadiazole is a heterocyclic aromatic chemical compound of azole family with molecular formula $C_2H_2N_2O$.

There are 4 isomers of oxadiazole namely,

1) 1,2,3 oxadiazole
2) 1,2,4 oxadiazole
3) 1,2,5 oxadiazole
4) 1,3,4 oxadiazole

In which we are going to see in brief about 1, 3, 4 oxadiazole,



1, 3, 4 oxadiazole is a 5membered aromatic ring containing one oxygen & 2 Nitrogen atoms seen in many synthetic molecules. Structural feature of 1, 3, 4

oxadiazole ring with pyridine type of Nitrogen atom is effective for its derivatives in binding with different enzymes.1, 3, 4 Oxadiazole with therapeutic potency are used to treat different ailments & entire medicinal chemistry such as anticancer , antifungal , antibacterial , anti tubercular ,anti inflammatory ,anti neuropathic ,anti hypertensive ,anti viral ,anti histaminic ,anti parasitic, anti obesity & other medicinal agents. Oxadiazole is an resultant from furan in which 2 methane groups is replaced by 2 pyridine type of Nitrogen atoms.[2]Reaction of acid hydrazides with acid chlorides are the most commonly used synthetic route for synthetics of 1, 3, 4 oxadiazole. Usually substituted aromatic acids are used as a starting material in 1, 3, 4 oxadiazole synthesis resulting in formation of corresponding esters and hydrazides. Ethyl ester is synthesized by Fischer esterification which further reacted with hydrazine hydrate in presence of ethanol to get hydrazide derivative.[3]

Anti-nociceptive is also called as painkiller causing relief from pain. They act on peripheral & CNS .Anti-nociceptive includes paracetamol. The NSAID such as salicylates, opioid drugs morphine & oxycodone choice of anti-nociceptive is based on the type of pain. For neuropathic pain traditional anti-nociceptive are not so effective. Topical NSAIDs provide muscle sprain relief and side effects are lesser. Based on the type of anti-nociceptive has the individual side effects these are classified based on their MOA. Paracetamol also called as an acetaminophen used to treat pain and fever. It's a combination of opioid and pain medication, paracetamol are nowadays used to treat severe pain like cancer pain and after surgery, used either by mouth (or) rectally also available intravenously and effective between 2-4 hrs. Lower doses decrease pain and lower fever and higher doses decreases inflammation for example Aspirin, Ibuprofen & naproxen. They are used in combination such as paracetamol and codeine psychotropic anti-nociceptive agents are Ketamine, clonidine and mexiletine. Certain drugs like nefopam, orphenadrine, pregabalin, cyclobenzaprine, and hyoscine are used along with anti-nociceptives to modify the opioid action when used specifically against neuropathic pain. Dexromethorphan exert additional analgesia effect and on NMDA receptors and slowing down development of tolerance to opioids.

Inflammation is a process in WBC and substances protect us from, infection from foreign organisms like bacteria and viruses usually inflammation is a response (i.e.) defense mechanism. MOA is to localize and eliminate the injurious agent,

removing damaged tissues so that the body begins to heal. Inflammation process are, vascular stasis: (i.e.) slowing of blood in the blood stream, based on the intensity and duration inflammation is mainly of 3 stages,

1. Acute – swelling stage
2. Sub acute – regenerative stage
3. Chronic – scar tissue maturation and remodeling stage.

Epilepsy may be neurological disease within which clusters of nerve cells, or neurons, within the brain typically signal abnormally. Neurons usually generate chemical science impulses that act on alternative neurons, glands, and muscles to supply human thoughts, feelings, and actions. In the neurological disorder, the normal pattern of neuronal activity becomes disturbed, causing strange sensations, emotions, and behavior, or sometimes convulsions, muscle spasms, and loss of consciousness.

For concerning eighty percent of these diagnosed with brain disorder, seizures can be controlled with modern medicines and surgical techniques. Having a seizure doesn't essentially mean that an individual has encephalopathy. Epilepsy isn't contagious and isn't caused by psychological state or sub normality. Some folks with sub normality might expertise seizures, however seizures don't essentially mean the person has or can develop mental impairment. Seizures typically do cause brain injury, significantly if they're severe.

However, most seizures don't appear to own a damaging result on the brain. Any changes that do occur are usually subtle, and it is often unclear whether these changes are caused by the seizures, themselves or by the underlying problem that caused the seizures. While encephalopathy cannot presently be cured, for a few folks it will eventually escape. This is a lot of possible if the encephalopathy has been well-controlled by medication or if the person has had encephalopathy surgery. Epilepsy is a disorder with many possible causes. Anything that disturbs the conventional pattern of nerve cell activity from health problem to brain injury to abnormal brain development will cause seizures.

Epilepsy would possibly develop due to Associate in Nursing abnormality in brain wiring, an imbalance of nerve signal chemicals referred to as neurotransmitters, or some combination of these factors One of the most-studied neurotransmitters that play a task in encephalopathy is amino acid, or gamma-amino butyric acid which is an inhibitory neurotransmitter. Research on amino acid has semiconductor diode to medicine that alters the quantity of this neurochemical within the brain or amendment, however, the brain responds to that. Researchers are also finding out excitation neurotransmitters like salt. In some cases, the brain's attempts to repair itself after a head injury, stroke, or other problem may inadvertently generate abnormal nerve connections that lead to epilepsy. Abnormalities in brain wiring that occurs throughout brain development additionally might disturb neural activity and cause encephalopathy.

Research has shown that the cell wall that surrounds every nerve cell plays a vital role in encephalopathy. The cell membranes were crucial for a nerve cell to come up with electrical impulses. For this reason, researchers are finding out details of the membrane structure, however molecules move in and out of membranes, and the way the cell nourishes and repairs the membrane. A disruption in any of those processes might cause encephalopathy. Studies in animals have shown that, as a result of the brain regularly adapts to changes in stimuli, a little amendment in neural activity, if repeated, may eventually lead to full-blown epilepsy.

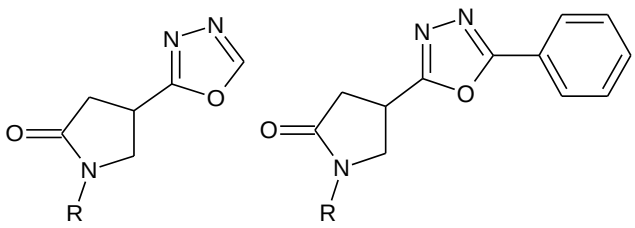
A chemical substance made by microorganism which has the ability to destroy or inhibit the growth of bacteria, fungi, viruses or protozoa. It has a high chemotherapeutical index to reduce the active process in organism in a diluted solution. Anti-microbial medicines are grouped according to the micro-organisms they act primarily against. They are classified according to their function. Agents that kill microbes are microbicidal whereas inhibit there are biostatic. This anti-microbial include antibacterial, antifungal, antiviral, antiparasitics. Wide ranges of natural & chemical compounds are also used as antimicrobials. The rapid rise in bacterial resistance to the traditional antibiotic such as penicillin& tetra cycline has been a key thing to continue search for new classes of compounds with novel modes of antimicrobial activity. The oxadiazoles have emerged as anti microbial agents of much interest because of their broad spectrum of in vitro activity & there in vivo chemotherapeutic activity.

The terminology anthelmintic is invariably meant for such drugs exerting their action locally to expel parasites from the GI tract exclusively. Nevertheless, there exists several varieties of *worms* which are able to penetrate other tissues as well ; therefore, the 'drugs' that predominantly act on these parasitic infections are frequently termed as anthelmintics. At this juncture one may come across *two* more terminologies, the 'drugs' that solely kill worms are called vermicides & the 'drugs' that specifically affect the worm in such a fashion that either the peristaltic activity or catharsis expels it from the intestinal tract are commonly known as vermifuges. Importantly, such absolute arbitrary categorization actually affords no useful and gainful objective as a host of anthelmintic has been recognized that particularly manifest both actions equally, as per the strength of dosages employed. Therefore, in a broader sense and perspective the anthelmintics are defined more appropriately as drugs used to combat any type of helminthiasis[4].

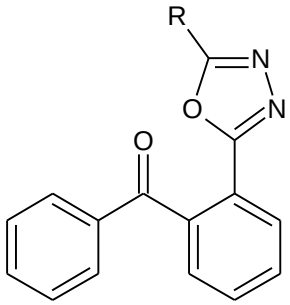
LITERATURE REVIEW

AS AN ANTI-MICROBIAL AGENTS

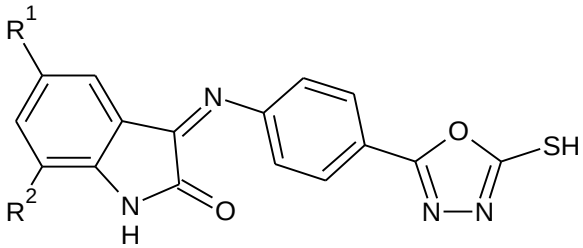
- V.mickevicius et al., [84] synthesized substituted 1, 3, 4-oxadiazole derivatives and screened for antimicrobial activity.



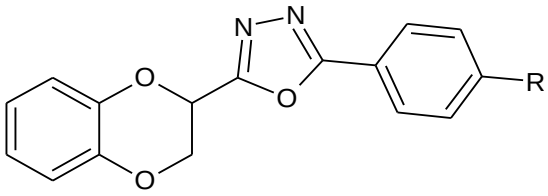
- Suman bala et al., [80] synthesized 1, 3, 4-oxadiazole derivatives screened for antimicrobial potential activity.



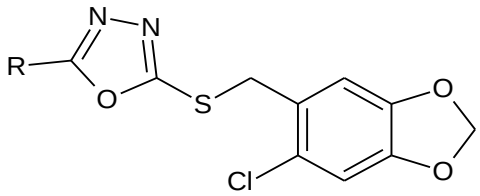
- Vishal Modi et al., [77] synthesized a novel achiral and chiral amides incorporating 1, 3, 4-oxadiazole ring and screened for anti microbial activity.



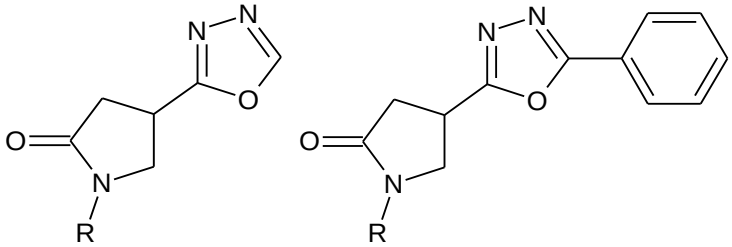
- Habibullah khalilullah et al., [78] synthesized a series of 1, 3, 4 oxadiazole containing 1, 4-benzodiaoxane ring system and evaluated antibacterial & anti fungal activities.



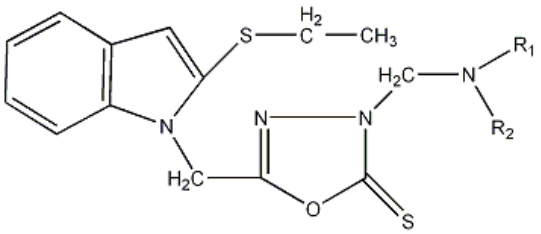
- Aziz-ur-Rehman et al., [74] synthesized some new 5-substituted-2-((6-chloro-3, 4-methylene dioxyphenyl) methyl thio-1, 3, 4-oxadiazole derivatives for bacterial inhibiting activity.



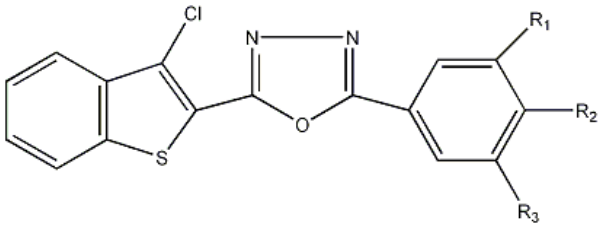
- V.mickevicius et al., [84] synthesized substituted 1, 3, 4-oxadiazole derivatives and screened for herbicidal activity.



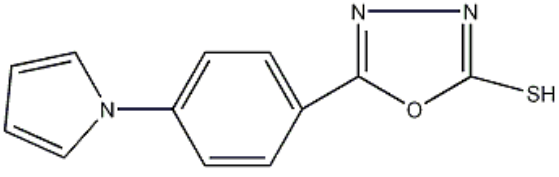
- R.R. Somani et al., [5] Synthesized and antimicrobial activity of some newer mannich bases.



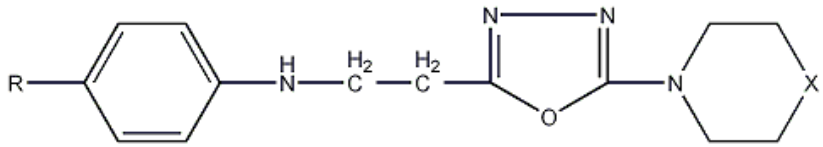
- Basavaraj Padmashali et al., [6] Synthesized and antimicrobial investigation of benzo (b) thiophen heterocycles.



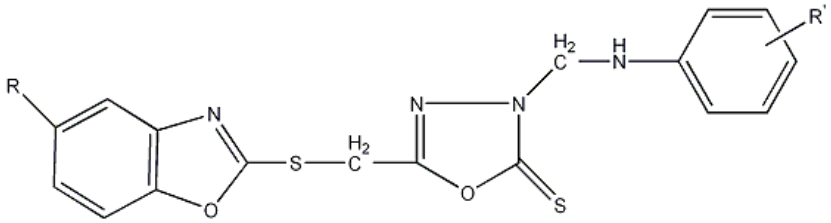
- H.M. Vagdevi et al., [7] synthesized some new pyrrole derivatives as potential antimicrobial and ant tubercular agents.



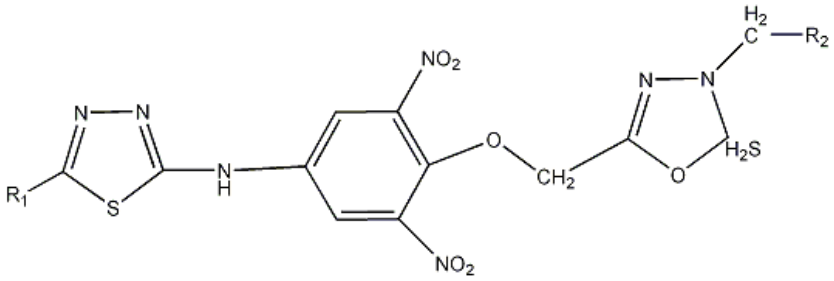
- K.R. Alaguwadi et al., [8] synthesized and antimicrobial evaluation of some 2-5 substituted oxadiazoles.



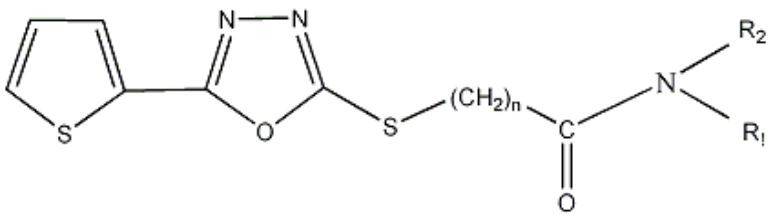
- H.M.Vagdevi et al., [9] synthesized and antimicrobial activity of some 1, 3, 4 oxadiazole incorporated benzoxazoles.



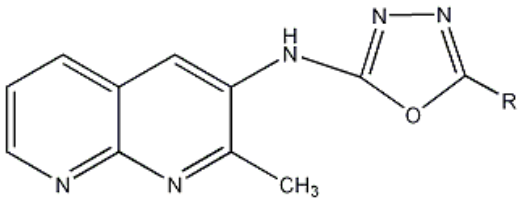
- Varrtika Rustagi et al., [10] Synthesized and evaluated the anti-microbial activity of some 5" -aryl substituted / N-benzoyl methylamino-2" - [{2', 6' - dinitro-4' - (5-alkyl-1, 3, 4-thiadiazole-2-yl)-amino}-phenoxy methyl] incorporated -1, 3, 4-oxadiazoles, 1, 3, 4 -oxadiazoline-5" -thiones and their mannich bases.



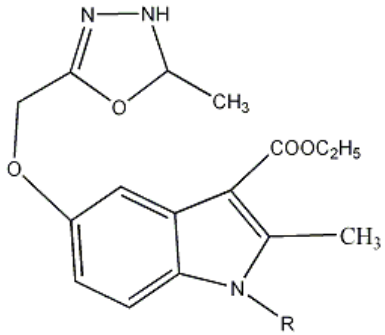
- I.M. Khazi et al., [11] Reported the synthesized and anti-microbial activity of some 2-(N-substituted carboxamido methyl/ethyl thio)-5-(2'-thienyl)-1, 3, 4-oxadiazoles.



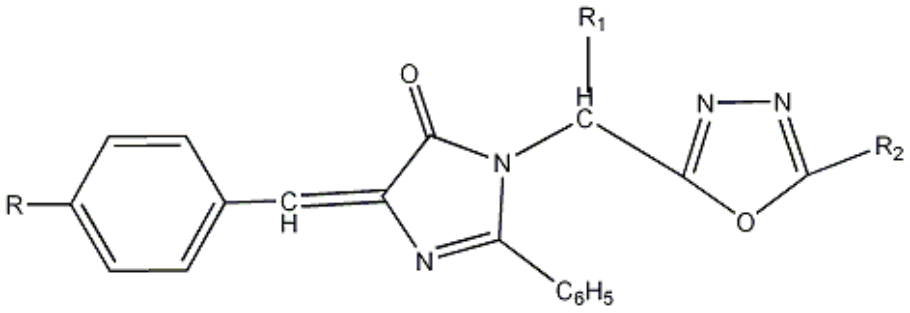
- D. Ramesh et al., [12] Synthesized and evaluated the anti-microbial activity of 2-methyl-3-(5'-aryl/aryloxymethyl-1', 3', 4'-oxadiazol-2'-yl) amino-1, 8-naphthyridines.



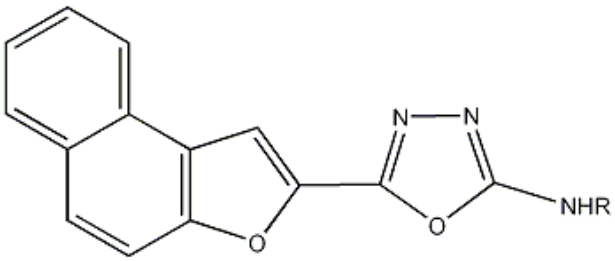
- G. Manjunath et al., [13] Reported the synthesized and anti-microbial activity of some new 1-substituted -2-methyl-3-ethoxy carbonyl-5-(1,2,3,4-tetrazolyl) / (1, 3, 4-oxadiazolyl) / 1,3,5-triazinyl) methoxy indoles.



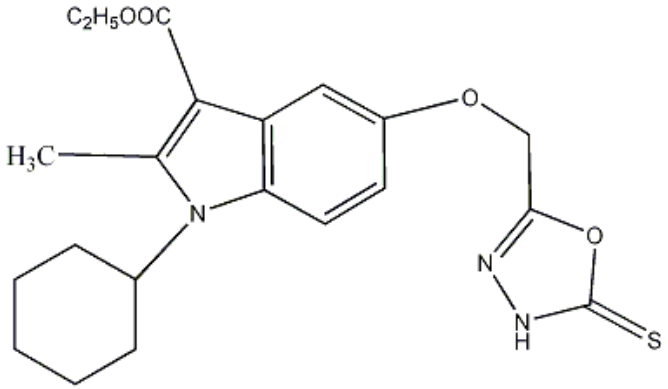
- Sangeeta Rajpurohit et al., [14] Reported the synthesized and anti-microbial activity of 5-aryl substituted - (4-benzylidine-4, 5-dihydro-5-oxo-1-(H)-imidazolo)-1, 3, 4-oxadiazoles.



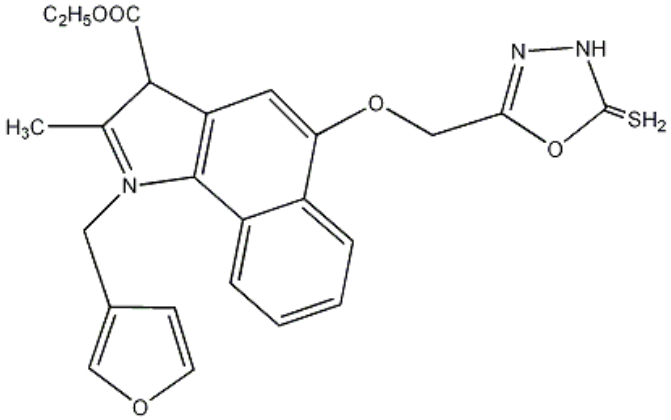
- K.C. Ravindra et al., [15] Reported the synthesized and anti-microbial activity of substituted bi heterocycles of oxadiazoles, thiadiazoles and triazoles involving naphtho [2, 1-b] furan.



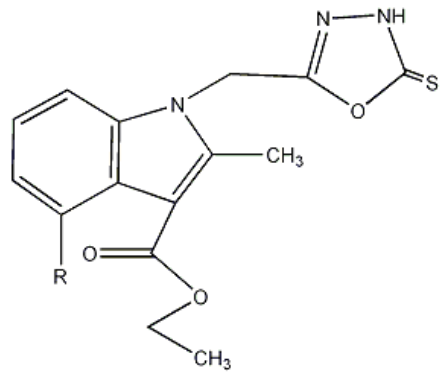
- S. Guru et al., [16] reported the synthesized and anti-microbial activity of some new 1-cyclohexyl-3-carbethoxy-2-methyl-5-oxadiazolyl and pyrrolyl amino carbonyl methoxy indoles.



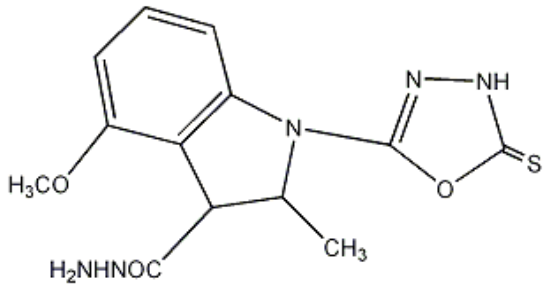
- Dundappa S Dona wade et al., [17] reported the synthesized and anti-microbial activity of some new triheterocycles-5-pyrrolyl amino carbonyl / mercapto oxadiazolyl / derivatives.



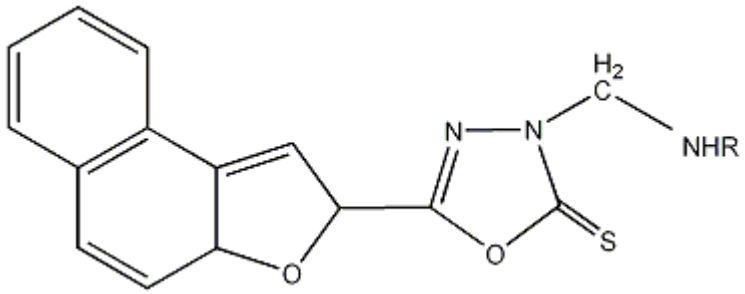
- Manjunath G Bhovi et al., [18] reported the synthesized and anti-microbial activity of some new 2-methyl-3-ethoxy carbonyl-1-oxadiazolyl methyl indoles.



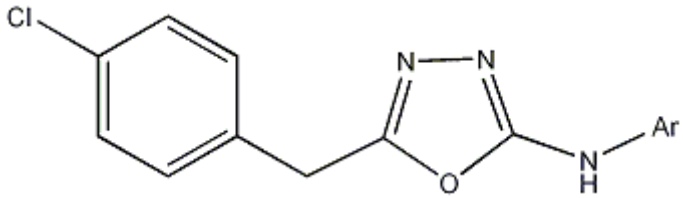
- Dundappa S Donawade et al., [19] reported the synthesized and anti-microbial activity of some new 1-substituted-3-pyrrolyl amino carbonyl oxadiazolyl 5-methoxy-2-methyl indoles.



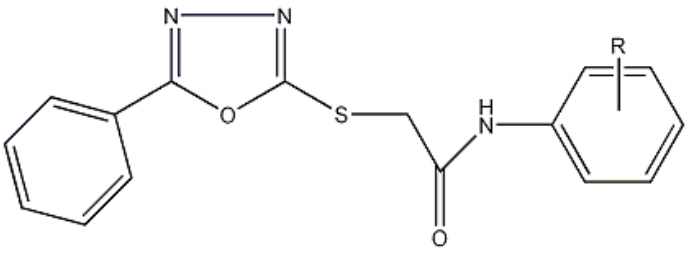
- K.C. Ravindra et al., [20] Synthesized and evaluated anti-microbial anti-inflammatory activities of 1, 3, 4-oxadiazoles linked to naphtho [2, 1-b] furan.



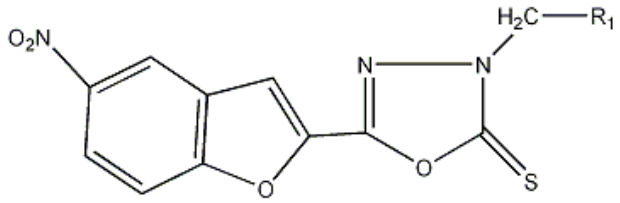
- N C Desai et al., [21] synthesized and QSAR studies of thio semi carbazides, 1, 2, 4-triazoles, 1, 3, 4-thiadiazoles and 1, 3, 4-oxadiazoles derivatives as potential antibacterial agents.



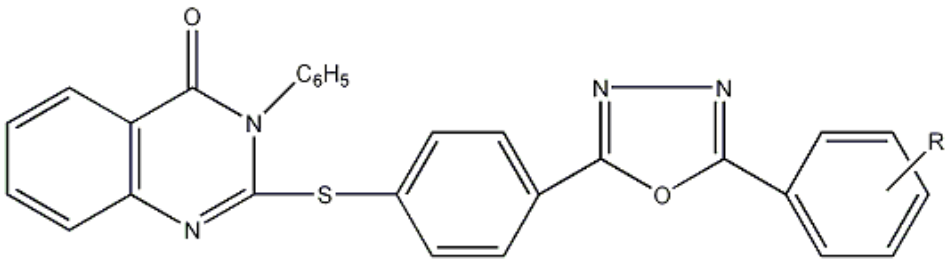
- S. Rajasekaran et al., [22] Microwave assisted synthesized of some 5-phenyl-2-[(N-substituted phenyl) thioacetamido]-1, 3, 4-oxadiazoles as antibacterial and antioxidant agents.



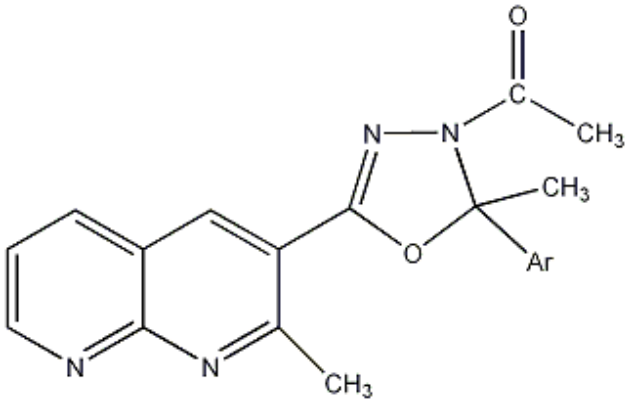
- Raddhi Madhu et al., [23] synthesized and antibacterial activities of some new 5-substituted benzoturans.



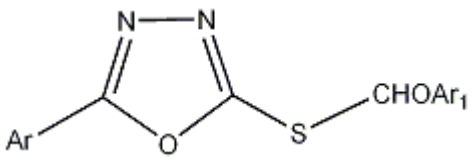
- Pramilla Sah et al., [24] synthesized and antibacterial activity of some 2-mercapto-3-phenyl 4-oxa (3H)-quinazolinyl substituted 1, 3, 4 oxadiazoles.



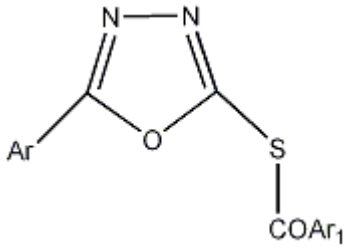
- K. Mogilaiah et al., [25] reported the synthesized and anti-bacterial activity of 1, 3, 4-oxadiazole and pyrozoline derivatives containing 1, 8-naphthyridine moiety.



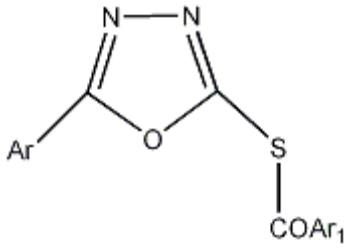
- Sandeep Jain et al., [26] reported the synthesized and anti-bacterial activity of 5-aryl-2-acyl thio-1, 3, 4-oxadiazoles.



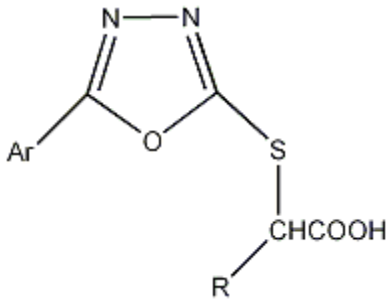
- Sandeep Jain et al., [27] synthesized some novel 5-aryl-2-acyl thio-1, 3, 4-oxadiazoles and evaluated their anti-bacterial activity.



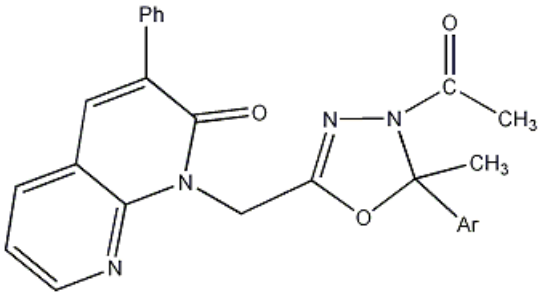
- Dharam Pal Pathak et al., [28] performed the synthesized and anti-bacterial activity of 5-aryl-1, 3, 4-oxadiazole-2-thioalkanoic acids.



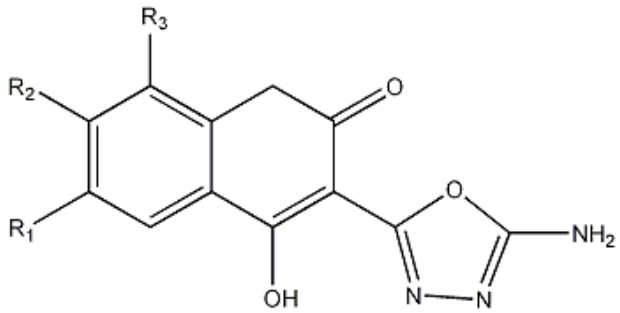
- Dharam Pal Pathak et al., [29] performed the synthesized some 5-aryl-1, 3, 4-oxadiazole-2-thiocarboxylic acids and evaluated their anti-bacterial activity.



- K. Mogilaiah et al., [30] synthesized and reported the anti-bacterial activity of 1, 3, 4-oxadiazolyl-1, 8-naphthyridines.

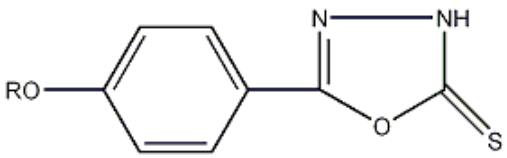


- V.V. Mulwad et al., [31] synthesized and evaluated anti-bacterial activity of new oxadiazolo [1, 3, 5]-triazine, 1, 2, 4-triazolo and thiadiazolo 1, 3, 4-oxadiazole derivatives.

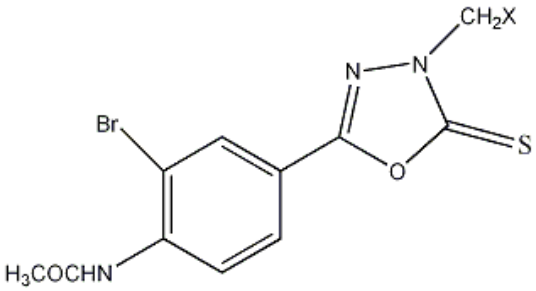


AS AN ANTI-FUNGAL AGENTS

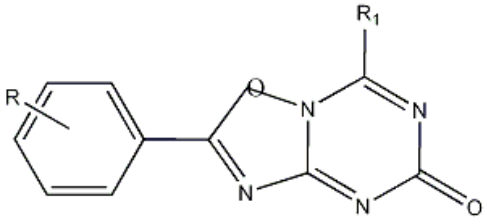
- Nisheeth Rastogi et al., [32] synthesized of 2-{4'-(3"-chlorobenzyloxy)-phenyl} 1, 3, 4 oxadiazolin-5-thione, 3-{4'-(3"-chlorobenzyloxy)-phenyl} -4-phenyl-1, 2, 4-triazolin-5-thione and their derivatives as potential antileishmanial agents.



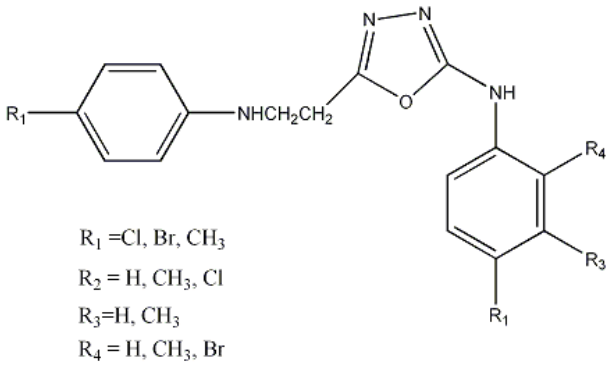
- R.S. Varma et al., [33] synthesized and reported anti-leishmanial activity of 4-substituted amino methyl-2-(4'-acetyl amino-3' -bromophenyl)-1, 3, 4-oxadiazolin-5-thiones.



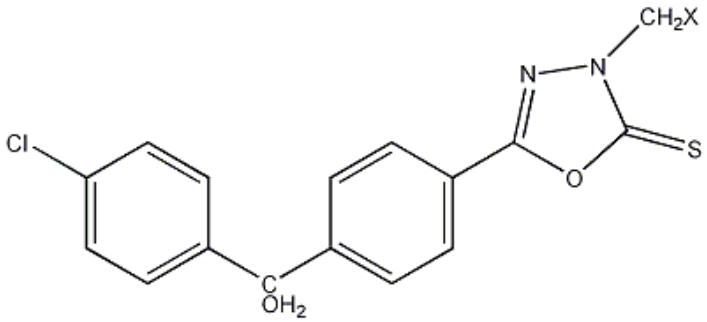
- Dharm Veer Singh et al., [34] reported the synthesized and anti-fungal activity of new 1, 3, 4-oxadiazolo[3,2-b]-S-triazine-5-ones and their thione analogues.



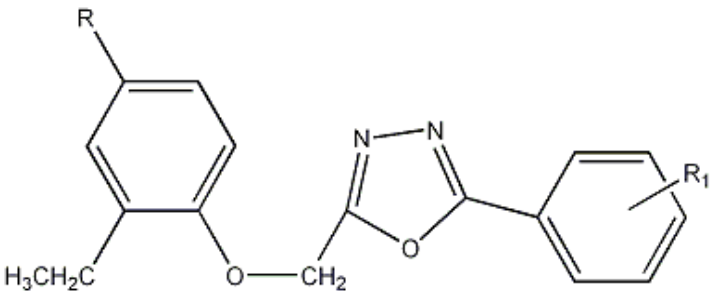
- Mohd. Afroz Bakht et al., [35] prepared and evaluated anti-fungal activity of some new 1, 3, 4-oxadiazoles.



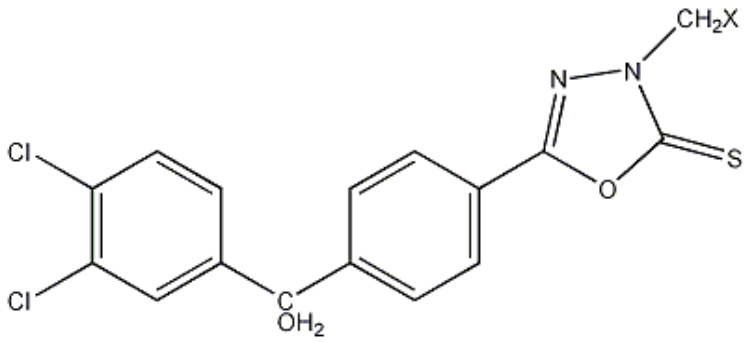
- Nisheeth Rastogi et al., [36] synthesized and reported anti-leishmanial activity of 4-aminomethyl-2-{4'-(4''-chlorobenzyloxy)-phenyl}-1, 3, 4-oxadiazolin-5-thiones.



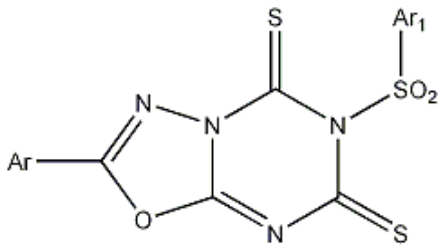
- R.P. Singh et al., [37] synthesized and reported anti-fungal activity of new oxadiazoles.



- Nisheeth Rastogi et al., [38] synthesized and reported anti-leishmanial activity of 2-{4'-(2"4"-dichlorobenzyloxy)-phenyl}-1, 3, 4-oxadiazolin-5-thiones.

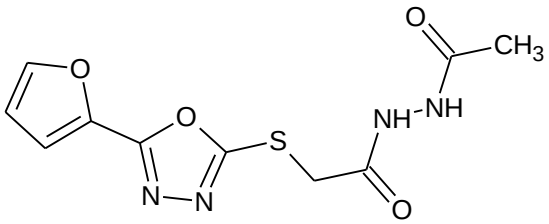


- Dayashankar Tripathi et al., [39] synthesized some new fungi toxic 2-aryl-1, 3, 4-oxadiazolo [3, 2-a]-S-triazine-5, 7-dithiones and their 6-aryl sulphonyl derivatives.

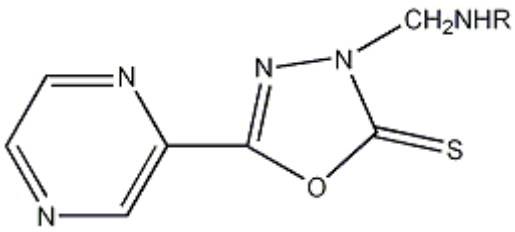


AS AN ANTI-TUBERCULOSIS AGENTS

- A.M.Comrie et al., [85] synthesized α-(5-(2-furyl-1, 3, 4-oxadiazol-2-yl-thio)acetohydrazide and related compound and evaluated for anti-tuberculosis activity.

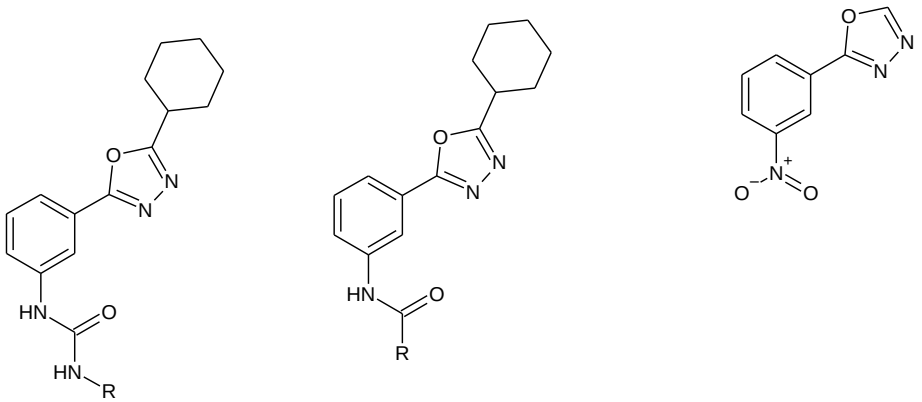


- R. Govindarajan et al., [40] reported the synthesized and anti-tubercular activity of pyrazinoyl and related heterocycles.

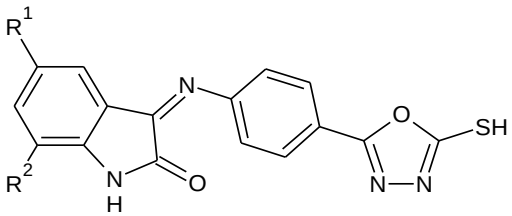


ANTICANCER ACTIVITY

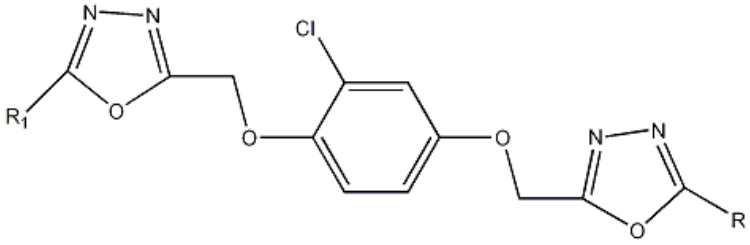
- Kavitha selvaraj et al., [75] synthesized a series of 3-(5-cyclohexyl)-1, 3, 4 oxadiazole-2-yl)-N-substituted aniline and screened for their anticancer activity.



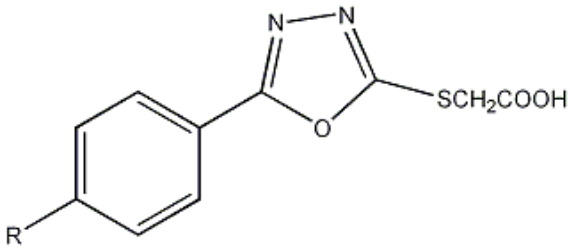
- Sarangapani manda et al., [76] synthesized a series of 5 or 7 substituted 3-(4-(5-mercapto-1, 3, 4-oxadiazole-2-yl) phenylimino)-indolin-2-one derivatives evaluated for anticancer activity.



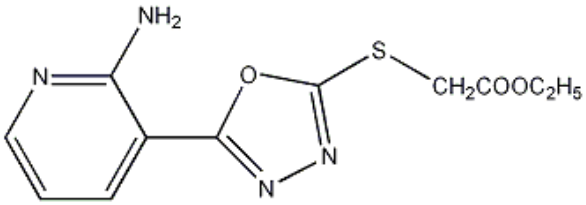
- B. Shivavarma Holla et al., [41] synthesized and evaluated the anti-cancer activity of 2-chloro-1,4-bis-(5-substituted-1, 3, 4-oxadiazol-2-ylmethyleneoxy)phenylene derivatives.



- T K Maity et al., [42] evaluation of anticancer activity of some 1, 3, 4-oxadiazole derivatives.

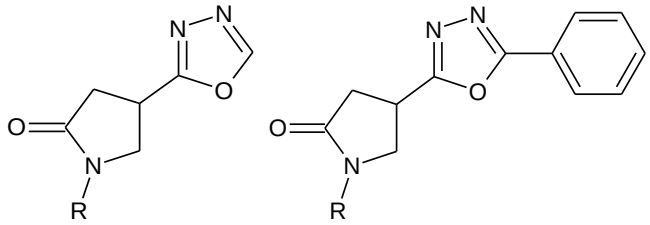


- H. Liszkiewica et al., [43] synthesized and evaluated the in-vitro anti-proliferative activity of new 5-(2-amino-3-pyrridyl)-2-thioxo-3H-1, 3, 4-oxadiazole derivatives.

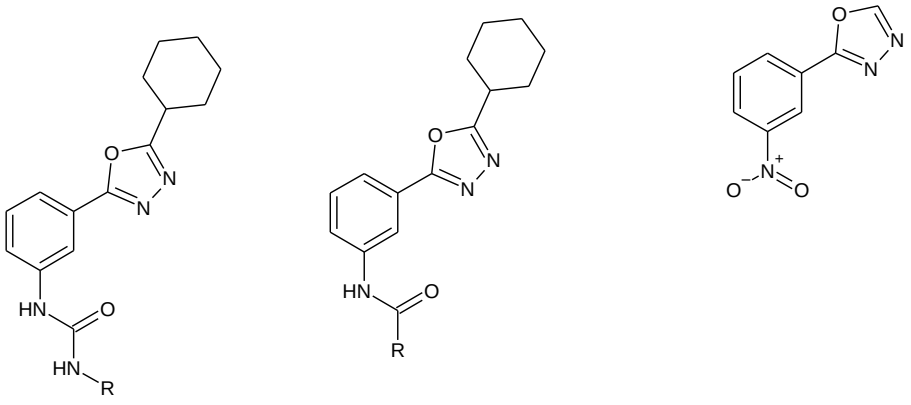


AS AN ANTI-INFLAMMATORY AGENTS

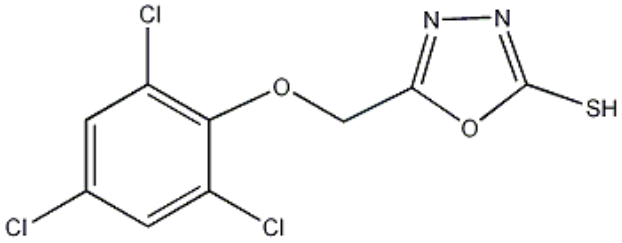
- V.mickevicius et al., [84] synthesized substituted 1, 3, 4-oxadiazole derivatives and screened for anti inflammatory activity.



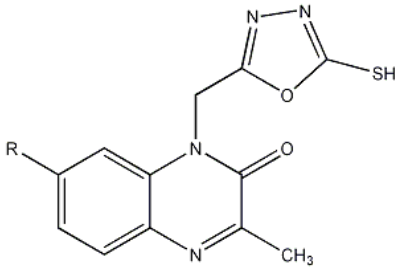
- Kavitha selvaraj et al., [75] synthesized a series of 3-(5-cyclohexyl)-1, 3, 4 oxadiazole-2-yl)-N-substituted aniline and screened for anti inflammatory activity.



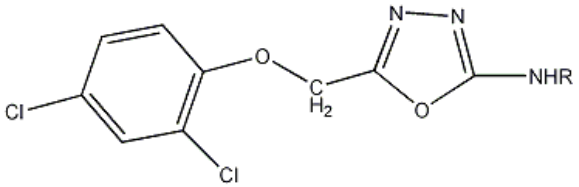
- Mohd Amir et al., [44] synthesized some 1, 3, 4-oxadiazole derivatives as potential anti-inflammatory agents.



- Airody Vasudeva Adhikari et al., [45] synthesized some new 2-(3-methyl-7-substituted-2-oxoquinoxalinyl)-5-(aryl)-1, 3, 4-oxadiazoles as potential non-steroidal anti-inflammatory and analgesic agents.

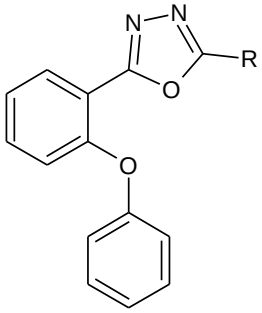


- Mohd. Amir et al., [46] synthesized and evaluated anti-inflammatory activity of some new 2,5-disubstituted 1, 3, 4-oxadiazole derivatives.

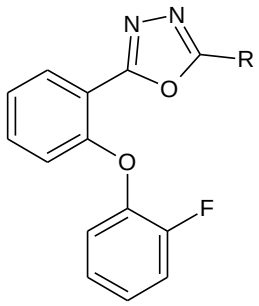


ANTICONVULSANT ACTIVITY

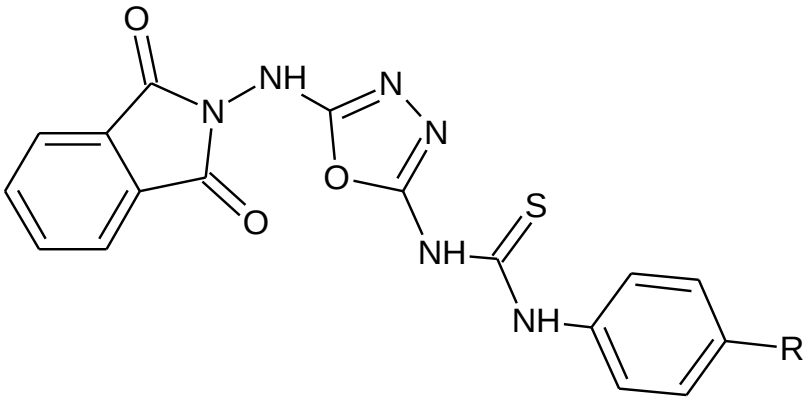
- Sayyed abbas tabatabai et al., [79] prepared 2-(2-2phenoxy)phenyl-1, 3, 4-oxadiazole derivatives screened for anticonvulsant activity.



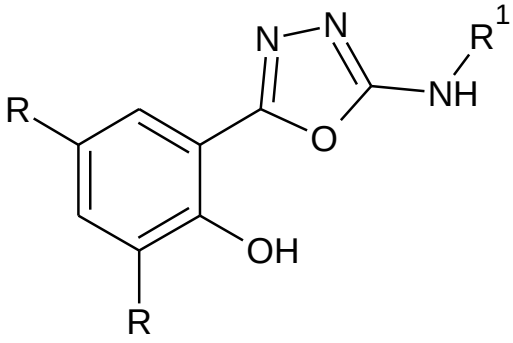
- Abbas shafiee et al., [74] synthesized new 2-substituted-5-(2-(2-fluorophenoxy) phenyl)-1, 3, 4-oxadiazoles and 1, 2, 4-triazoles screened for anticonvulsant activity.



- Mashooq A.Bhat et al., [82] synthesized some novel 1, 3, 4-oxadiazole derivatives of phthalimide and screened anticonvulsant activity.

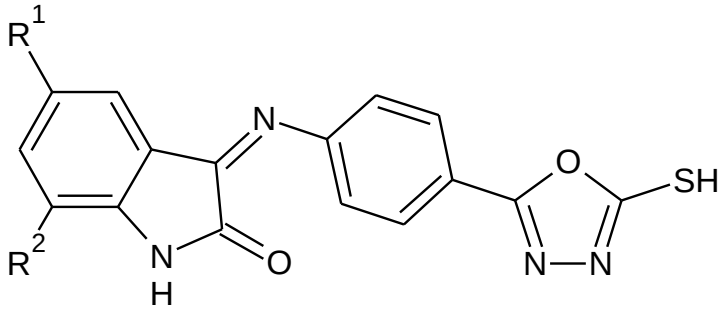


- M.E.Omar et al., [86] synthesized novel series of 2 substituted (amino-5-aryl)1, 3, 4-oxadiazole derivatives and screened for anti-convulsant activity.



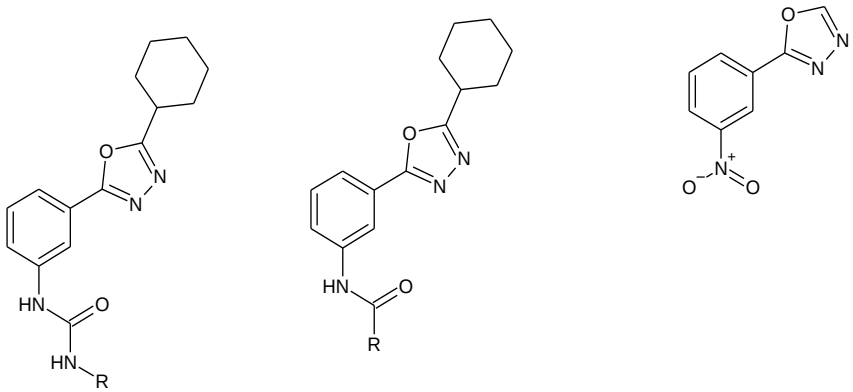
CYTOTOXIC ACTIVITY

- Vishal Modi et al., [77] synthesized a novel achiral and chiral amides incorporating 1, 3, 4-oxadiazole ring and screened for cytotoxic activities.



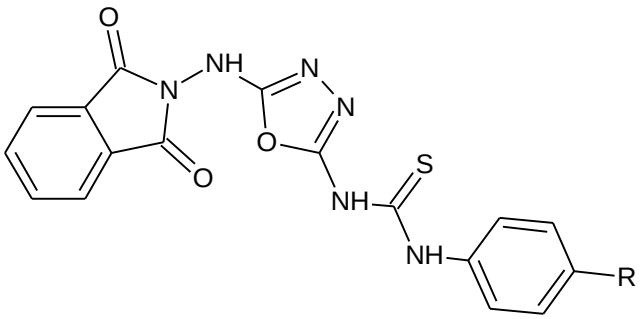
ANTIDIABETIC ACTIVITY

- Kavitha selvaraj et al., [75] synthesized a series of 3-(5-cyclohexyl)-1, 3, 4 oxadiazole-2-yl)-N-substituted aniline and screened for their ant diabetic activity.



NEUROTOXICITY

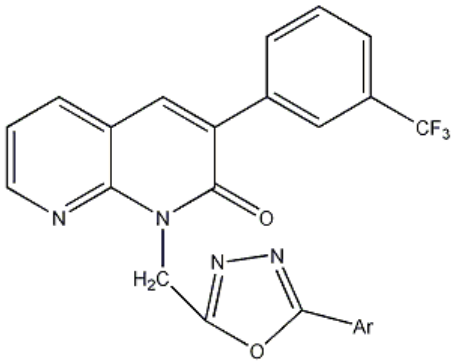
- Mashooq A.Bhat et al., [82] synthesized some novel 1, 3, 4-oxadiazole derivatives of phthalimide and screened neurotoxicity.



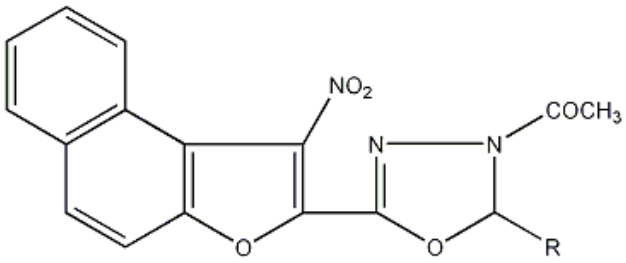
R=H,2Cl,3Cl,4Cl,2CH_3,3CH_3,4CH_3,2OCH_3,3OCH_3,4OCH_3

MISCELLENEOUS

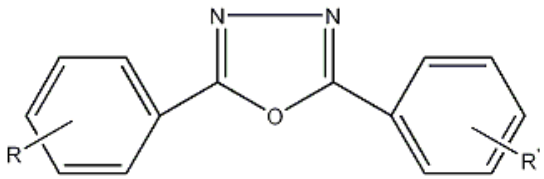
- K Mogilaiah et al., [47] Facile and efficient synthesized 1, 3, 4-oxadiazolyl 1, 8-naphthyridines under microwave irradiation.



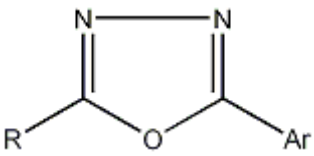
- V.P.Vaidya et al., [48] synthesized and biological evaluation of 2(3nitronaphtho [2, 1-b] furan-2yl) substituted 1, 3, 4 oxadiazoles.



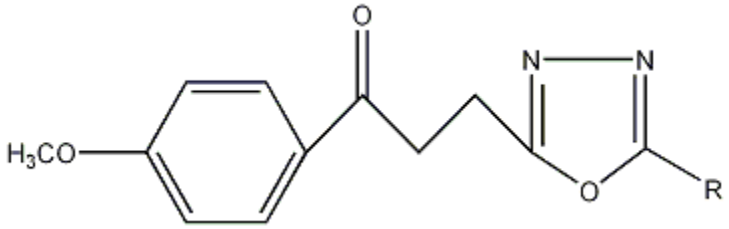
- J. K. Makranli et al., [49]reported a facial synthesized symmetrical and unsymmetrical 2, 5 di substituted 1, 3, 4 oxadiazoles.



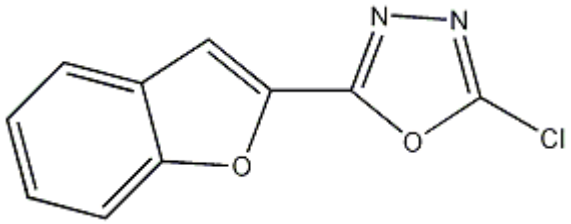
- B. kalluraya et al., [50] Microwave assisted one pot synthesized some 2,5 di substituted 1, 3, 4 oxadiazoles.



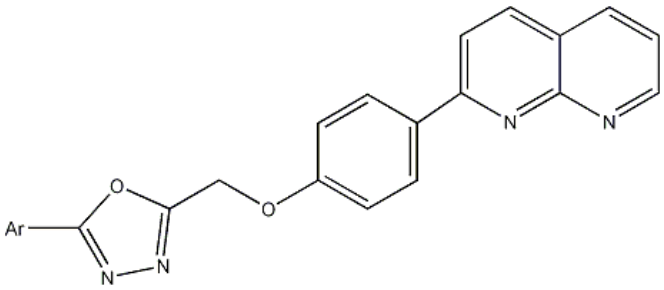
- Asif Husain et Al., [51] synthesized and biological evaluation of 2-[3-(4-methoxy phenyl) propane-3-one]-5-(substituted phenyl)-1, 3, 4 oxadiazoles.



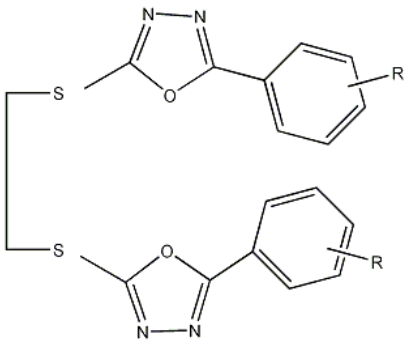
- K.M. Basa Varaja et al., [52] synthesized and evaluated biological activity of bi heterocyclic oxadiazolyl benzo furans.



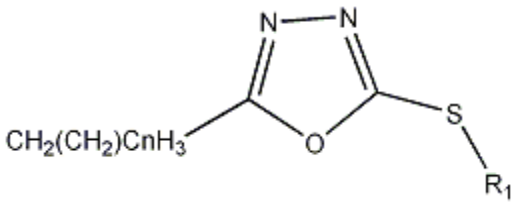
- K. Mogilaiah et al., [53] synthesized 5-aryl-2-[p-(1, 8-naphthyridin-2-yl) phenoxy methyl]-1, 3, 4-oxadiazoles using microwave irradiation.



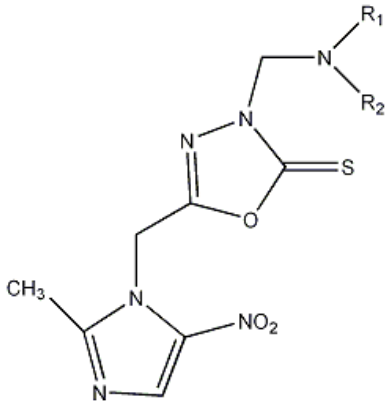
- A.D. Pandey et al., [54] synthesized tweezers incorporating 2-mercapto-5-aryl-1, 3, 4-oxadiazoless as heterocyclic sub units.



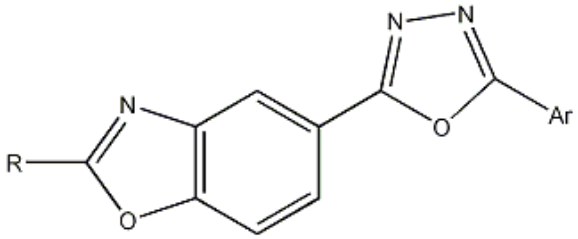
- K.R. Alagawadi et al., [55] synthesized 2-alkyl / aryl thio-5-n-alkyl-1, 3, 4-oxadiazoles.



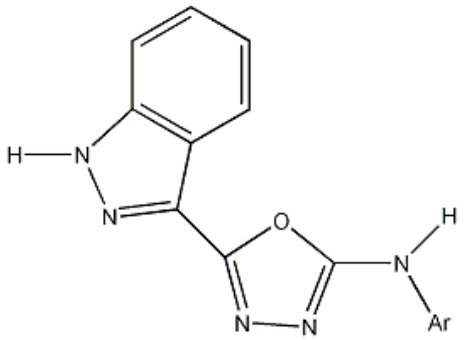
- P.V. Frank et al., [56] reported the region specific synthesized some oxadiazole derivatives from imidazoles.



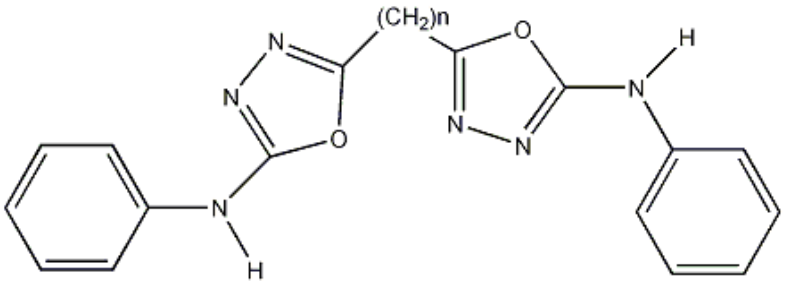
- D. Sridhar et al., [57] synthesized some new 2-(2-substituted benzoxazol-5-yl) 5-aryl-1, 3, 4-oxadiazoles.



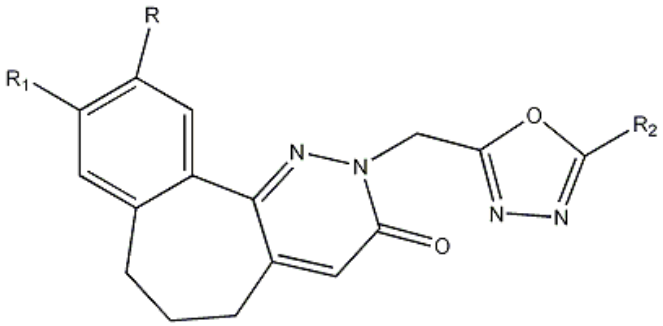
- M.S. More et al., [58] synthesized 5-(1H-indazol-3-yl)-n-phenyl-1, 3, 4-oxadiazol-2-amine by conventional and non-conventional method.



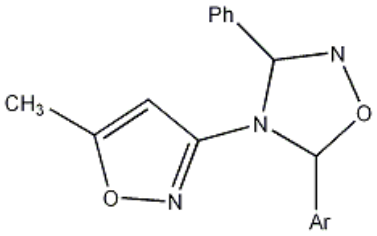
- Ajay K Behera et al., [59] synthesized bis oxadiazolyl alkanes from discarboxylic acids and evaluated their biological activity.



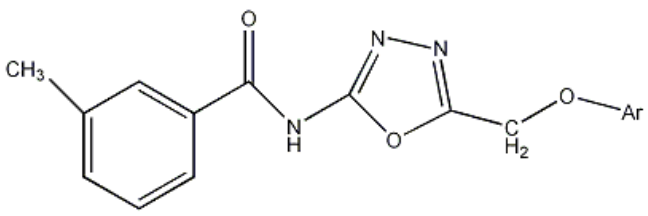
- Venkateswarlu Peesappati et al., [60] synthesized 2, 5-disubstituted -1, 3, 4-oxadiazoles as biologically active heterocycles.



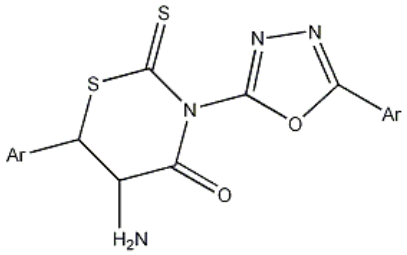
- E. Rajanarendar et al., [61] synthesized isoxazolyl oxadiazolines.



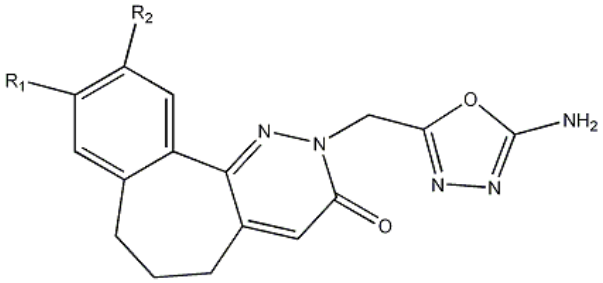
- Zhang Li et al., [62] synthesized 2-(3-methyl benzoylamino)-5-aryloxymethyl-1, 3, 4-oxadiazoles.



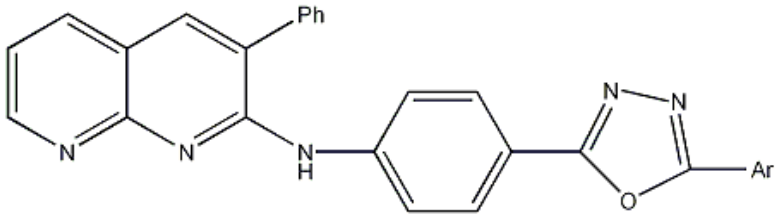
- LDS Yadav et al., [63] synthesized 5-amino-6-aryl-3-(5-aryl-1, 3, 4-oxadiazol-2-yl)-5, 6-dihydro-2-thioxo-1,3-thiazine-4-ones.



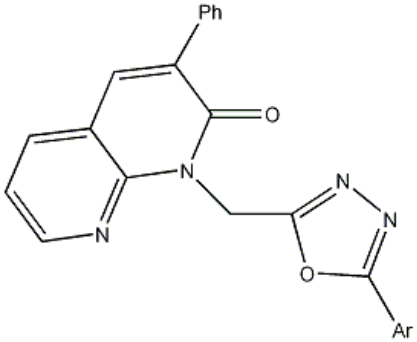
- Venkateswarlu Peesappati et al., [64] synthesized some oxadiazolo benzazocinones.



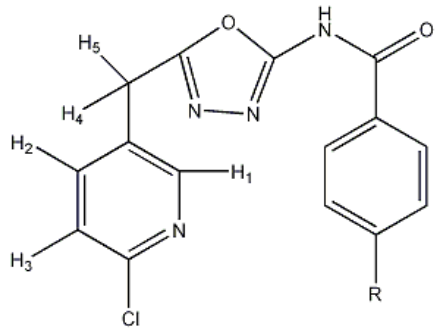
- K. Mogilaiah et al., [65] reported microwave irradiation assisted heterocyclic synthesized 1,8-naphthyridinyl-1, 3, 4-oxadiazoles.



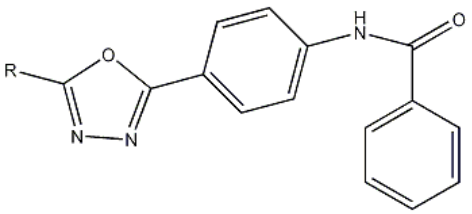
- K. Mogilaiah et al., [66] reported chloramines-T mediated synthesized 1,8-naphthyridinyl-1, 3, 4-oxadiazoles.



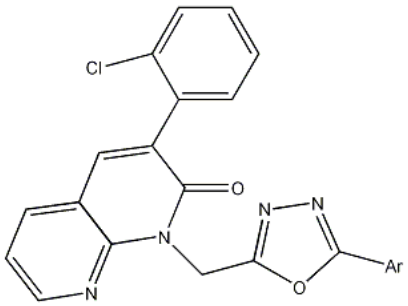
- B. Shivarama Holla et al., [67] synthesized and characterization of 1, 3, 4-oxadiazole derivatives containing 2-chloropyridin-5-yl-methyl moiety.



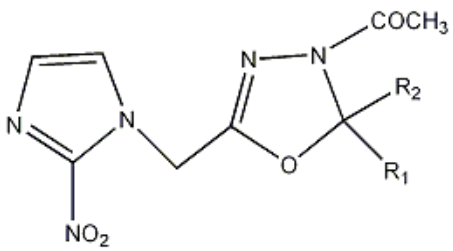
- Mohd. Amir et al., [68] reported the synthesized, characterization and biological activities of oxadiazole derivatives.



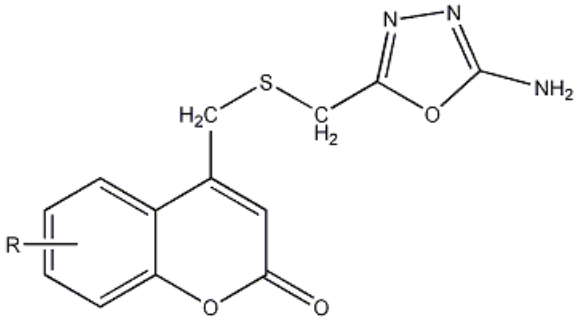
- K. Mogilaiah et al., [69] reported chloramines -T mediated synthesis of 1, 8-naphthyridinyl-1, 3, 4-oxadiazoles.



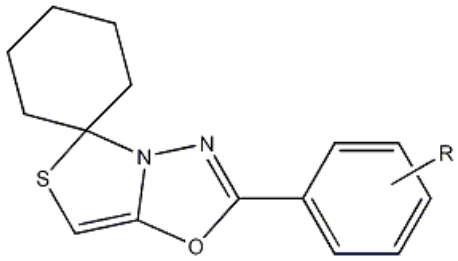
- Priya V Frank et al., [70] synthesized 1, 3, 4-oxadiazoles carrying imidazole moiety.



- Ganesh N. Alawandi et al., [71] performed chemo selective knoevenagel reaction as a novel route for the synthesis of amino oxadiazolyl coumarins.

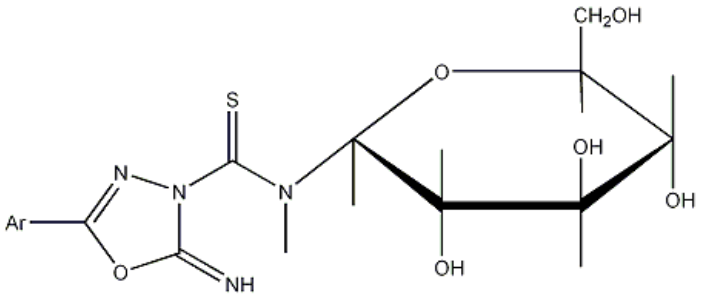


- Nizamuddin et al., [72] synthesized and evaluated the mollusicidal activity of (2-substituted)-Spiro (cyclo hexane)-1', 5-[1, 3, 4] oxadiazolo [3, 2-c] hiazolines.



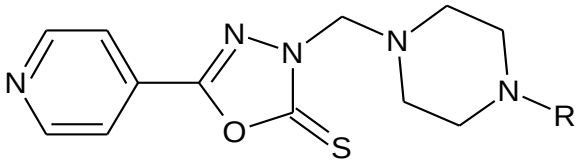
R = H, 2-Cl, 4-Cl, 2-CH_3, 3-CH_3, 4-CH_3

- Deepa Chauhan et al., [73] synthesized some novel nucleosides and evaluated their anti-herpetic activity.

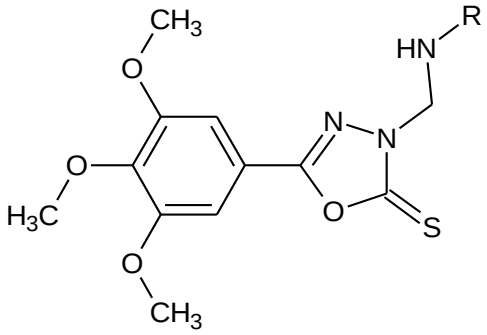


MANNICH BASE:

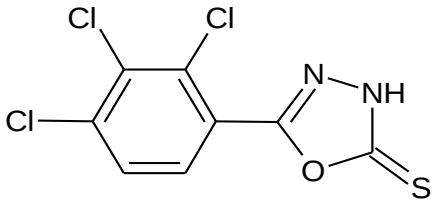
- Shadab Miyan Siddiqui et al., [87] synthesized mannich base derivatives of 5-(pyridine-4-yl) - 1, 3, and 4-oxadiazole-2-(3H)-thione with substituted piperazine and screening against Entamoeba histolytica (2012).



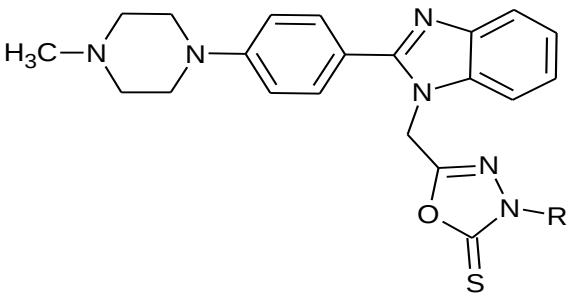
- Muhammad Akram et al.,[88] synthesized Mannich bases derived from 1, 3, 4-oxadiazole- 2-thiones and evaluated potent urease inhibition and antioxidant activities and anti-ulcer (2017)



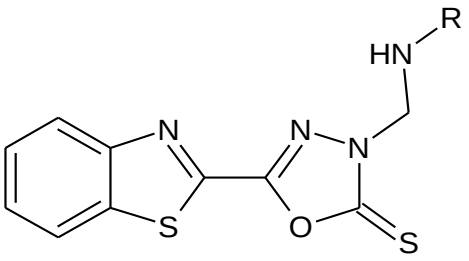
- Jagadeesh Prasad D et al., [89] synthesized some new mannich Bases Bearing 1, 3, 4-Oxadiazoline Ring System and screened antimicrobial activity (2015).



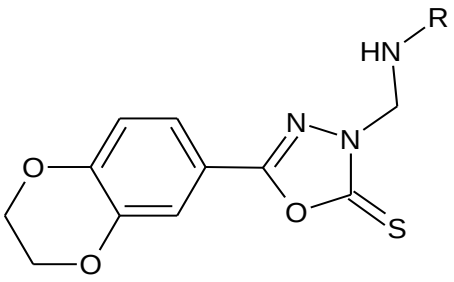
- Pramilla Sah et al.,[90] synthesized Mannich Bases of 1, 3, 4- oxadiazole Bearing Benzimidazole and Piperazine moieties and evaluated antimicrobial activity(2013).



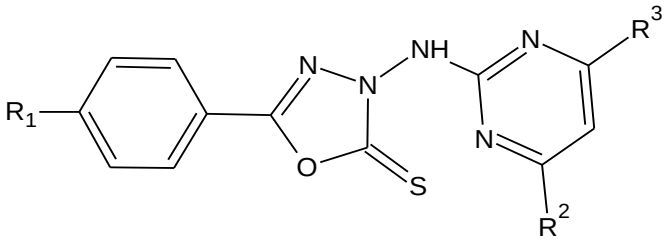
- S.m. Shantakumar et al.,[91] synthesized Some Mannich Bases of Benzothiazolyl oxadiazoles and screened antibacterial, anti-inflammatory and analgesic activity(2009).



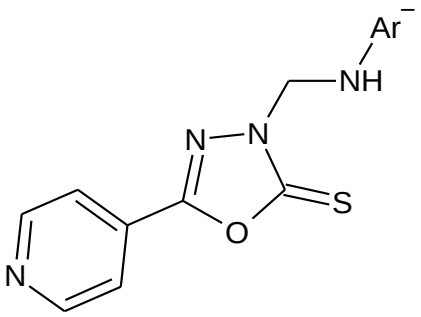
- Dong-Dong Lib et al.,[92] synthesized Mannich base of 1, 3, 4-oxadiazole derivatives possessing 1,4-benzodioxan and evaluated antioxidant activity.(2013)



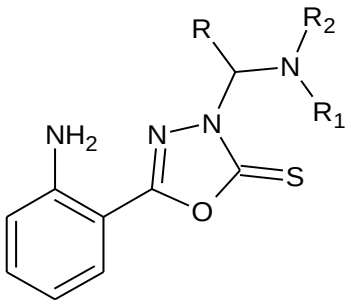
- Xiaohong Sun et al.,[93] synthesized some novel aryl substituted 1, 3, 4-oxadiazole Mannich base containing pyrimidine rings and screened anti fungal activity.(2014)



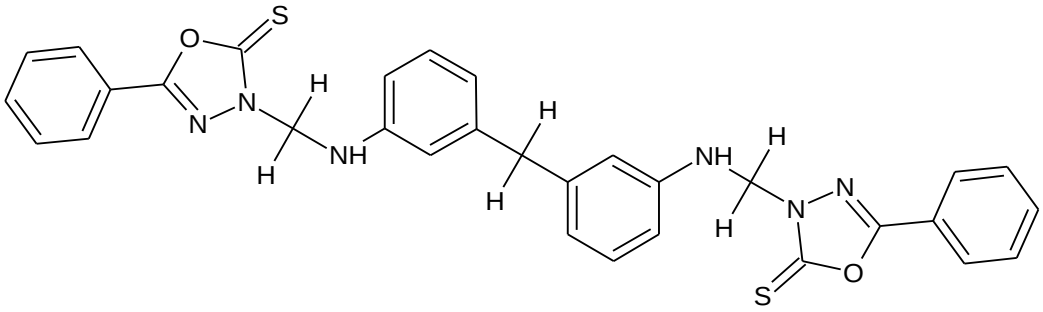
- Somani R. R. et al.,[94] synthesized Some 1, 3, 4-oxadiazole based Mannich Bases and evaluated anti-tubercular and antibacterial activity.(2013)



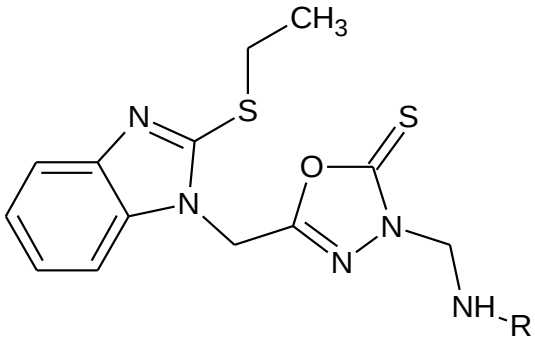
- Selvakumar Kanthiah et al.,[95] synthesized 5-(2-Aminophenyl)-1, 3, 4-oxadiazole-2(3h)-Thione Derivatives based Mannich Bases and screened antimicrobial activity.(2011)



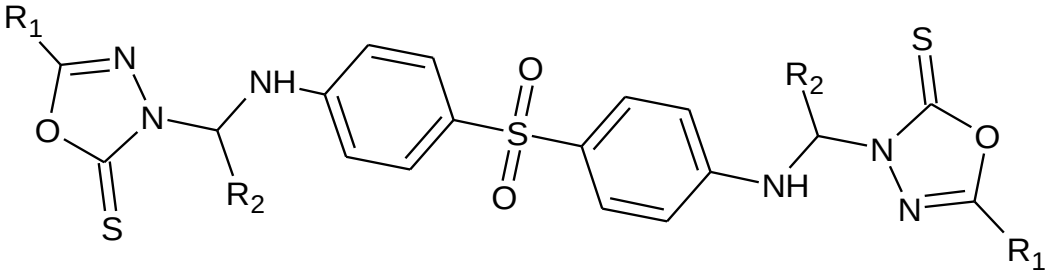
- Shahriar Ghammamy et al.,[96] synthesized Some Mannich Base New 1, 3, 4-oxadiazole-2-Thione Derivatives.(2012)



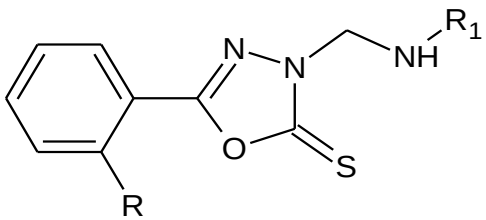
- Somani R. R. et al.,[97] synthesized some mannich bases of 1, 3, 4-oxadiazole and evaluated anticonvulsant, sedative, hypnotic, anxiolytic, CNS depressant activity.(2010)



- Humaira Nadeem et al.,[99] synthesized mannich bases of mercapto oxadiazoles and their molecular docking studies and screened antimicrobial and α-Glucosidase Inhibitory Potential.(2018)



- Mohammed Shaharyar et al.,[98] synthesized oxadiazole mannich bases and evaluated anti mycobacterial activity.(2007)



AIM OF THE PRESENT WORK

- From the literature review it is known that the synthesis of 1, 3, 4-oxadiazoles is of considerable interest due to their various biological activities.
- Reported activities were: antimicrobial, antifungal, anti-inflammatory, anti-nociceptive, anticancer, anticonvulsant, antitumor and antihypertensive activities.
- Hence we have carried out investigations towards the synthesis of various 1, 3, 4-oxadiazole derivatives in order to exploit some of their activities.
- In the present investigation I have reported the synthesis of new members of this applicably important type of compounds that are various N- substituted 1, 3, 4-oxadiazoles from salicylic acid and p-hydroxy benzoic acid by four steps esterification, hydrazinolysis, cyclization and mannich condensation.
- The synthesized compounds are characterized and screened for anti-inflammatory, anti-nociceptive and anticonvulsant activities.
- Others screening like antibacterial, antifungal activity and anthelmintic activity also carried out because of many of the substituted compounds possessing above activities.

PLAN OF THE PRESENT WORK

The plan of the present work can be summarized as follows.

1. Synthesis of substituted oxadiazole by reacting salicylic acid and /or p-hydroxy benzoic acid with ethanol in presence of sulphuric acid followed by reacting with hydrazine hydrate, carbon disulphide and alkali.
2. Synthesis of titled oxadiazole derivatives by making substitution at free N-(H) position of oxadiazole through mannich condensation with secondary amine bearing compounds and aldehyde (formaldehyde).
3. Characterization of the synthesized compounds by various analytical techniques like TLC, IR and NMR.
4. The synthesized compounds were screened for anti-inflammatory, anti-nociceptive, anti-convulsant activity, anti microbial activity and anthelmintic activity.
5. The synthesized compounds were screened for anti-bacterial activity against G (+ve) organism like *Staphylococcus aureus* and *Streptococcus pyogenes* and G (-ve) organism like *Escherichia coli* and *Pseudomonas auruginosa.*
6. The synthesized compounds were screened for anti-fungal activity against *Candida albicans and Aspergillus Niger*.
7. The synthesized compounds were screened for anthelmintic activity against *Pheritima posthuma* worm.

SYNTHETIC METHODOLOGY

STEP I: SYNTHESIS OF SUBSTITUTED OXADIAZOLE

SCHEME I:

Esterification:

0.01 mol of salicylic acid was dissolved in 20 ml absolute ethanol to this solution 0.5ml of conc. H_2SO_4 drop wise added and refluxed for 4 hrs. Distilled off excess of alcohol on water bath and allowed to cool. The residue was added in 250 ml distilled water in separating funnel and to this 10 ml CCl_4 added then neutralized by strong solution of $NaHCO_3$. Lower layer was separated and dried by pouring into a small conical flask containing 5 g, $MgSO_4$, shaked for 5 min. and allowed to stand for ½ hours. Filtered the ester solution, distilled off CCl_4, and ester product was collected.

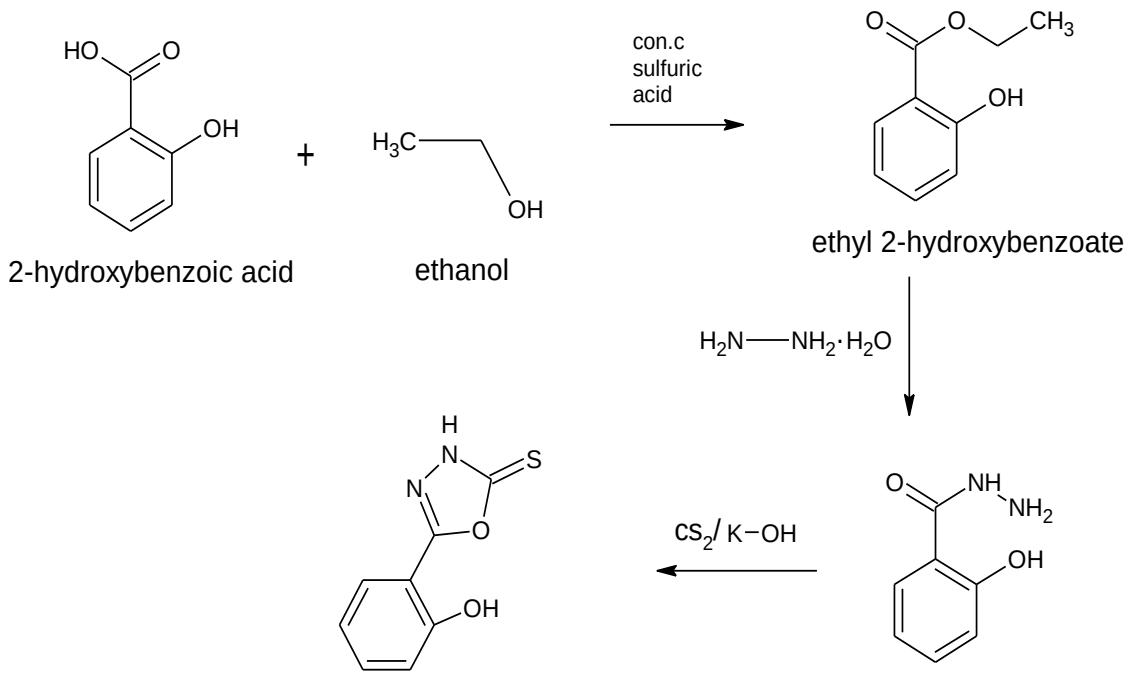
Hydrozinolysis

To the ester product (0.01 mol),hydrazine hydrate(0.04 mol) was added and refluxed in absolute ethanol for 5 h. the reaction mixture was cooled and poured into crushed ice. The separated solid was filtered, dried, and recrystallized using ethanol.

Cyclization

A mixture of hydrazide (0. 05 mol) potassium hydroxide (0.005 mol) and carbon disulphide (5 ml) in ethanol (50 ml) was refluxed on a steam bath for 10 hr. The solution was allowed to cool overnight and then concentrated. It was again cooled at room temp and then dissolved in ice cold water. The resulting solution was acidified with dil. HCl and allowed to stand for 12 hr. The separated solid was dried and recrystallized from ethanol.

SCHEME I:



2-hydroxybenzoic acid

ethanol

ethyl 2-hydroxybenzoate

2-hydroxybenzohydrazide

5-(2-hydroxyphenyl)-1,3,4-oxadiazole
-2(3*H*)-thione

SCHEME II:

Esterification

0.01 mol of p-hydroxy benzoic acid was dissolved in 20 ml absolute ethanol to this solution 0.5ml of conc. H_2SO_4 drop wise added and refluxed for 4 hrs. Distilled off excess of alcohol on water bath and allowed to cool. The residue was added in 250 ml distilled water in separating funnel and to this 10 ml CCl_4 added then neutralized by strong solution of $NaHCO_3$. Lower layer was separated and dried by pouring into a small conical flask containing 5 g, $MgSO_4$, shaked for 5 min. and allowed to stand for ½ hours. Filtered the ester solution, distilled off CCl_4, and ester product was collected.

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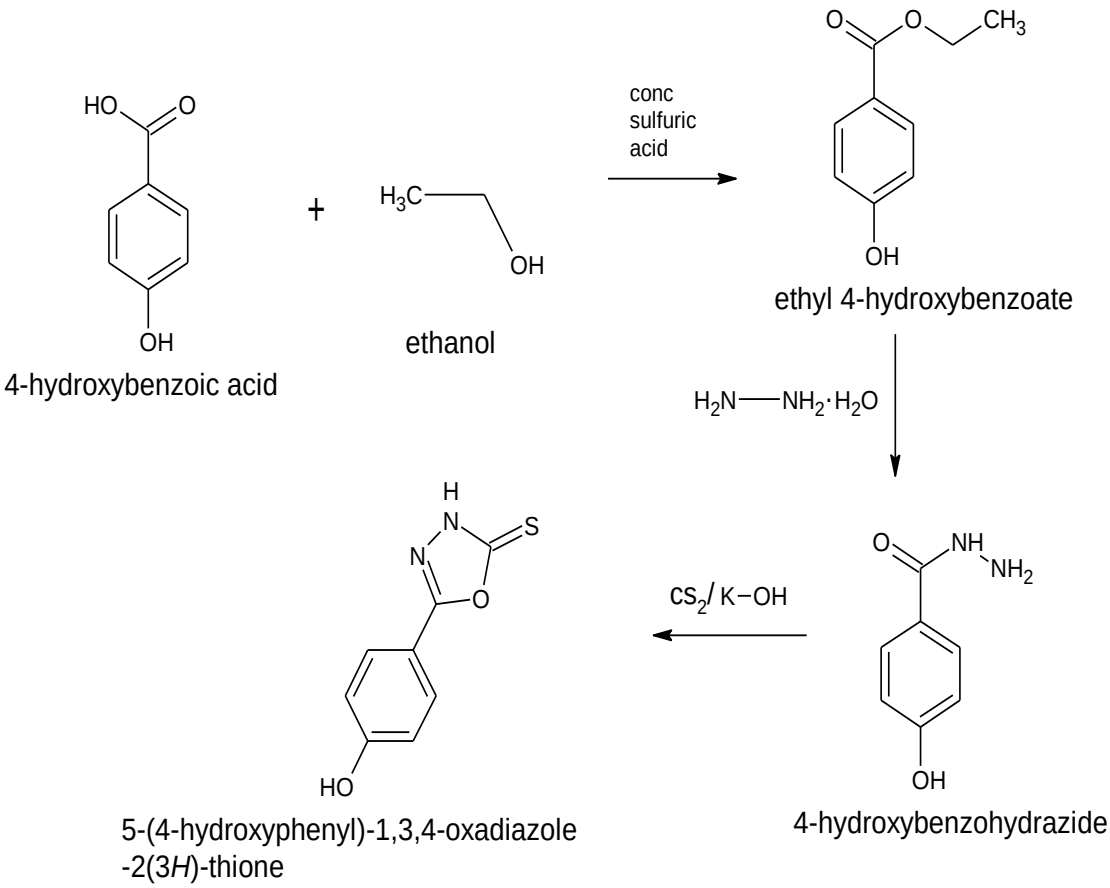

HO
O
OH
4-hydroxybenzoic acid
+
H3C
OH
ethanol
conc
sulfuric
acid
O
O
CH3
OH
ethyl 4-hydroxybenzoate
H2N—NH2·H2O
O
NH
NH2
OH
4-hydroxybenzohydrazide
CS2/ K−OH
H
N
N
S
O
HO
5-(4-hydroxyphenyl)-1,3,4-oxadiazole
-2(3H)-thione

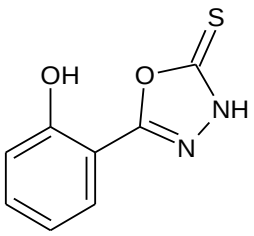
STEP II:

SYNTHESIS OF TITLED OXADIAZOLE DERIVATIVES BY MANNICH

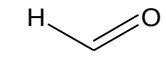
CONDENSATION

To the solution of 5-(2-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione and/or 5-(4-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione (0.005 mol)(synthesized in scheme I) in absolute alcohol, formaldehyde (0.5 ml,37%) and amines (0.005 mol) were added and vigorous stirred at 2-5^{0}C temp, for 3 hours, and then kept it on room temp. overnight. Solid compounds thus obtained were filtered, dried and recrystallized from suitable solvent.

II) A



5-(2-hydroxyphenyl)-1,3,4-oxadiazole
-2(3*H*)-thione



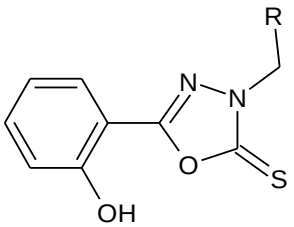
formaldehyde

RH

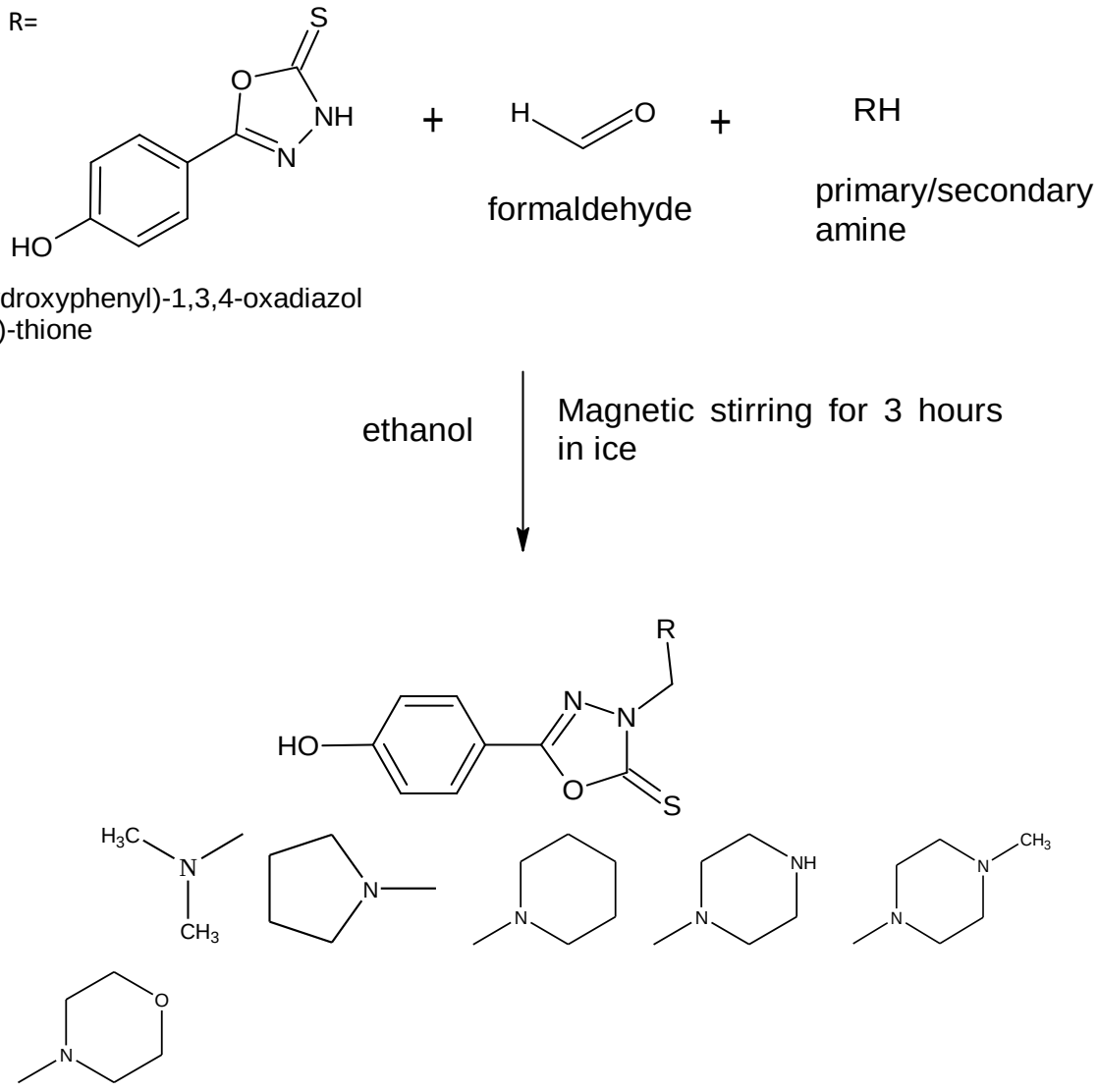
primary/secondary amine

ethanol

Magnetic stirring for 3 hours in ice



II) B


R=
S
O
NH
N
HO
+
H
O
+
RH
formaldehyde
primary/secondary amine
5-(4-hydroxyphenyl)-1,3,4-oxadiazole-2(3H)-thione
ethanol
Magnetic stirring for 3 hours in ice
R
N
N
HO
O
S
H3C
N
CH3
N
N
NH
N
CH3
N
N
O
N

IUPAC NAMES OF SYNTHESIZED COMPOUNDS

ODAZ 01

3-[(dimethylamino)methyl]-5-(2-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione

ODAZ 02

5-(2-hydroxyphenyl)-3-[(pyrrolidin-1-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

ODAZ 03

5-(2-hydroxyphenyl)-3-[(piperidin-1-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

ODAZ 04

5-(2-hydroxyphenyl)-3-[(piperazin-1-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

ODAZ 05

5-(2-hydroxyphenyl)-3-[(4-methylpiperazin-1-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

ODAZ 06

5-(2-hydroxyphenyl)-3-[(morpholin-4-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

PDAZ 01

3-[(dimethylamino)methyl]-5-(4-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione

PDAZ 02

5-(4-hydroxyphenyl)-3-[(pyrrolidin-1-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

PDAZ 03

5-(4-hydroxyphenyl)-3-[(piperidin-1-yl) methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

PDAZ 04

5-(4-hydroxyphenyl)-3-[(piperazin-1-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

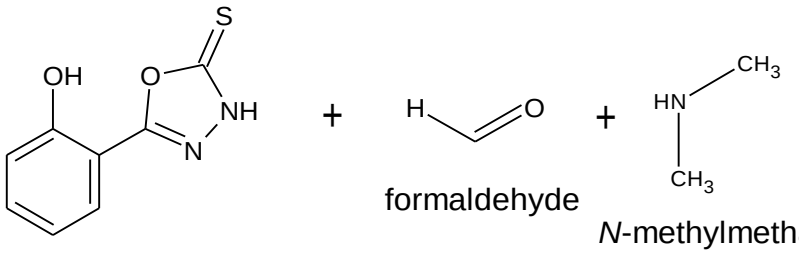
PDAZ 05

5-(4-hydroxyphenyl)-3-[(4-methylpiperazin-1-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

PDAZ 06

5-(4-hydroxyphenyl)-3-[(morpholin-4-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione

ODAZ 01



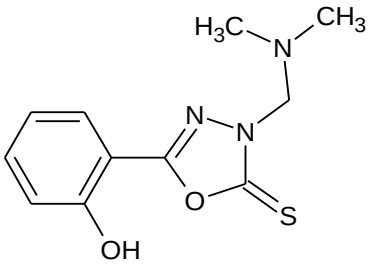
formaldehyde

N-methylmethanamine

5-(2-hydroxyphenyl)-1,3,4-oxadiazole
-2(3*H*)-thione

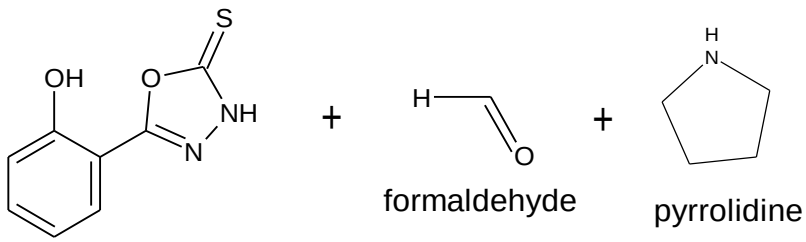
ethanol

Magnetic stirring for 3 hours
in ice



3-[(dimethylamino)methyl]-5-(2-hydroxyphenyl)-
1,3,4-oxadiazole-2(3*H*)-thione

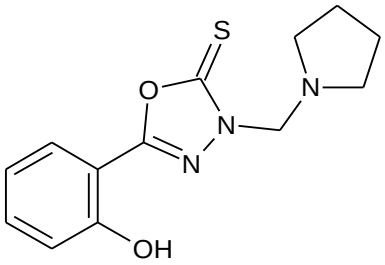
ODAZ O2



5-(2-hydroxyphenyl)-1,3,4-oxadiazole
-2(3*H*)-thione

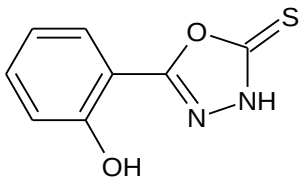
ethanol

Magnetic stirring for 3 hours in ice



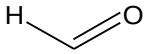
5-(2-hydroxyphenyl)-3-[(pyrrolidin-1-yl)methyl]-
1,3,4-oxadiazole-2(3*H*)-thione

ODAZ 03



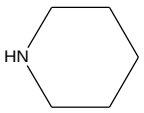
5-(2-hydroxyphenyl)-1,3,4-oxadiazole
-2(3*H*)-thione

+



formaldehyde

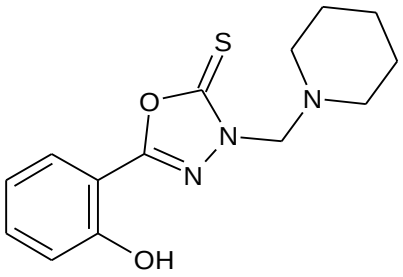
+



piperidine

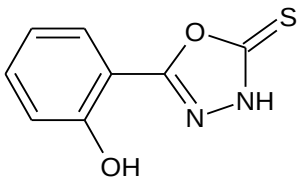
ethanol

Magnetic stirring for 3 hours
in ice



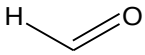
5-(2-hydroxyphenyl)-3-[(piperidin-1-yl)methyl]
-1,3,4-oxadiazole-2(3*H*)-thione

ODAZ 04



5-(2-hydroxyphenyl)-1,3,4-oxadiazole
-2(3*H*)-thione

\+



formaldehyde

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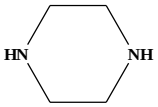
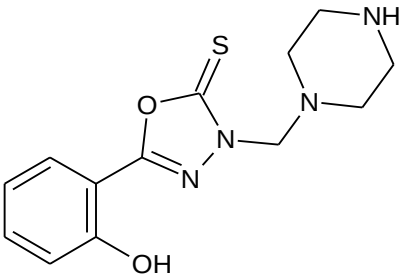


piperazine

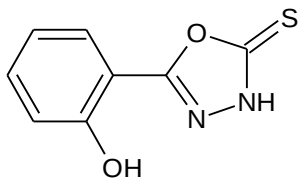
ethanol

Magnetic stirring for 3 hours in ice



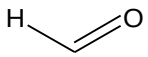
5-(2-hydroxyphenyl)-3-[(piperazin-1-yl)methyl]-
1,3,4-oxadiazole-2(3*H*)-thione

ODAZ 05



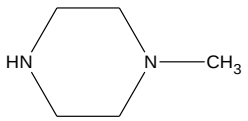
5-(2-hydroxyphenyl)-1,3,4-oxadiazole
-2(3*H*)-thione

+



formaldehyde

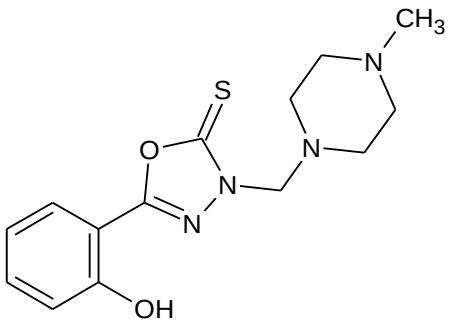
+



1-methylpiperazine

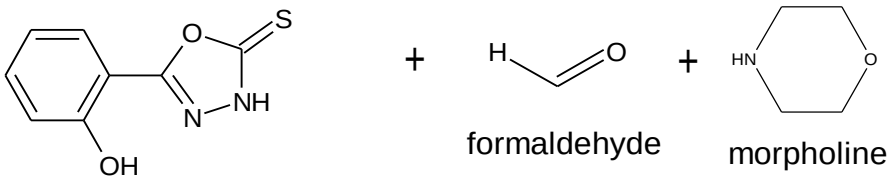
ethanol

Magnetic stirring for 3 hours
in ice



5-(2-hydroxyphenyl)-3-[(4-methylpiperazin-1-yl)
methyl]-1,3,4-oxadiazole-2(3*H*)-thione

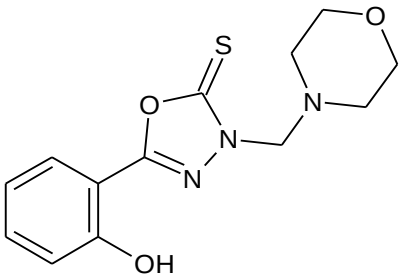
ODAZ 06



5-(2-hydroxyphenyl)-1,3,4-oxadiazole
-2(3*H*)-thione

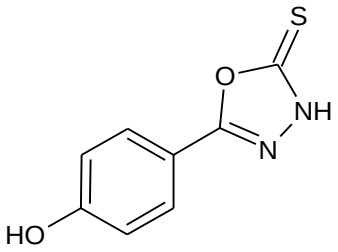
ethanol

Magnetic stirring for 3 hours in ice



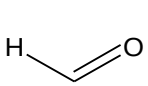
5-(2-hydroxyphenyl)-3-[(morpholin-4-yl)methyl]-
1,3,4-oxadiazole-2(3*H*)-thione

PDAZ 01



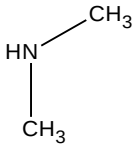
5-(4-hydroxyphenyl)-1,3,4-oxadiazol
e-2(3*H*)-thione

+



formaldehyde

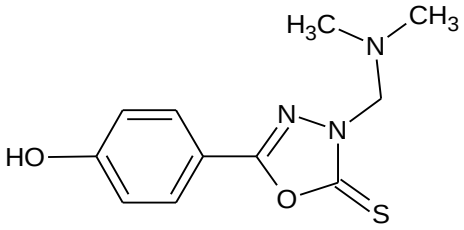
+



N-methylmethanamine

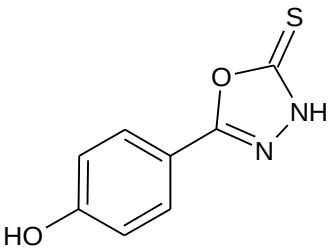
ethanol

Magnetic stirring for 3 hours
in ice



3-[(dimethylamino)methyl]-5-(4-hydroxyphenyl)
-1,3,4-oxadiazole-2(3*H*)-thione

PDAZ 02



5-(4-hydroxyphenyl)-1,3,4-oxadiazol
e-2(3*H*)-thione

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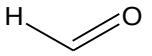

formaldehyde

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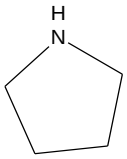
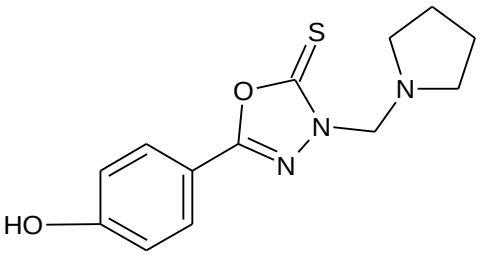


pyrrolidine

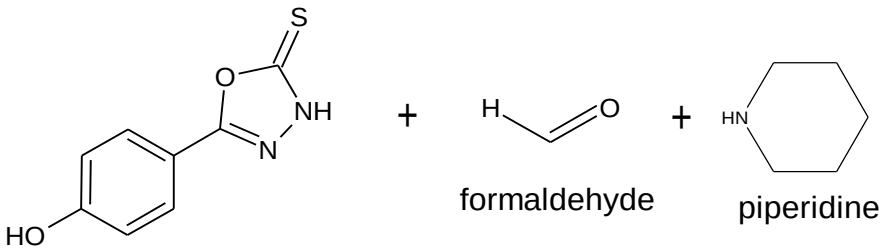
ethanol

Magnetic stirring for 3 hours
in ice



5-(4-hydroxyphenyl)-3-[(pyrrolidin-1-yl)methyl]
-1,3,4-oxadiazole-2(3*H*)-thione

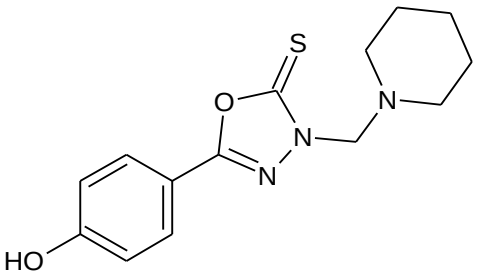
PDAZ 03



5-(4-hydroxyphenyl)-1,3,4-oxadiazol
e-2(3*H*)-thione

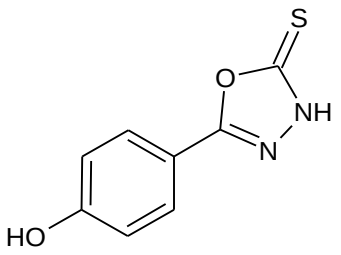
ethanol

Magnetic stirring for 3 hours
in ice



5-(4-hydroxyphenyl)-3-[(piperidin-1-yl)methyl]
-1,3,4-oxadiazole-2(3*H*)-thione

PDAZ 04



5-(4-hydroxyphenyl)-1,3,4-oxadiazol
e-2(3*H*)-thione

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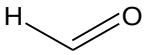

formaldehyde

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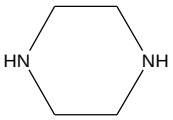
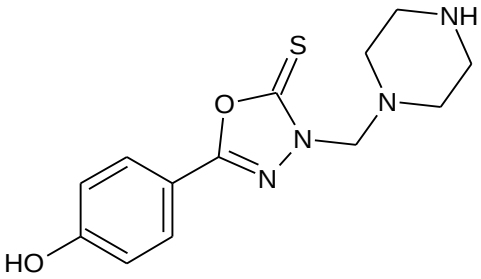


piperazine

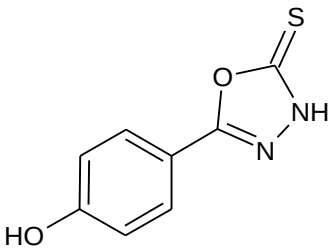
ethanol

Magnetic stirring for 3 hours
in ice



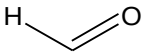
5-(4-hydroxyphenyl)-3-[(piperazin-1-yl)methyl]
-1,3,4-oxadiazole-2(3*H*)-thione

PDAZ 05



5-(4-hydroxyphenyl)-1,3,4-oxadiazol
e-2(3*H*)-thione

\+



formaldehyde

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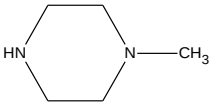
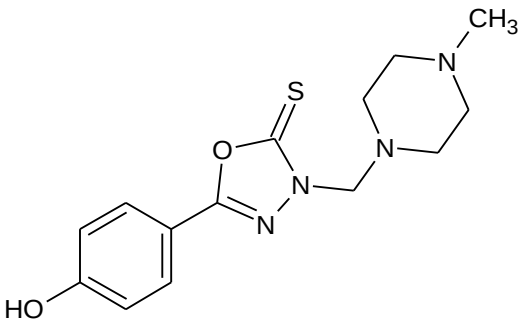


1-methylpiperazine

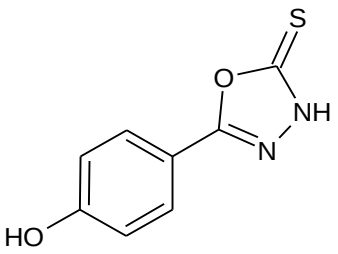
ethanol

Magnetic stirring for 3 hours
in ice



5-(4-hydroxyphenyl)-3-[(4-methylpiperazin-1-yl)
methyl]-1,3,4-oxadiazole-2(3*H*)-thione

PDAZ 06



5-(4-hydroxyphenyl)-1,3,4-oxadiazol
e-2(3*H*)-thione

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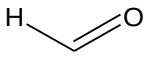

formaldehyde

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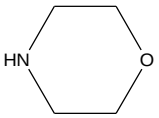
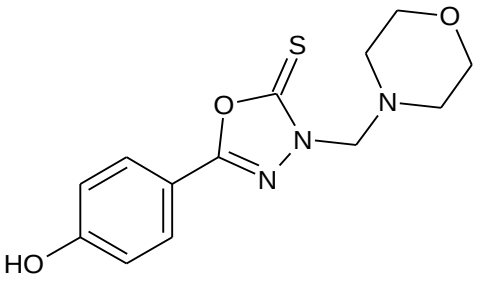


morpholine

ethanol

Magnetic stirring for 3 hours
in ice



5-(4-hydroxyphenyl)-3-[(morpholin-4-yl)methyl]
-1,3,4-oxadiazole-2(3*H*)-thione

CHEMICALS AND INSTRUMENTS

CHEMICALS

Salicylic acid	P-hydroxy benzoic acid
Ethanol	Conc. Sulphuric acid
Carbon tetrachloride	Magnesium sulphate
Hydrazine hydrate	Carbon disulphide
Potassium hydroxide	Formaldehyde
Dimethylamine	Piperidine
Pyrrolidine	Methyl piperazine
Morpholine	Piperazine
Ether	Chloroform
DMF	Methanol
Silica gel – G	Iodine crystals

All the chemicals and reagents used were analytical grade.

INSTRUMENTS

- Melting point apparatus
- FT-IR Spectrophotometer
- NMR Spectrophotometer
- Heating mantle
- Magnetic stirrer
- Analgesiometer
- Electroconvulsiometer
- Plethysmogram

CHARACTERIZATION

SOLUBILITY

Solubility analysis has been carried out for all the synthesized compounds and reported in table No. 1.

S. No.	Comp. Code	Alcohol
1	ODAZ 01	Soluble
2	ODAZ 02	Soluble
3	ODAZ 03	Soluble
4	ODAZ 04	Soluble
5	ODAZ 05	Soluble
6	ODAZ 06	Soluble
7	PDAZ 01	Soluble
8	PDAZ 02	Soluble
9	PDAZ 03	Soluble
10	PDAZ 04	Soluble
11	PDAZ 05	Soluble
12	PDAZ 06	Soluble

MELTING POINT

Melting point was found in a one end sealed capillary tube method by electrically heated melting point apparatus. The melting points of the synthesized compounds were given in the Table No. 2.

Table No. 2.

S. No	Compound Code	Melting Point (^{0}C)
1.	SALICYLIC ACID	158.6°C
2.	PARA HYDROXY BENZOIC ACID	214.5°C
3.	ODAZ 01	132°C
4.	ODAZ 02	120°C
5.	ODAZ 03	131°C
6.	ODAZ 04	136°C
7.	ODAZ 05	144°C
8.	ODAZ 06	148°C
9.	PDAZ 01	170°C
10.	PDAZ 02	228°C
11.	PDAZ 03	171°C
12.	PDAZ 04	189°C
13.	PDAZ 05	190°C
14.	PDAZ 06	211°C

Molecular Formula, Molecular Weight, & Percentage Yield

Table No. 3

S. No.	Compound Code	Molecular Formula	Molecular Weight	% Yield
1	ODAZ 01	$C_{11}H_{13}N_3O_2S$	251.07	70.50%
2	ODAZ 02	$C_{13}H_{15}N_3O_2S$	277.09	68.20%
3	ODAZ 03	$C_{14}H_{17}N_3O_2S$	291.10	65.75%
4	ODAZ 04	$C_{13}H_{16}N_4O_2S$	292.10	66.69%
5	ODAZ 05	$C_{14}H_{17}N_3O_2S$	306.12	75.04%
6	ODAZ 06	$C_{13}H_{15}N_3O_3S$	293.08	67.69%
7	PDAZ 01	$C_{11}H_{13}N_3O_2S$	251.07	74.75%
8	PDAZ 02	$C_{13}H_{15}N_3O_2S$	277.09	73.92%
9	PDAZ 03	$C_{14}H_{17}N_3O_2S$	291.10	68.65%
10	PDAZ 04	$C_{13}H_{16}N_4O_2S$	292.10	73.79%
11	PDAZ 05	$C_{14}H_{18}N_4O_2S$	306.12	65.64%
12	PDAZ 06	$C_{13}H_{15}N_3O_3S$	293.08	69.29%

THIN LAYER CHROMATOGRAPHY[100]

The purity of the compound was ascertained by TLC.

Adsorbent used: Silica gel –G, Detecting agent: Iodine vapor

R_f Values of the synthesized compounds were calculated by the following formula,

$$R_f \text{ value} = \frac{\text{Distance traveled by the solute}}{\text{Distance traveled by the solvent front}}$$

R_f VALUES OF TITLED COMPOUNDS

TABLE No. 4

S.No	Compound Code	Solvent System and Ratio	R_f Value
1	ODAZ 01	Chloroform : Diethyl Ether (80:20)	0.812
2	ODAZ 02	Chloroform : Diethyl Ether : Methanol (70:20:10)	0.785
3	ODAZ 03	Chloroform : Diethyl Ether (80:20)	0.728
4	ODAZ 04	Chloroform : Diethyl Ether (80:20)	0.680
5	ODAZ 05	Chloroform : Diethyl Ether : Methanol (70:20:10)	0.864
6	ODAZ 06	Chloroform : Diethyl Ether (80:20)	0.757
7	PDAZ 01	Chloroform : Diethyl Ether : Methanol (70:20:10)	0.644
8	PDAZ 02	Chloroform : Diethyl Ether : Methanol (70:20:10)	0.902
9	PDAZ 03	Chloroform : Diethyl Ether (80:20)	0.675
10	PDAZ 04	Chloroform : Diethyl Ether : Methanol (70:20:10)	0.858
11	PDAZ 05	Chloroform : Diethyl Ether (80:20)	0.923
12	PDAZ 06	Chloroform : Diethyl Ether (80:20)	0.559

INFRA-RED SPECTRAL ANALYSIS[101, 102]

The structure of the synthesized was elucidated by Shimadzu 8400 series Fourier transformer – Infrared Spectrophotometer in KBr- pellet method. IR values are measured in cm^{-1} and results are shown below.

ODAZ 01

Groups assigned	Frequency (cm^{-1})
O-H	3412.73
	1482.15
C-N	1182.32
C-O	1135.31
C=S	1070.30
C-H	2982.35
CH_2	1455.35

ODAZ 02

Groups assigned	Frequency (cm^{-1})
O-H	3389.15
	1471.32
C-N	1179.13
C-O	1241.62
C=S	1228.41
C-H	2975.32
CH_2	1468.15
C=C	1659.13

ODAZ 03

Groups assigned	Frequency (cm^{-1})
O-H	3471.34
	1468.56
C-N	1180.61
C-O	1238.62
C=S	1240.35
C-H	2978.61
CH_2	1450.31
C=C	1634.35

ODAZ 04

Groups assigned	Frequency (cm^{-1})
O-H	3331.53
	1657.31
C-N	1188.72
C-O	1238.72
C=S	1248.31
C-H	2988.73
CH_2	1461.32

ODAZ 05

Groups assigned	Frequency (cm^{-1})
O-H	3348.17
	1483.41
C-N	1168.38
C-O	1138.61
C=S	1081.33
C-H	2991.37
CH_2	1452.35
C=C	1651.38

ODAZ 06

Groups assigned	Frequency (cm^{-1})
O-H	3441.73
	1473.64
C-N	1191.39
C-O	1243.51
C=S	1238.41
C-H	2876.15
CH_2	1461.71
C=C	1652.84

PDAZ 01

Groups assigned	Frequency (cm^{-1})
O-H	3317.56
	1471.69
C-N	1195.87
C-O	1143.79
C=S	1082.07
C-H	2983.88
CH_2	1433.11

PDAZ 02

Groups assigned	Frequency (cm^{-1})
O-H	3413.13
	1451.18
C-N	1121.91
C-O	1241.32
C=S	1231.43
C-H	2913.71
CH_2	1471.61
C=C	1649.73

PDAZ 03

Groups assigned	Frequency (cm^{-1})
O-H	3318.15
	1470.63
C-N	1132.43
C-O	1248.12
C=S	1231.01
C-H	2971.32
CH_2	1456.73
C=C	1653.18

PDAZ 04

Groups assigned	Frequency (cm^{-1})
	1450.47
C-N	1163.08
C=S	1240.23
C-H	2877.79
CH_2	1450.47

PDAZ 05

Groups assigned	Frequency (cm^{-1})
C-N	1101.35
C-O	1134.14
C=S	1134.14
C-H	2881.65

PDAZ 06

Groups assigned	Frequency (cm^{-1})
O-H	3400
	1469.76
C-N	1128.36
C-O	1240.23
C=S	1240.23
C-H	2981.95
CH_2	1469.76
C=C	1645.28

3318.15
2971.32
2783.91
2512.56
1653.18
1470.63
1456.73
1257.12
1248.12
1241.01
1132.43
882.97
654.51
4000
3500
3000
2500
2000
1750
1500
1250
1000
750
500
cm-1
4
3
2
1
Abs
ODAZ01

612.86
871.64
979.32
1179.13
1228.41
1241.62
1367.78
1468.15
1471.32
1631.15
1659.13
2389.15
2881.81
2975.32
3389.15
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3500
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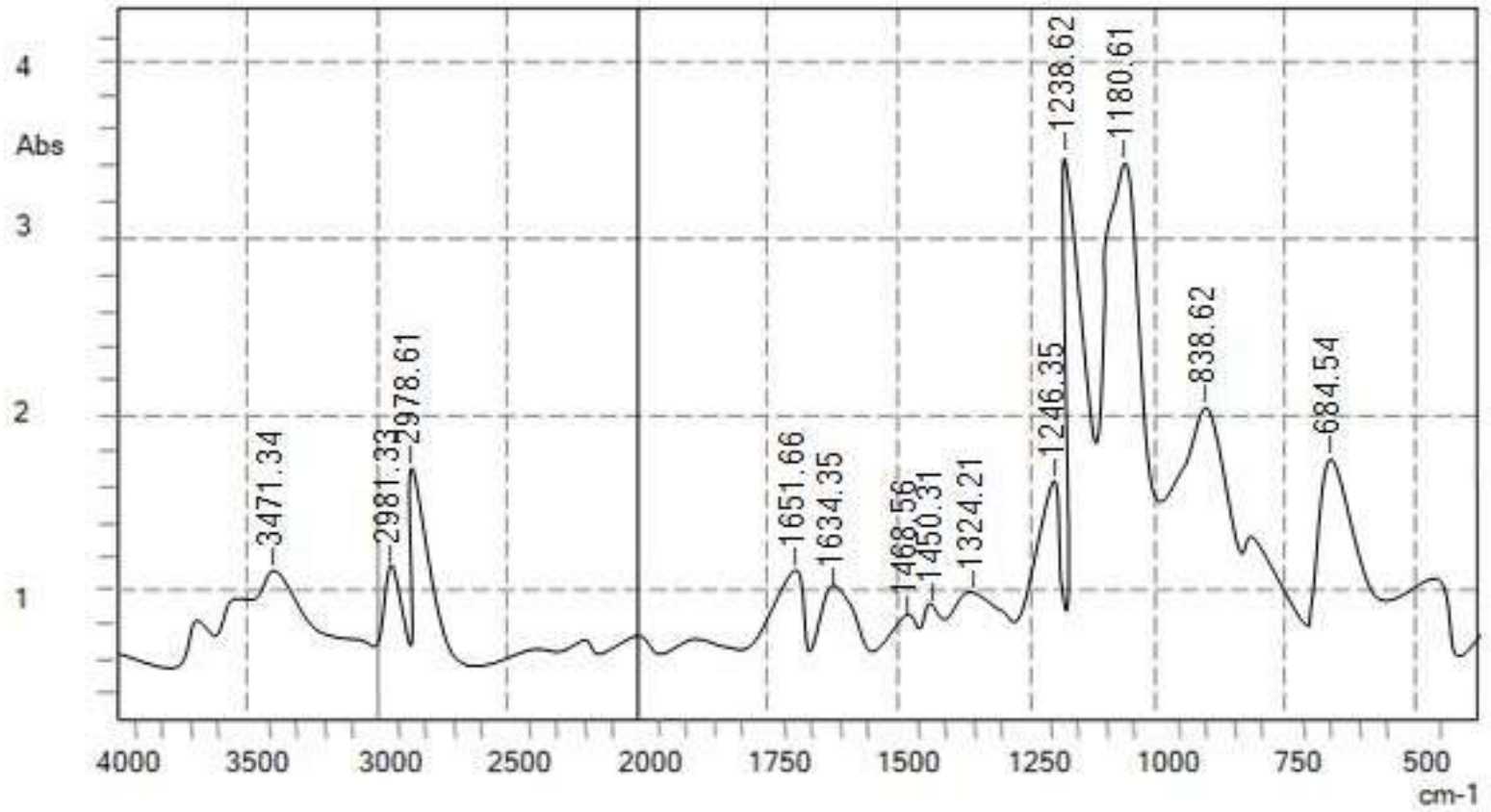
2500
2000
1750
1500
1250
1000
750
500
cm-1
Abs
4
3
2
1

ODAZ 02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1246.35
1238.62
1180.61
838.62
684.54
4000
3500
3000
2500
2000
1750
1500
1250
1000
750
500
cm-1

ODAZ 03

Abs
4
3
2
1
4000
3500
3000
2500
2000
1750
1500
1250
1000
750
500
cm-1
3331.53
2988.73
2976.57
2593.42
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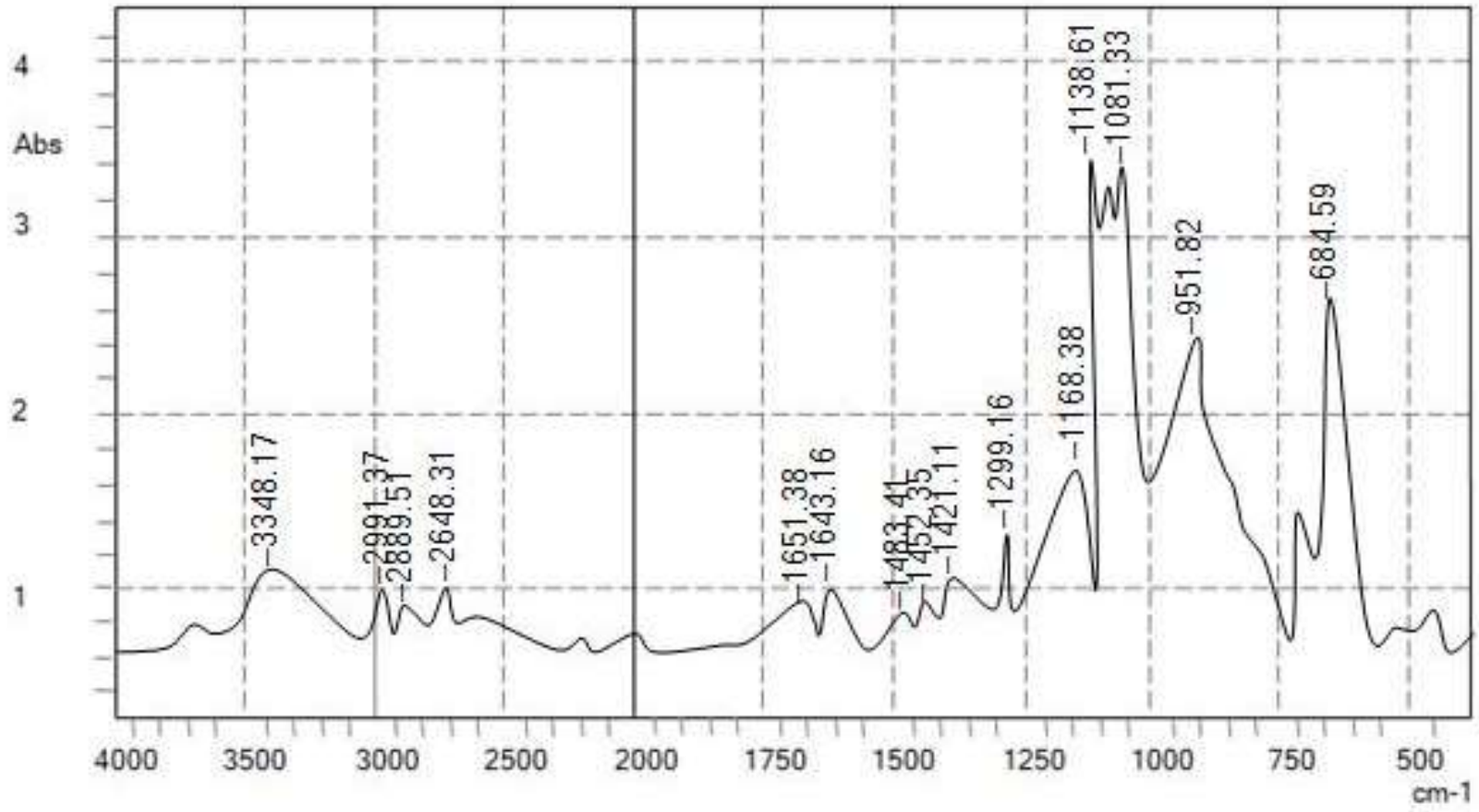
890.41
648.67

ODAZ04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2
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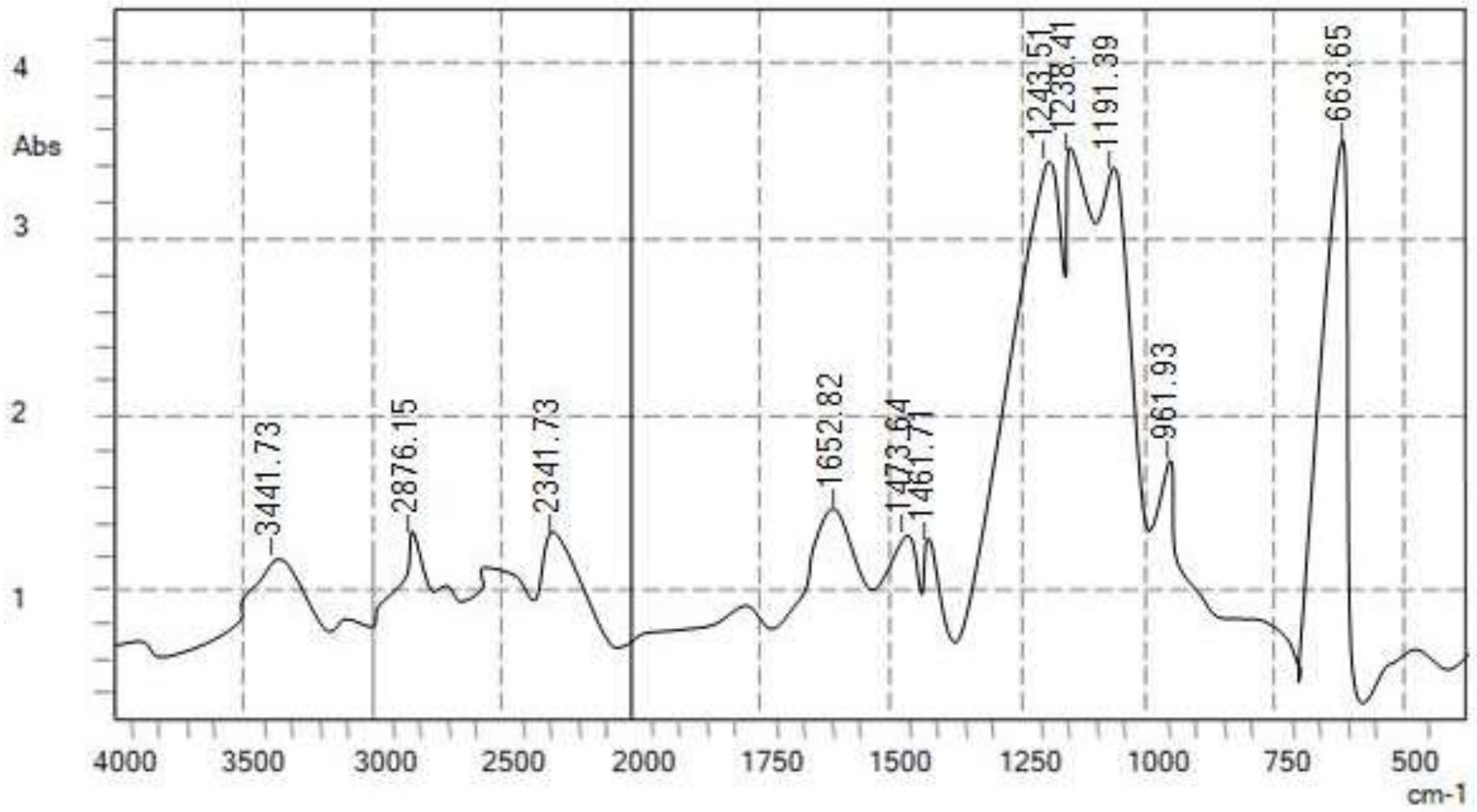
1452.35
1421.11
1299.16
1168.38
1138.61
1081.33
951.82
684.59
4000
3500
3000
2500
2000
1750
1500
1250
1000
750
500
cm-1

ODAZ05


4
Abs
3
2
1
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2876.15
2341.73
1652.82
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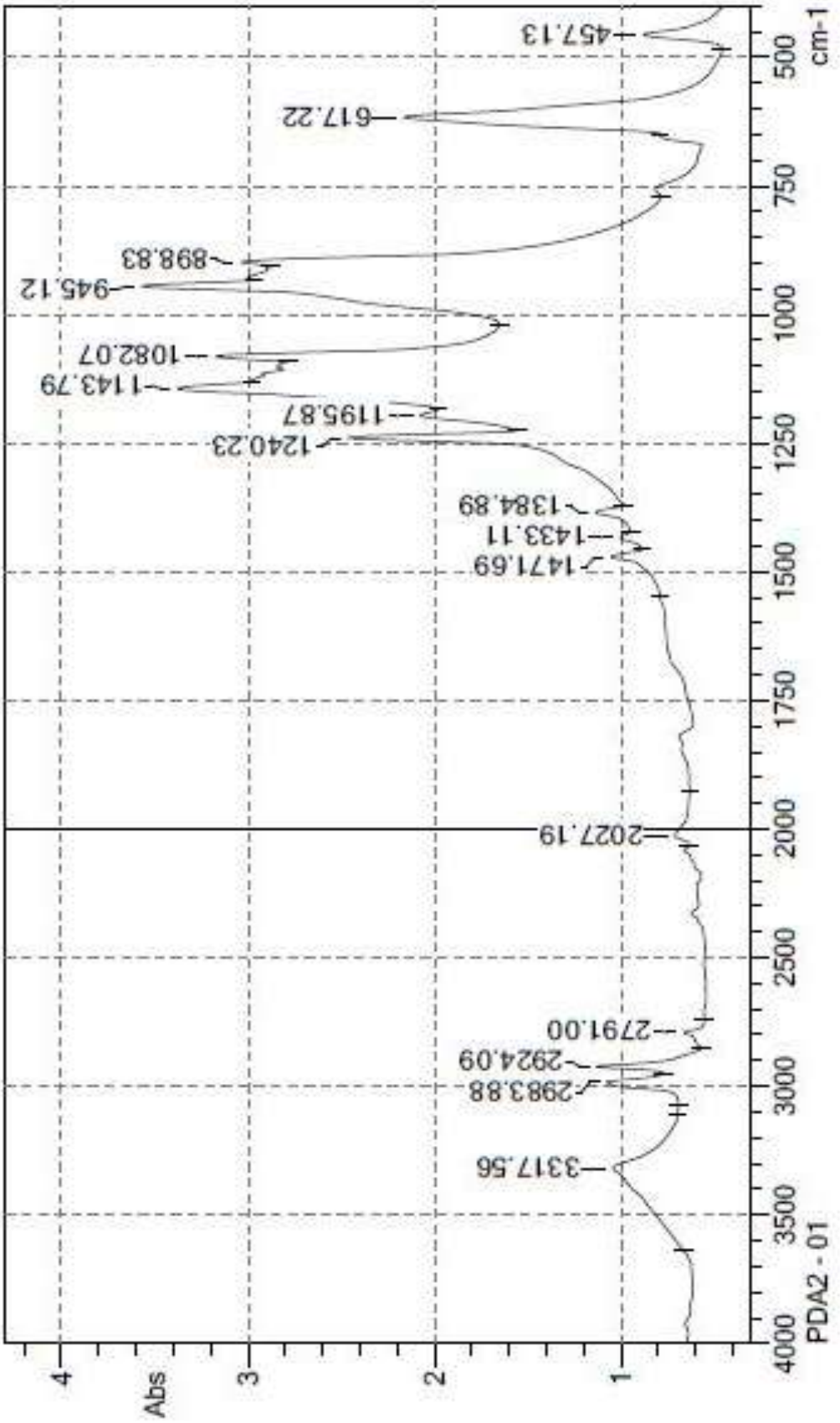
1461.71
1243.51
1238.41
1191.39
961.93
663.65
4000
3500
3000
2500
2000
1750
1500
1250
1000
750
500
cm-1

ODAZ 06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1471.69
2027.19
2791.00
2924.09
2983.88
3317.56
cm-1
4000
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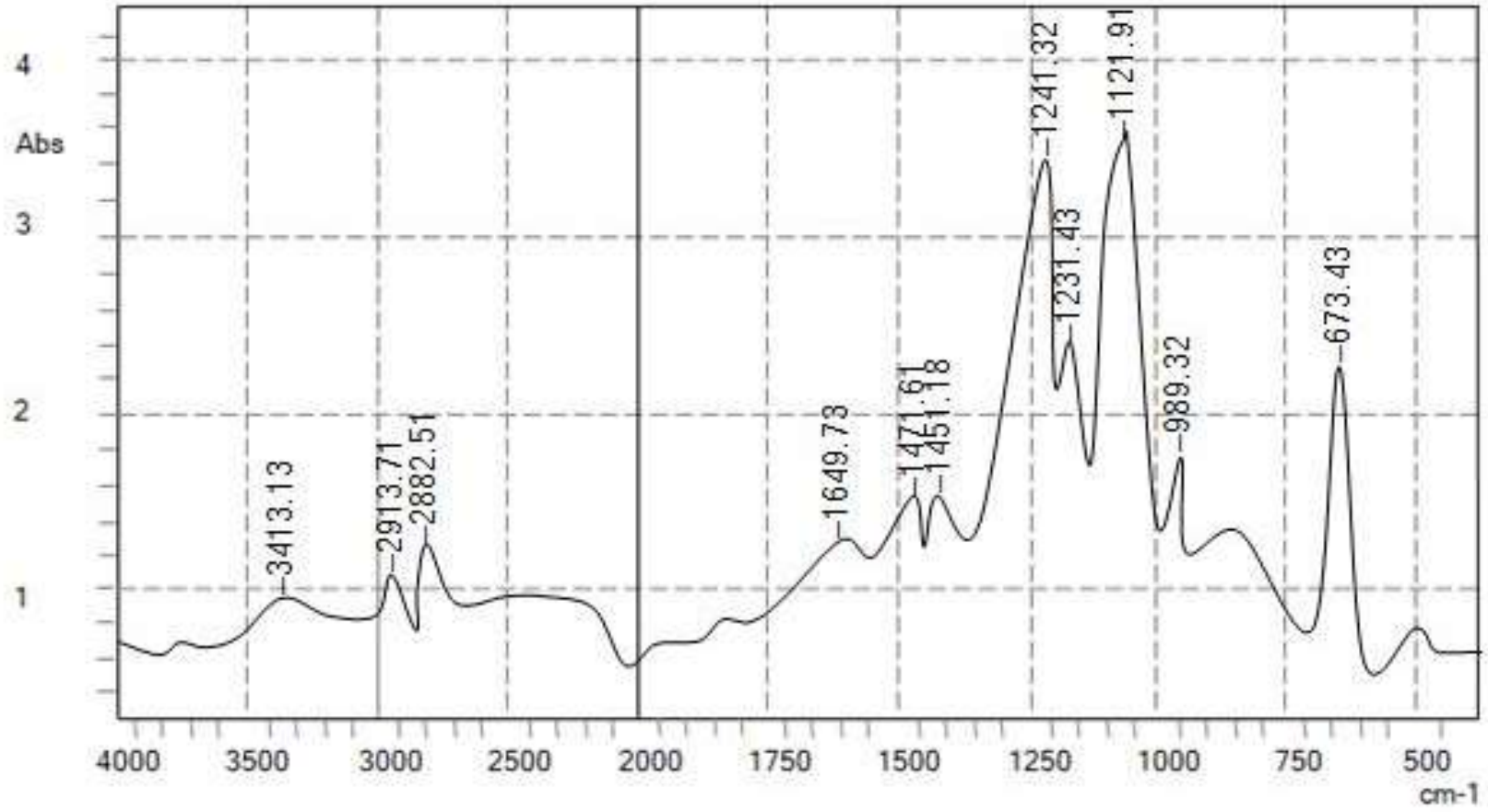
2000
1750
1500
1250
1000
750
500
PDA2 - 01
Abs
4
3
2
1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3
2
1
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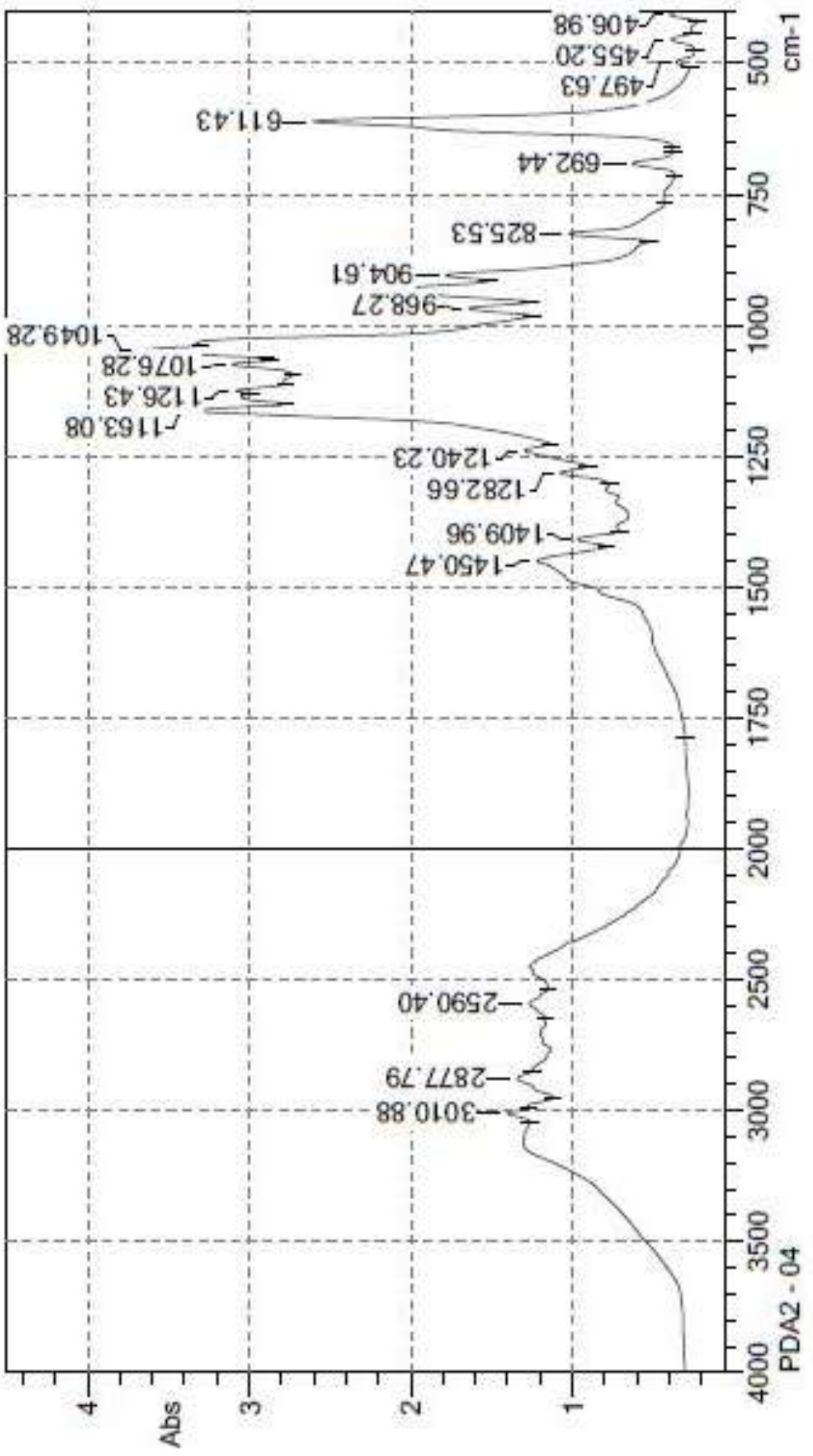
1649.73
1471.61
1451.18
1241.32
1231.43
1121.91
989.32
673.43
4000
3500
3000
2500
2000
1750
1500
1250
1000
750
500
cm-1

PDAZ02

649.71
802.31
953.42
1017.32
1132.43
1231.01
1248.12
1456.73
1470.73
1653.18
2597.23
2783.91
2971.32
3318.15
4000
3500
3000
2500
2000
1750
1500
1250
1000
750
500
cm-1
4
Abs
3
2
1
PDAZ 03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1240.23
1282.66
1409.96
1450.47
2590.40
2877.79
3010.88
cm-1
500
750
1000
1250
1500
1750
2000
2500
3000
3500
4000
PDA2 - 04
Abs
1
2
3
4

617.22
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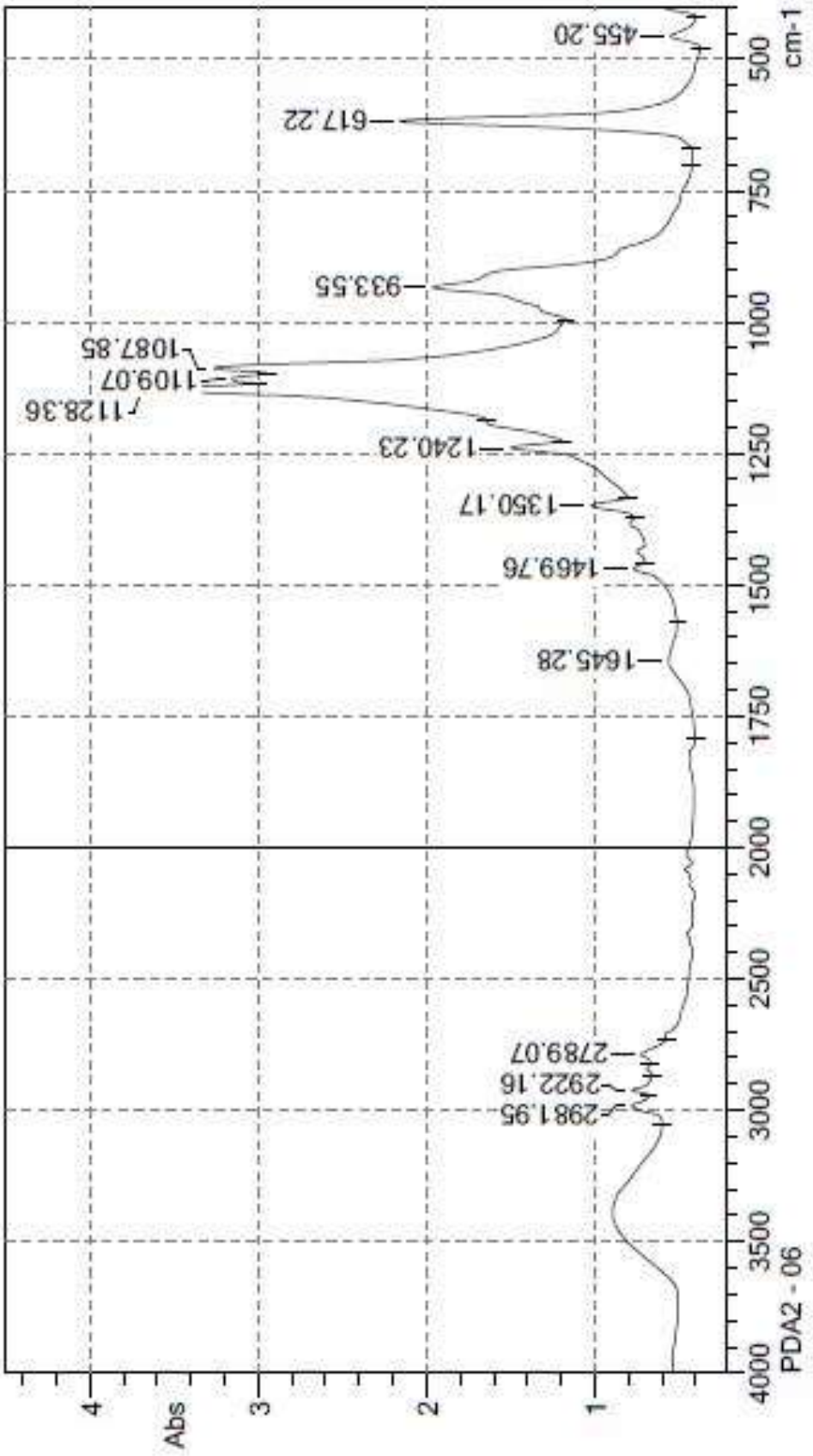
Abs
cm-1
PDA2 - 05


Abs
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3
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1
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cm-1
PDA2 - 06
2981.95
2922.16
2789.07
1645.28
1469.76
1350.17
1240.23
1128.36
1109.07
1087.85
933.55
617.22
455.20

^{1}H NMR SPECTRAL ANALYSIS[101, 102]

The structure of synthesized compounds was predicted by FT-1H NMR, 13C NMR Spectrophotometer. The sample was dissolved in DMSO and the values were measured in δ ppm and the predicted values were reported as follows.

ODAZ

Groups assigned	**Chemical shift (ppm)**
C-H (Benzylideimine)	7.1,7.4
C-H (Benzylideimine)	6.7-6.8
OH	4.9
NH (Hydrazide)	6.9

ODAZ 03

Groups assigned	**Chemical shift (ppm)**
C-H (Benzylideimine)	7.2-7.4
C-H (Benzylideimine)	6.6-6.8
N-CH_2-N(Methylene)	3.71
OH	4.9
CH_2(Piperidine)	1.49,2.23

ODAZ 05

Groups assigned	**Chemical shift (ppm)**
C-H (Benzylideimine)	7.2-7.3
C-H (Benzylideimine)	6.7-6.8
N-CH_2-N(Methylene)	3.73
OH	4.9
CH_2	2.46-2.47
CH_3(Methyl)	2.26

ODAZ 06

Groups assigned	**Chemical shift (ppm)**
C-H (Benzylideimine)	7.1-7.3
C-H (Benzylideimine)	6.7-6.8
N-CH_2-N(Methylene)	3.74
OH	5.1
CH_2	2.36-2.38, 3.64-3.66

PDAZ

Groups assigned	**Chemical shift (ppm)**
C-H (Benzylideimine)	7.4,7.5
C-H (Benzylideimine)	6.7,6.8
NH (Hydrazide)	6.9
OH	4.9

PDAZ 03

Groups assigned	**Chemical shift (ppm)**
C-H (Benzylideimine)	7.3-7.5
C-H (Benzylideimine)	6.7-6.8
OH	5.1
N-CH_2-N(Methylene)	3.73
CH_2(Piperidine)	1.51,2.25

PDAZ 05

Groups assigned	**Chemical shift (ppm)**
C-H (Benzylideimine)	7.3-7.4
C-H (Benzylideimine)	6.6-6.8
OH	5.0
N-CH_2-N(Methylene)	3.72
CH_2(Methylene)	2.44-2.47
CH_3(Methyl)	2.28

PDAZ 06

Groups assigned	**Chemical shift (ppm)**
C-H (Benzylideimine)	7.3-7.4
C-H (Benzylideimine)	6.6-6.7
OH	5.1
N-CH_2-N(Methylene)	3.73
CH_2	3.65-3.67, 2.37-2.38

13C NMR

ODAZ

Groups assigned	**Chemical shift (ppm)**
CH(Benzene)	121.9,132.8,116.4,131.2
C(Benzene)	161.4,127.3
C(imine)	155.2
C(Thiocarboxyl)	157.8

ODAZ 03

Groups assigned	**Chemical shift (ppm)**
CH(Benzene)	121.7,133.2,116.3,130.8
C(Benzene)	161.5,127.7
C(imine)	155.3
C(Thiocarboxyl)	177.4
N-CH_2-N	66.2
CH_2(Piperidine)	25.6,52.6, 25.6,52.6,25.6

ODAZ 05

Groups assigned	**Chemical shift (ppm)**
CH(Benzene)	121.4,132.7,117.1,130.4
C(Benzene)	162.2,127.3
C(imine)	155.7
C(Thiocarboxyl)	177.2
N-CH_2-N	66.4
CH_2(Cyclohexane)	49.6,55.2, 49.6,55.2
CH_3(Aliphatic)	43.4

ODAZ 06

Groups assigned	**Chemical shift (ppm)**
CH(Benzene)	122.4,131.9,116.9,131.2
C(Benzene)	161.7,128.2
C(imine)	155.1
C(Thiocarboxyl)	177.7
CH_2(Aliphatic)	66.8
CH_2(Cyclohexane)	49.9,67.2, 49.9,67.2

PDAZ

Groups assigned	**Chemical shift (ppm)**
CH(Benzene)	116.9,130.8,116.9,130.8
C(Benzene)	161.6,122.9
C(imine)	155.2
C(Thiocarboxyl)	158.1

PDAZ 03

Groups assigned	**Chemical shift (ppm)**
CH(Benzene)	116.3,131.2,116.3, 131.2
C(Benzene)	117.1,126.3
C(imine)	155.6
C(Thiocarboxyl)	178.1
CH_2(Aliphatic)	66.8
CH_2(Piperidine)	25.8,52.5, 25.8,52.5, 26.1

PDAZ 05

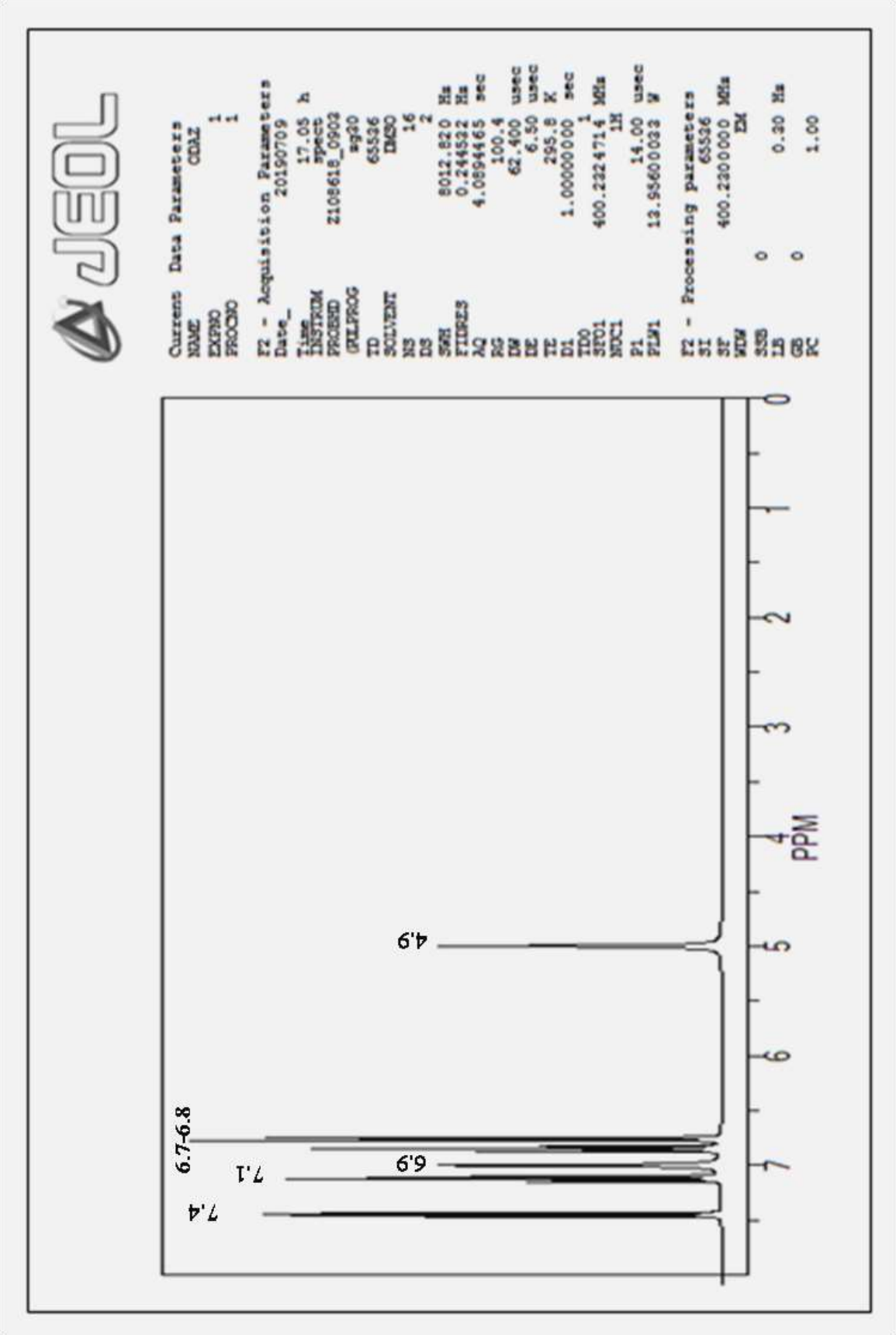
Groups assigned	**Chemical shift (ppm)**
CH(Benzene)	116.8,131.2,116.8,131.2
C(Benzene)	161.3,121.9
C(imine)	155.1
C(Thiocarboxyl)	177.8
N-CH_2-N	66.2
CH_2(Cyclohexane)	48.9,54.8, 48.9,54.8
CH_3(Aliphatic)	43.7

PDAZ 06

Groups assigned	**Chemical shift (ppm)**
CH(Benzene)	117.4,131.1, 117.4,131.1
C(Benzene)	160.9,122.2
C(imine)	155.3
C(Thiocarboxyl)	177.2
N-CH_2-N	66.3
CH_2(Cyclohexane)	50.5,66.2, 50.5,66.2

1H NMR

ODAZ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SOLVENT DMSO
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DS 2
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FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 100.4
DW 62.400 usec
DE 6.50 usec
TE 295.8 K
D1 1.00000000 sec
TD0 1
SFO1 400.2224714 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.95600033 W
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GB
PC 1.00
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6.9
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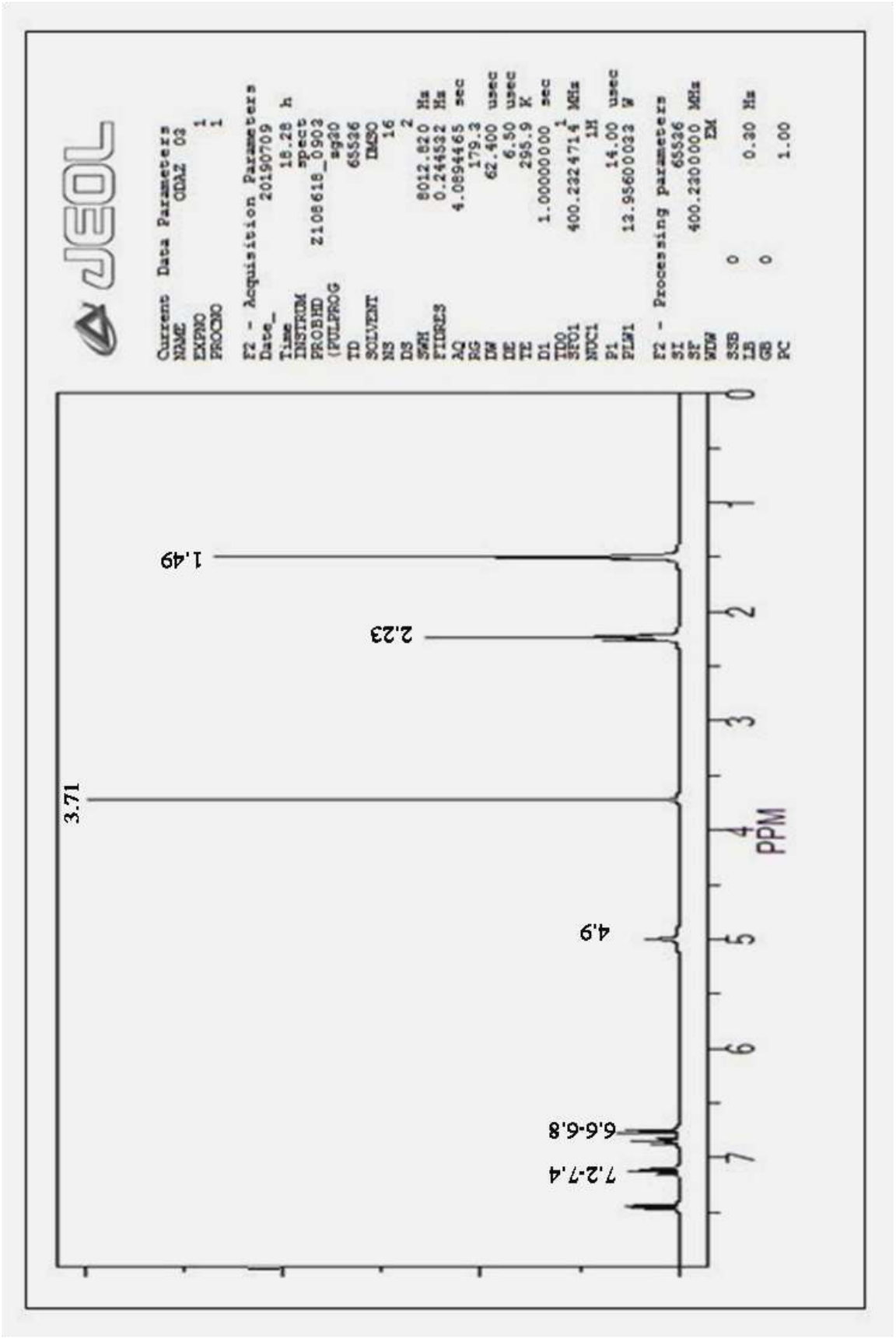
PPM

ODAZ 03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DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 179.3
DW 62.400 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1
SFO1 400.2324714 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.95600032 W
F2 - Processing parameters
SI 65536
SF 400.2300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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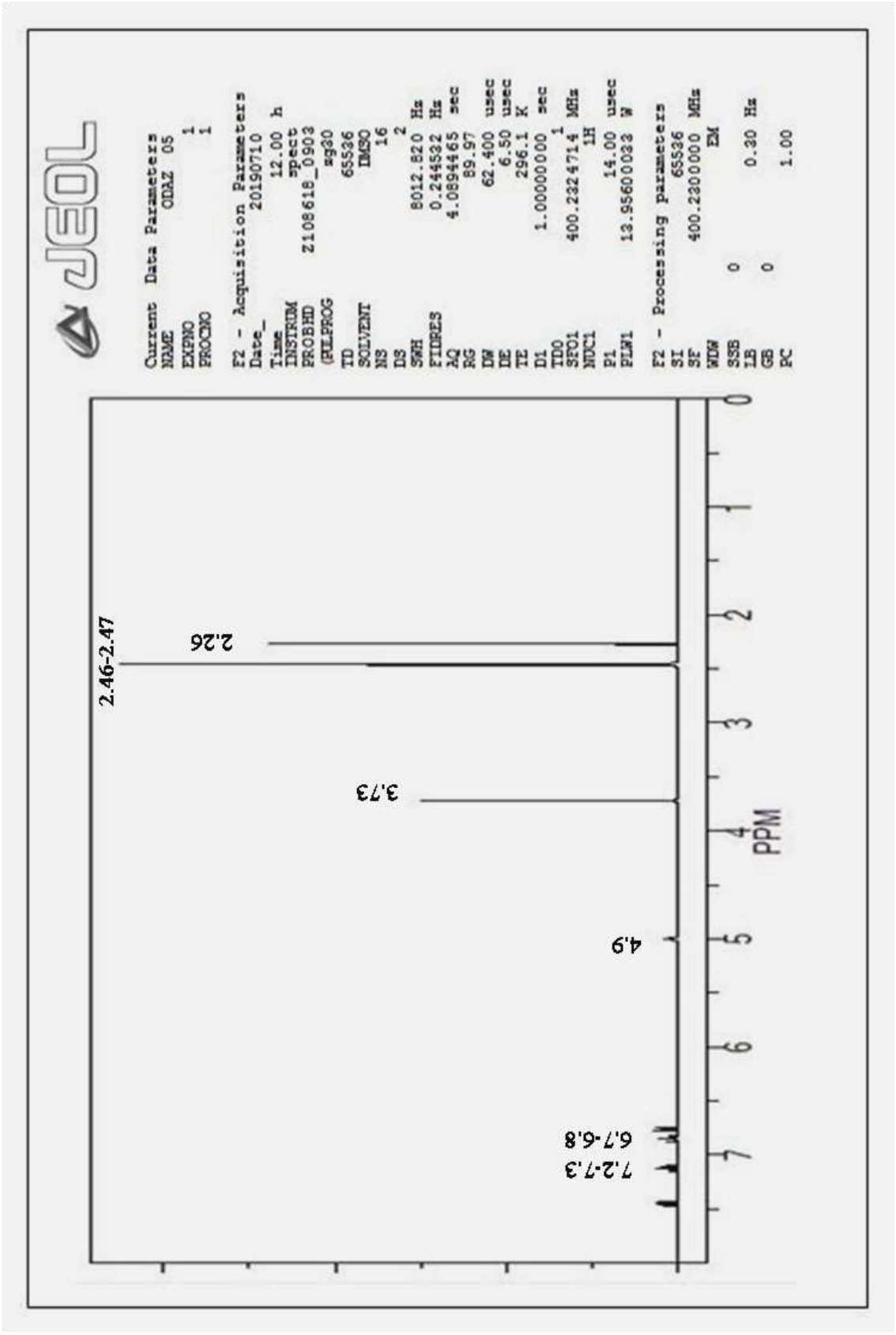
4.9
6.6-6.8
7.2-7.4
PPM

ODAZ 05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SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 89.97
DW 62.400 usec
DE 6.50 usec
TE 296.1 K
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TD0 1
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NUC1 1H
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WDW EM
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LB 0.30 Hz
GB 0
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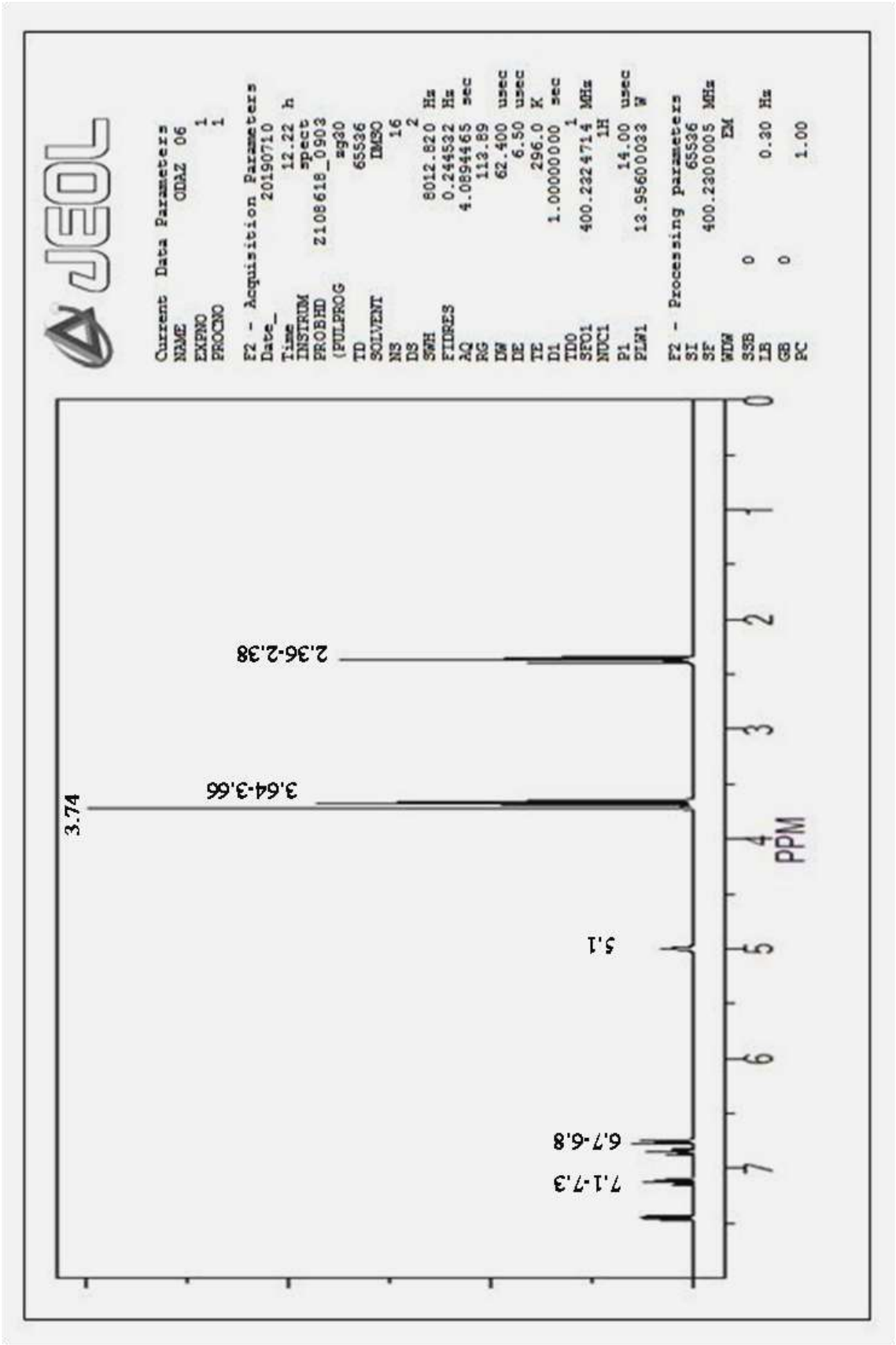
3.73
4.9
7.2-7.3
6.7-6.8
PPM

ODAZ 06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PROCNO 1
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SOLVENT DMSO
NS 16
DS 2
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FIDRES 0.244532 Hz
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RG 113.89
DW 62.400 usec
DE 6.50 usec
TE 296.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.2324714 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.95600033 W
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SF 400.2300005 MHz
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LB 0.30 Hz
GB 0
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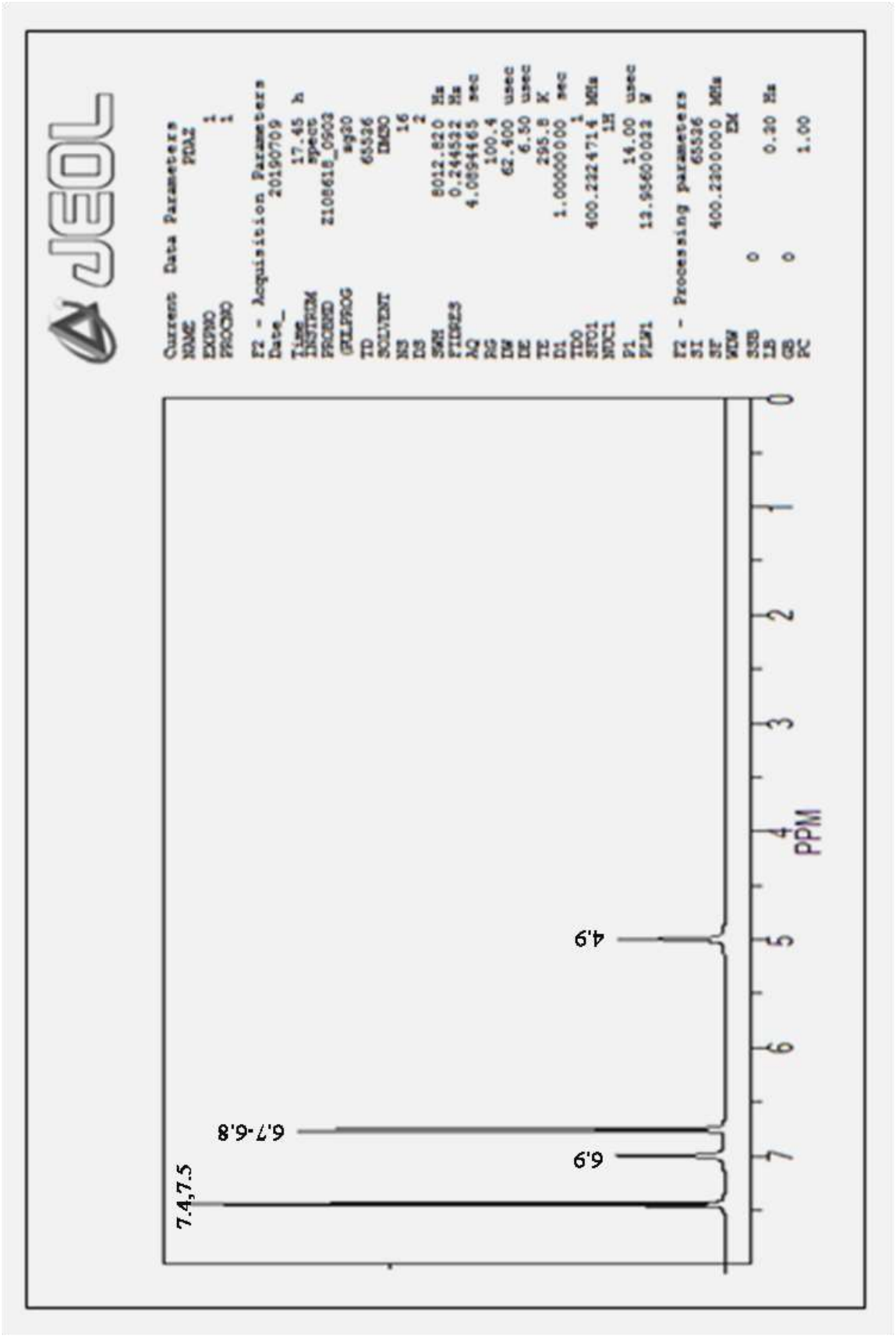
3.64-3.66
2.36-2.38
5.1
6.7-6.8
7.1-7.3
PPM

PDAZ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PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 100.4
DW 62.400 usec
DE 6.50 usec
TE 295.8 K
D1 1.00000000 sec
TD0 1
SFO1 400.2224714 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.56600023 W
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SF 400.2200000 MHz
WDW EM
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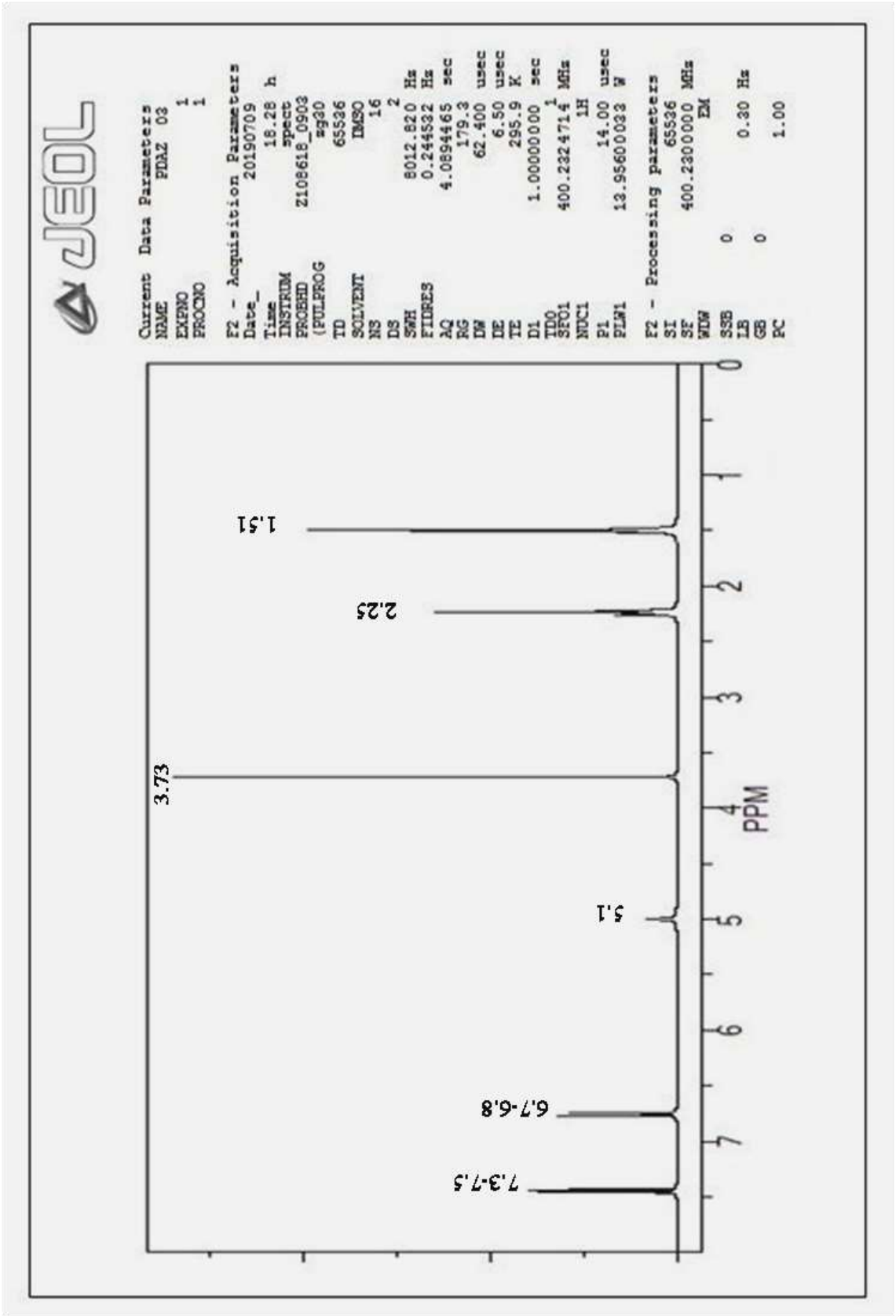
GB 0
PC 1.00
7.4,7.5
6.7-6.8
6.9
4.9
PPM

PDAZ 03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PROCNO 1
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(PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 179.3
DW 62.400 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1
SFO1 400.2324714 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.95600033 W
F2 - Processing parameters
SI 65536
SF 400.2300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
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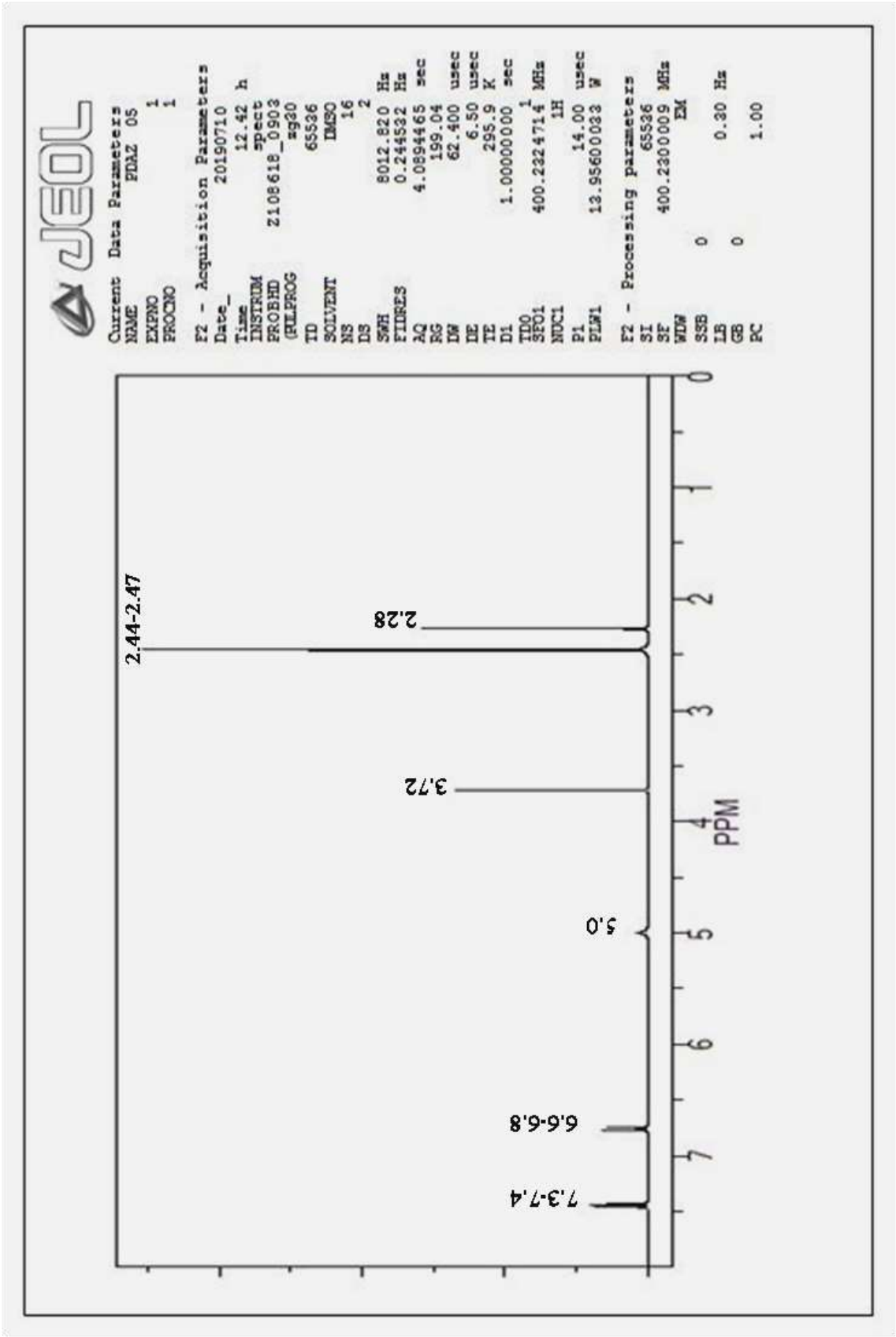
PC 1.00
1.51
2.25
3.73
5.1
6.7-6.8
7.3-7.5
PPM

PDAZ 05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EXPNO 1
PROCNO 1
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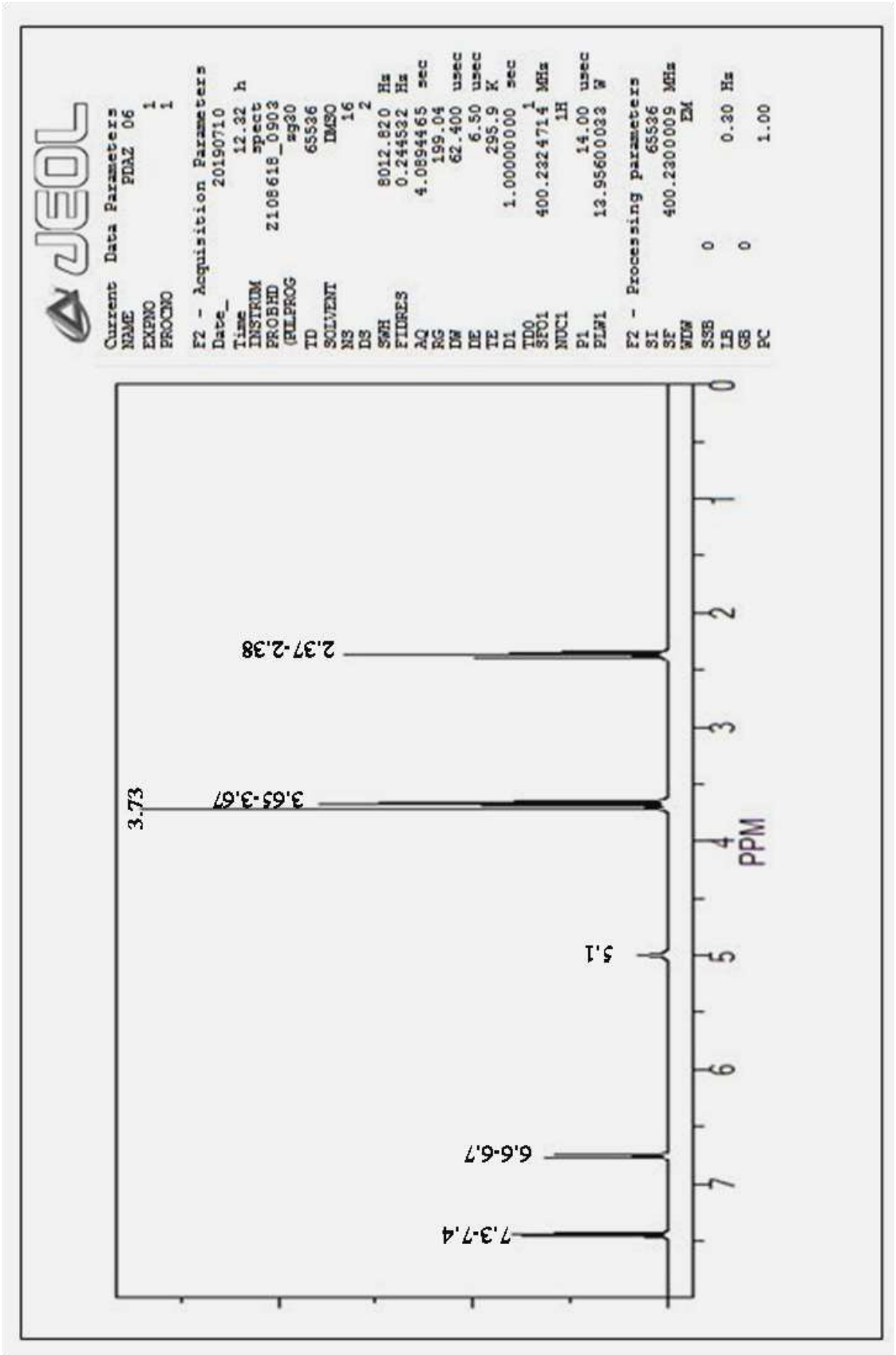
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 199.04
DW 62.400 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1
SFO1 400.2324714 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.95600033 W
F2 - Processing parameters
SI 65536
SF 400.2300009 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
2.44-2.47
2.28
3.72
5.0
6.6-6.8
7.3-7.4
PPM
0
1
2
3
4
5
6
7

PDAZ 06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PROCNO 1
F2 - Acquisition Parameters
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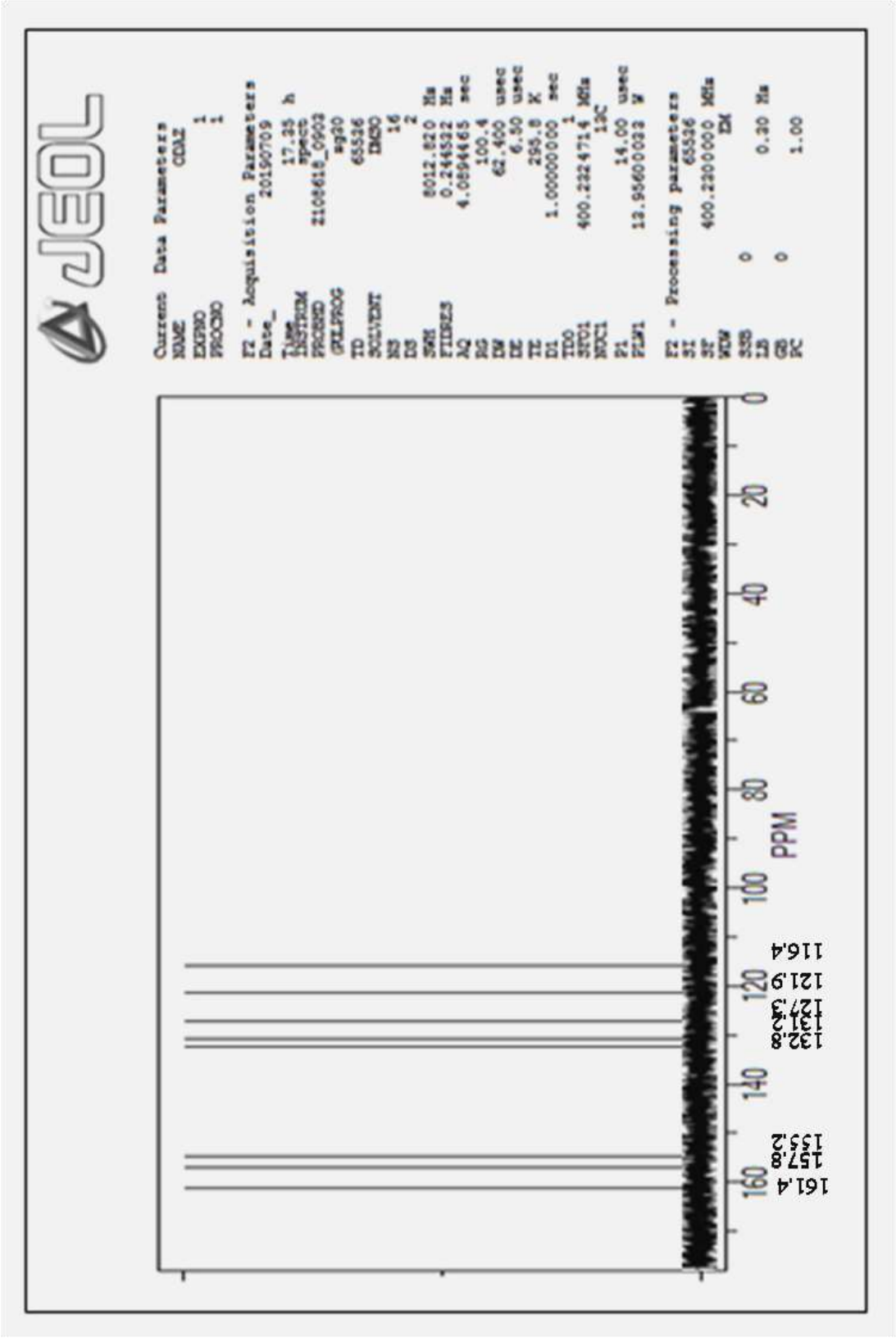
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 199.04
DW 62.400 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1
SFO1 400.2324714 MHz
NUC1 1H
P1 14.00 usec
PLW1 13.95600033 W
F2 - Processing parameters
SI 65536
SF 400.2300009 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
2.37-2.38
3.65-3.67
3.73
5.1
6.6-6.7
7.3-7.4
PPM

13C NMR:

ODAZ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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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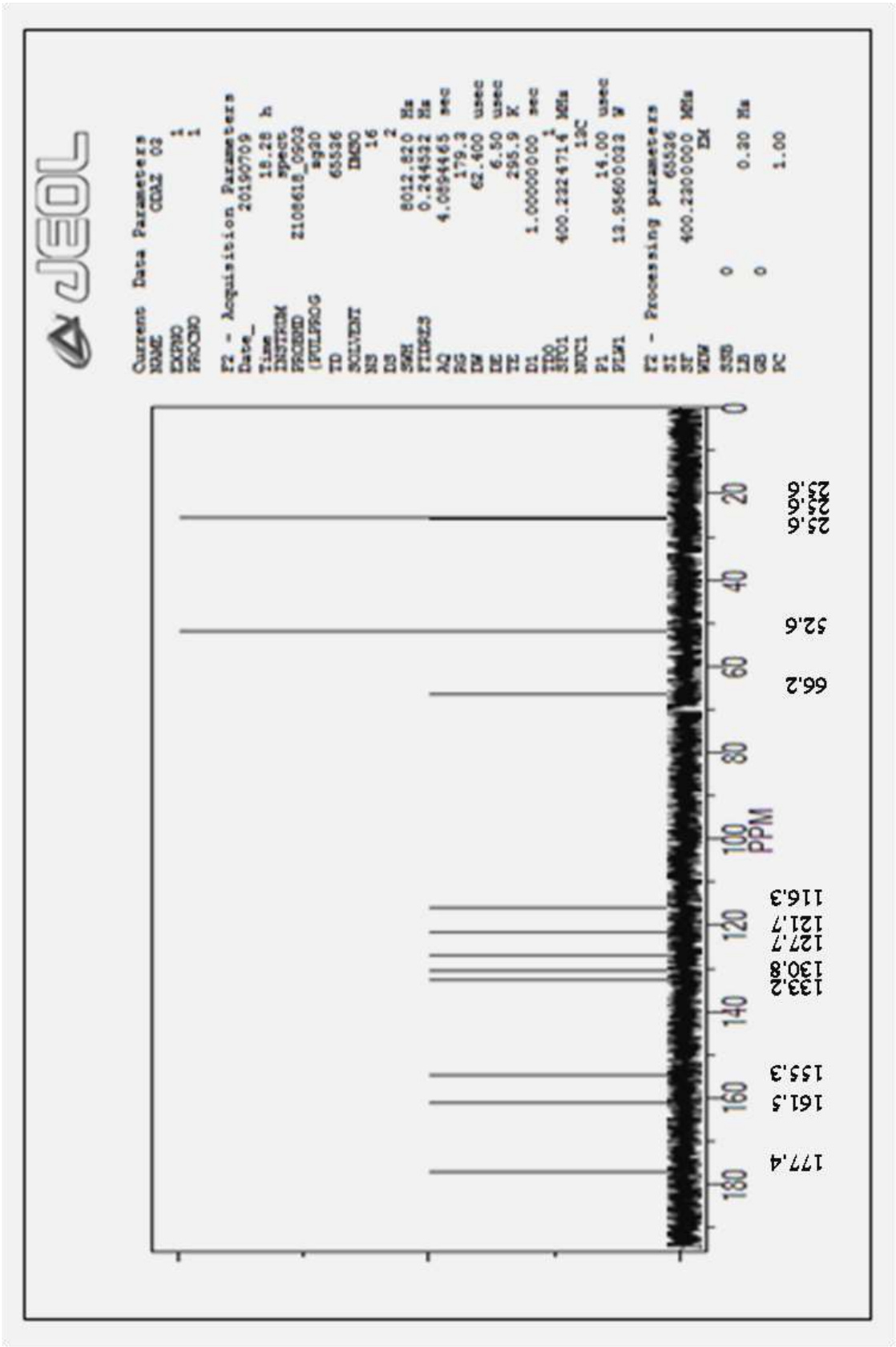
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 100.4
DW 62.400 usec
DE 6.50 usec
TE 298.8 K
D1 1.00000000 sec
TD0 1
SFO1 400.2224714 MHz
NUC1 13C
P1 14.00 usec
PLW1 13.95600033 W
F2 - Processing parameters
SI 65536
SF 400.2300000 MHz
WDW EM
SSB 0 0.30 Hz
LB
GB
PC 1.00
PPM
0
20
40
60
80
100
120
140
160
116.4
121.9
127.3
131.2
132.8
155.2
157.8
161.4

ODAZ 03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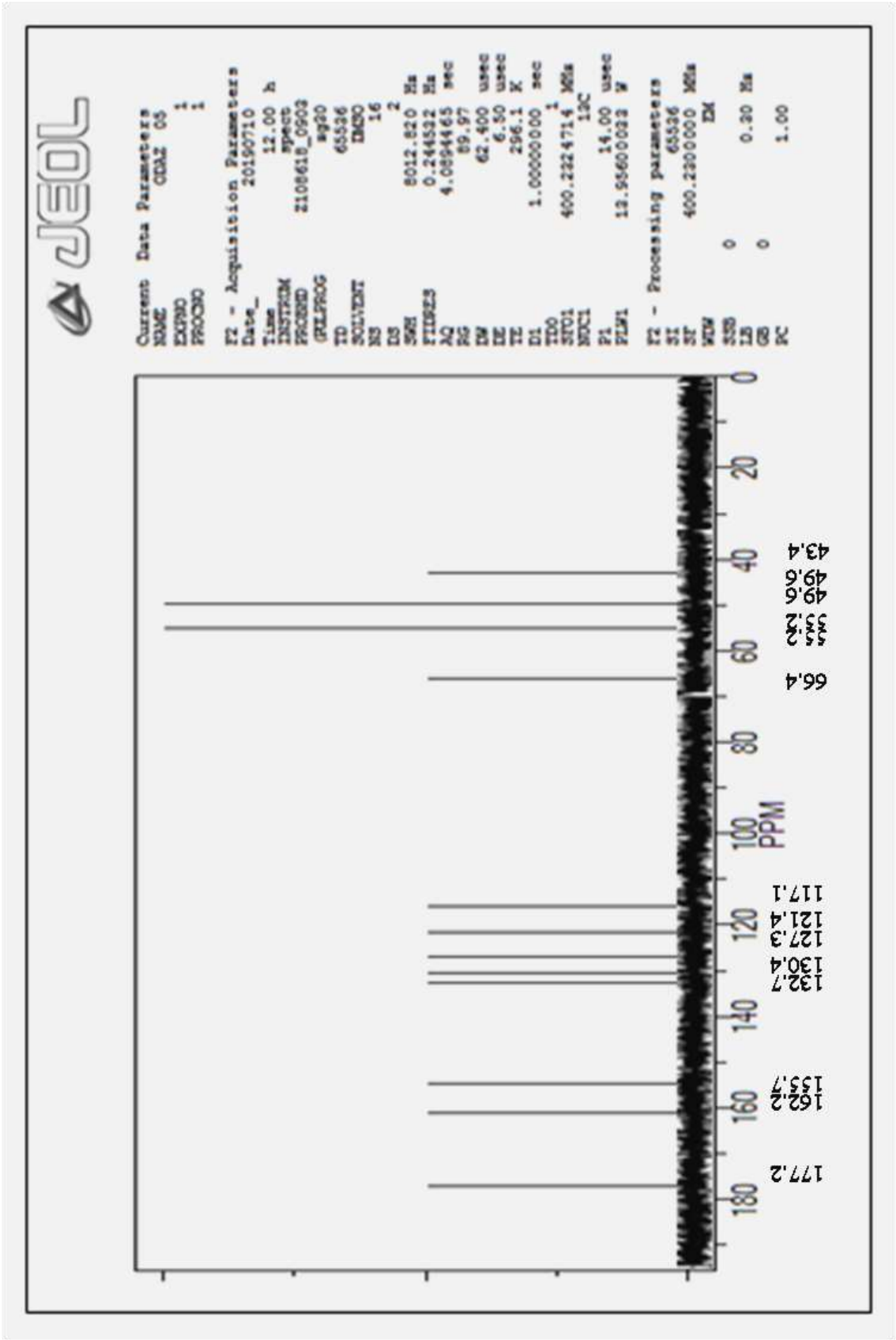
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190709
Time 18.28 h
INSTRUM spect
PROBHD 2108618_0903 (PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 179.3
DW 62.400 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1
SFO1 400.2224714 MHz
NUC1 13C
P1 14.00 usec
PLW1 12.95600033 W
F2 - Processing parameters
SI 65536
SF 400.2200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
177.4
161.5
155.3
133.2
130.8
127.7
121.7
116.3
66.2
52.6
25.6
25.6
PPM

ODAZ 05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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190710
Time 12.00 h
INSTRUM spect
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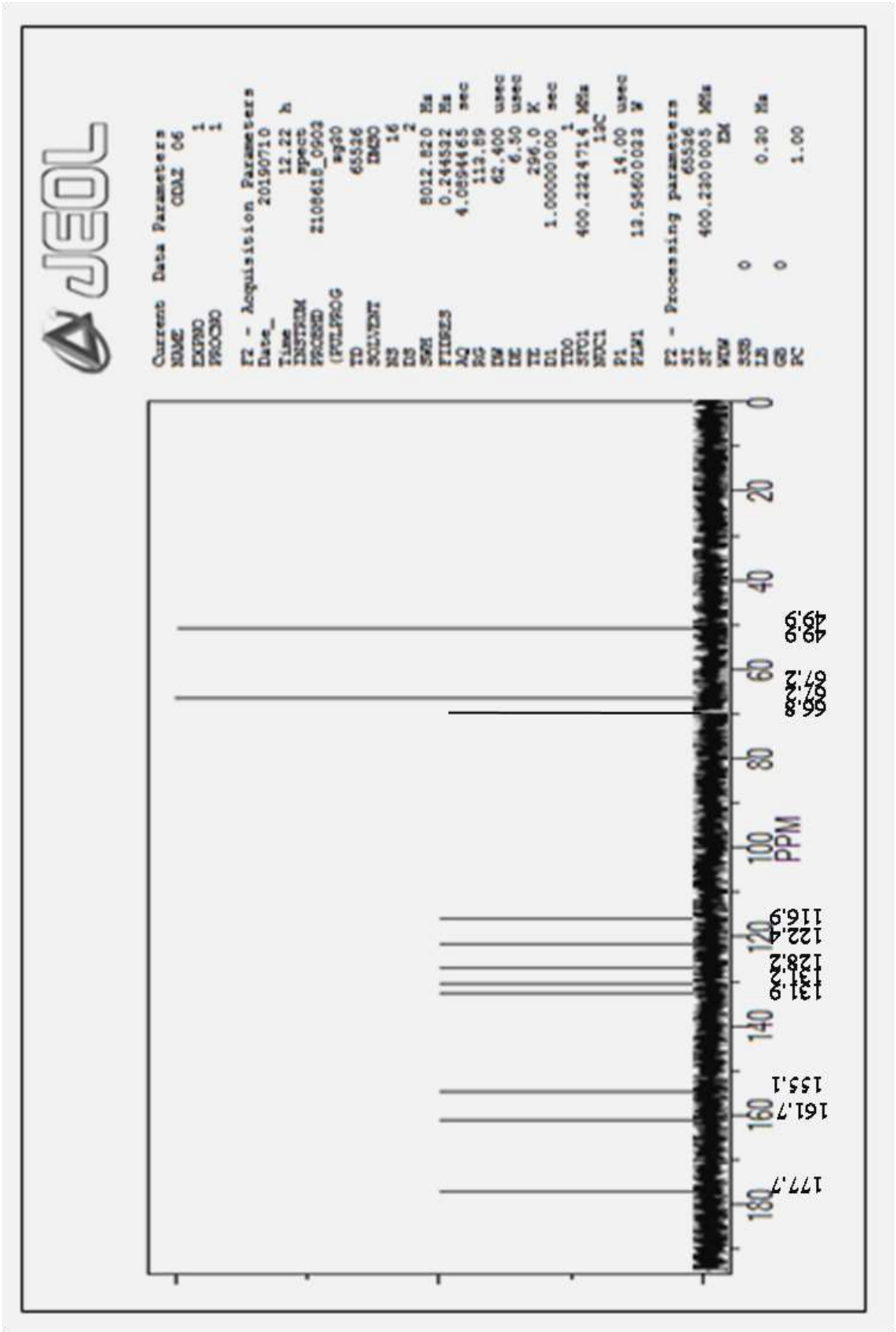
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 89.97
DW 62.400 usec
DE 6.50 usec
TE 296.1 K
D1 1.00000000 sec
TD0 1
SFO1 400.2224714 MHz
NUC1 13C
P1 14.00 usec
PLW1 12.95600033 W
F2 - Processing parameters
SI 65536
SF 400.2300000 MHz
WDW EM
SSB 0 0.30 Hz
LB
GB 0
PC 1.00
0
20
40
60
80
100
120
140
160
180
PPM
177.2
162.2
155.7
132.7
130.4
127.3
121.4
117.1
66.4
53.2
49.6
43.4

ODAZ 06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PROCNO 1
F2 - Acquisition Parameters
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Time 12.22 h
INSTRUM spect
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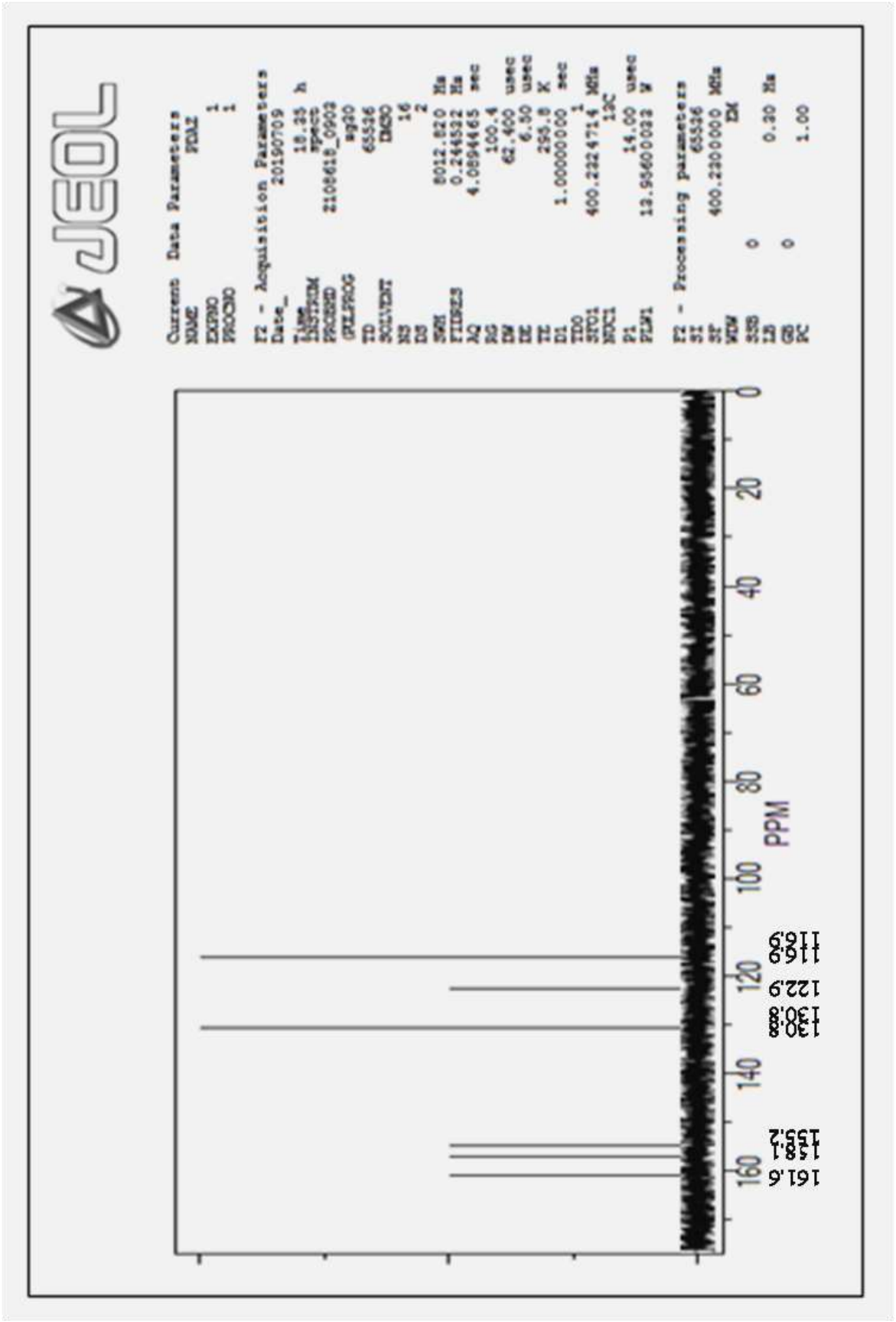
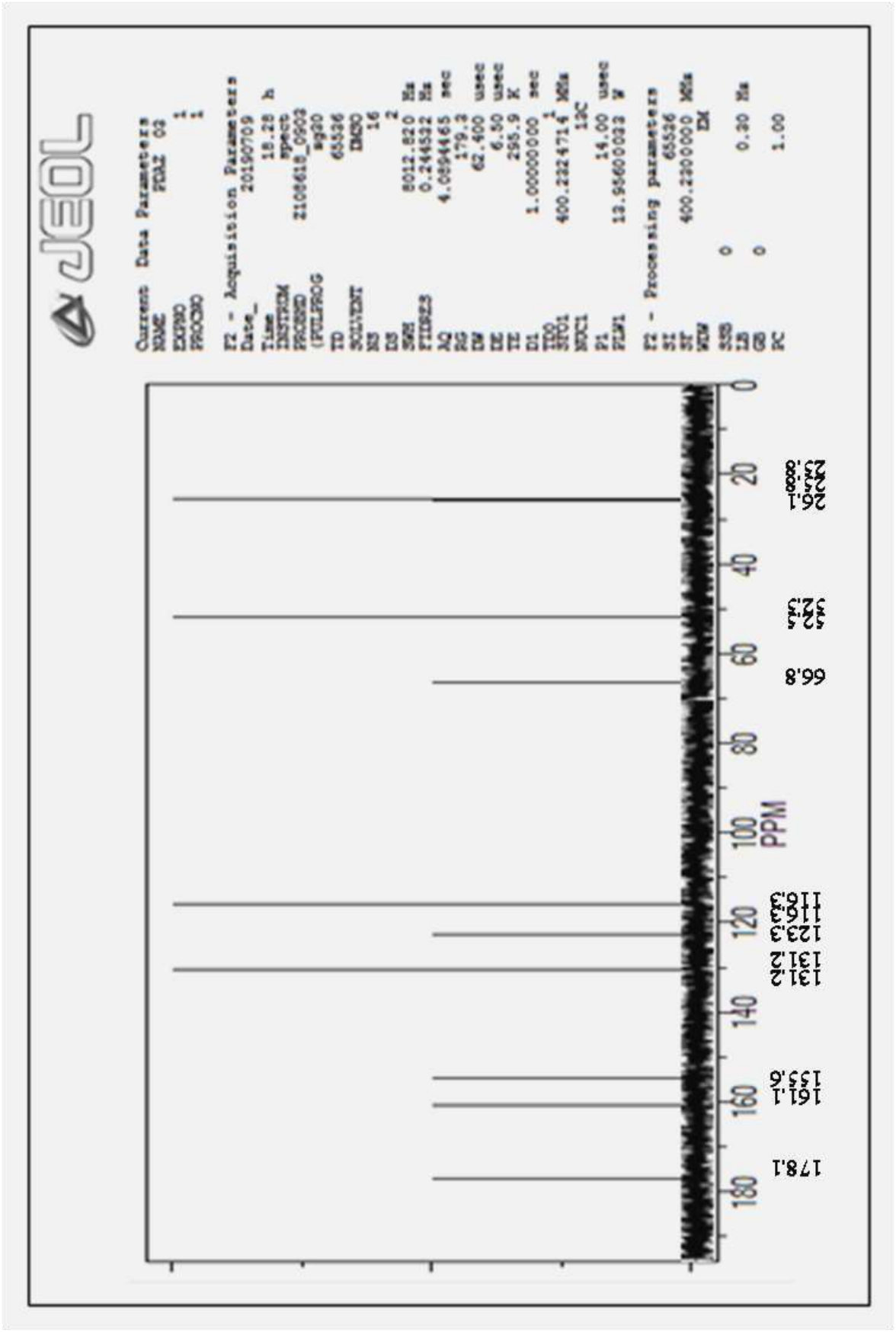
(PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 113.89
DW 62.400 usec
DE 6.50 usec
TE 296.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.2224714 MHz
NUC1 13C
P1 14.00 usec
PLW1 13.95600033 W
F2 - Processing parameters
SI 65536
SF 400.2300005 MHz
WDW EM
SSB 0 0.20 Hz
LB
GB
PC 1.00
0
20
40
60
80
100
120
140
160
180
PPM
49.9
67.2
69.8
116.9
122.4
128.2
131.9
155.1
161.7
177.7

PDAZ


JEOL
Current Data Parameters
NAME PDAZ
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190709
PPM
161.6
155.2
158.1
130.8
130.8
122.9
116.9
116.9

PDAZ 03


JEOL
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NAME PDAZ 03
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20190709
Time 18.28 h
INSTRUM spect
PROBHD 2108618_0003
(PULPROG zg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 179.2
DW 62.400 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1
SFO1 400.2224714 MHz
NUC1 13C
P1 14.00 usec
PLW1 13.96600003 W
F2 - Processing parameters
SI 65536
SF 400.2200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
178.1
161.1
155.6
131.2
131.2
123.3
116.3
116.3
66.8
32.5
32.5
26.1
25.8
PPM
0
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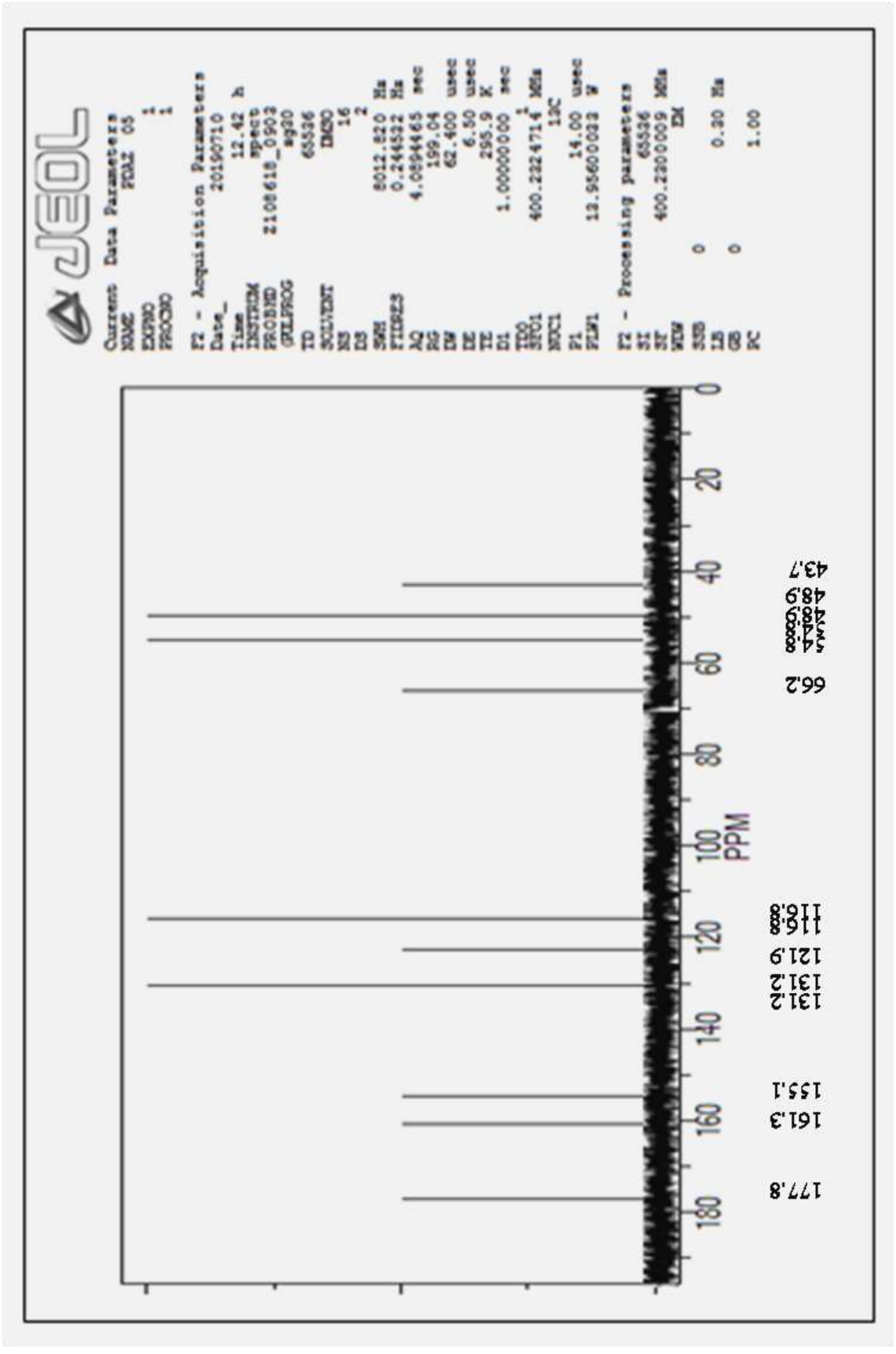
40
60
80
100
120
140
160
180

PDAZ 05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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
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PULPROG zgpg30
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 199.04
DW 62.400 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1
SFO1 400.2224714 MHz
NUC1 13C
P1 14.00 usec
PLW1 13.95600033 W
F2 - Processing parameters
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SF 400.2300009 MHz
WDW EM
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GB
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PPM
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120
140
160
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177.8
161.3
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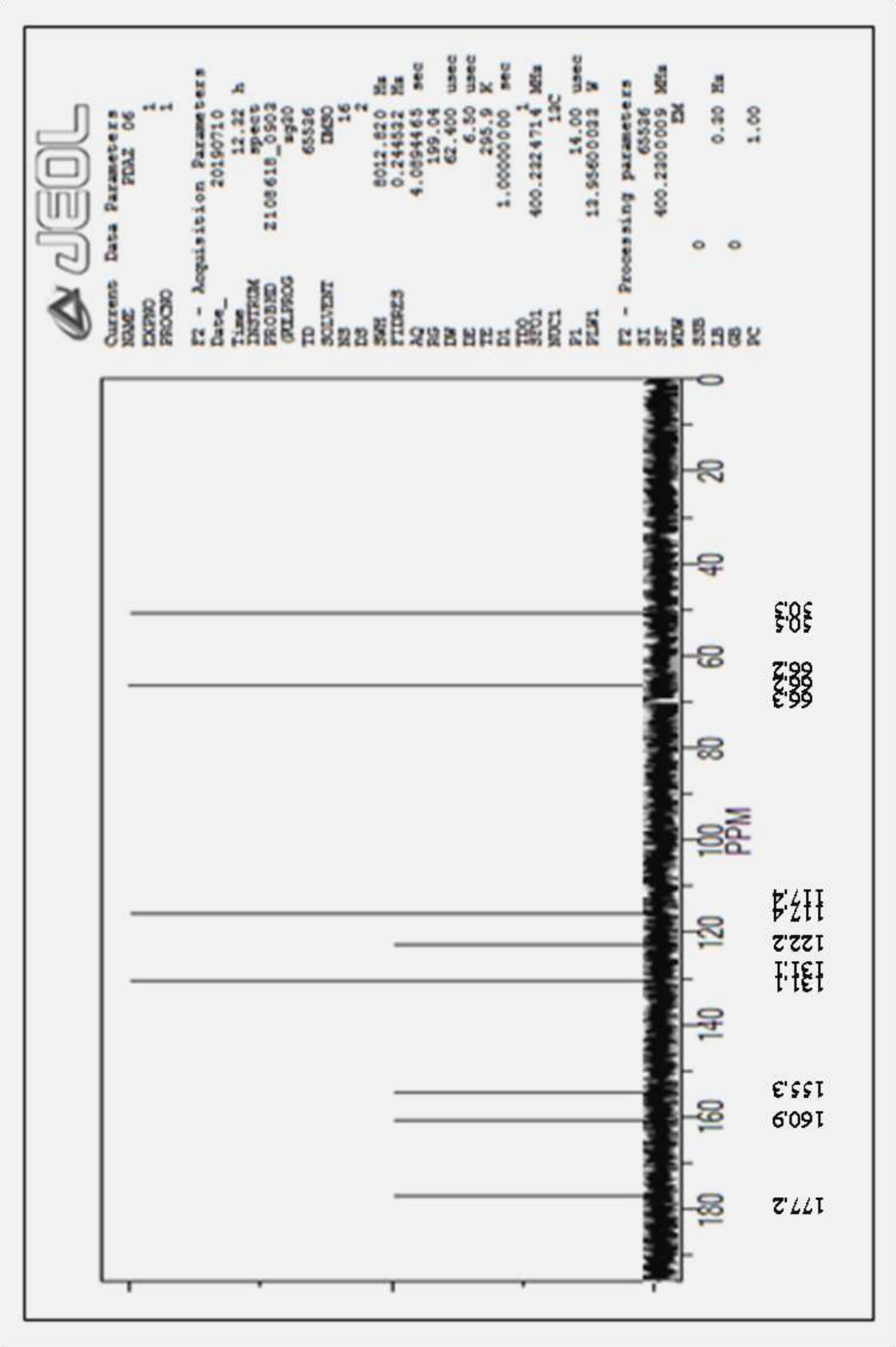
PDAZ 06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EXPNO 1
PROCNO 1
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Time 12.32 h
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PULPROG zgdc
TD 65536
SOLVENT DMSO
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 4.0894465 sec
RG 199.04
DW 62.400 usec
DE 6.50 usec
TE 295.9 K
D1 1.00000000 sec
TD0 1
SFO1 400.2324714 MHz
NUC1 13C
P1 14.00 usec
PLW1 13.95600033 W
F2 - Processing parameters
SI 65536
SF 400.2300009 MHz
WDW EM
SSB 0 0.30 Hz
LB 0
GB 0
PC 1.00
0
20
40
60
80
100
120
140
160
180
PPM
177.2
160.9
155.3
131.1
122.2
117.4
66.3
66.2
30.5
30.3

BIOLOGICAL EVALUATION

EVALUATION OF ACUTE TOXICITY STUDIES[103-105]

The study was performed based on Miller and Tainer method. The method is used to determine LD_{50} value of the synthesized compounds. Male Albino mice (25-30 g) were used for this study (AKCP/IAEC/82/18-19). The animals were divided into 15 groups of 6 mice each. The synthesized compounds were administered orally. The animals were observed for 2h for death because of acute toxicity. The LD_{50} value of the synthesized compounds found to be 200mg/kg. The doses of test compounds were fixed based on their acute toxicity.

A. ANTICONVULSANT ACTIVITY [106]

Anti convulsant activity was carried out by using maximal electro shock (MES) induced convulsion method. Albino mice of either sex (25-30g) were used for the study and divide to 14 groups of 6 mices each. They were given electrical shock through corneal electrodes of 150mA for 0.2 sec by using electro convulsiometer. Group I were treated with 0.5% tween 80 suspension and served as a control. Group II were treated with phenytoin (25mg/kg) serve as standard.

Group III-XIV were treated with synthesized ODAZ 01,ODAZ 02, ODAZ 03, ODAZ 04, ODAZ 05, ODAZ 06,PDAZ 01,PDAZ 02, PDAZ 03, PDAZ 04, PDAZ 05, PDAZ 06 compounds (20 mg/kg) respectively. After 30 min, seizure induction onset time of tonic flexion, extension and clonic, phase was noted. The protective index was observed as reduction time of tonic extensor phase and all the data was observed as reduction time of tonic extensor phase and all the data (Mean±SEM) were analyzed statistically by students “t” test and tabulated in table No.6.

Anticonvulsant Activity

Table No: 6

S.No.	Treatment	Extensor(sec) (Mean±SEM)	Clonus(sec) (Mean±SEM)	Stupor(sec) (Mean±SEM)	Mortality
1.	Control	28.83±0.9098	22.67±0.8433	51.67±0.8819	Recovery
2.	STD	10.00±0.5774**	11.50±0.8851	28.17±0.6540	Recovery
3.	ODAZ 01	22.13±0.0014*	27.52±0.7654	39.54±0.3426	Recovery
4.	ODAZ 02	17.17±0.7032**	21.78±0.7865	32.14±0.5432	Recovery
5.	ODAZ 03	15.17±0.7032**	19.03±0.5643	29.67±0.8768	Recovery
6.	ODAZ 04	20.33±0.8028**	25.15±0.5123	34.45±0.7612	Recovery
7.	ODAZ 05	14.17±0.6009**	18.12±0.4325	24.15±0.5674	Recovery
8.	ODAZ 06	12.67±0.6146**	16.56±0.6123	22.15±0.4536	Recovery
9.	PDAZ 01	23.83±0.4014*	28.45±0.6723	40.65±0.5613	Recovery
10.	PDAZ 02	18.15±0.3251**	22.51±0.8564	33.43±0.6156	Recovery
11.	PDAZ 03	15.71±0.3256**	20.41±0.5432	30.23±0.8912	Recovery
12.	PDAZ 04	21.17±0.7923**	26.12±0.2345	35.23±0.3412	Recovery
13.	PDAZ 05	14.72±0.5091**	19.45±0.4567	25.67±0.8612	Recovery
14.	PDAZ 06	12.97±0.4566**	17.43±0.4327	23.56±0.7126	Recovery

** P < 0 .001 indicates the highly significant difference compared with control.

* P < 0 .05 indicates the significant difference compared with control.

BBB predictor results

Table No: 7

S.NO	COMPOUND NAME	SCORE	BBB+/BBB-
1.	Valproic acid	0.089	BBB+
2.	Phenytoin	0.081	BBB+
3.	ODAZ 01	0.016	BBB-
4.	ODAZ 02	0.053	BBB+
5.	ODAZ 03	0.059	BBB+
6.	ODAZ 04	0.022	BBB+
7.	ODAZ 05	0.063	BBB+
8.	ODAZ 06	0.072	BBB+
9.	PDAZ 01	0.013	BBB-
10.	PDAZ 02	0.049	BBB+
11.	PDAZ 03	0.054	BBB+
12.	PDAZ 04	0.016	BBB-
13.	PDAZ 05	0.060	BBB+
14.	PDAZ 06	0.066	BBB+

B. **ANTI-INFLAMMATORY ACTIVITY** [107]

Anti-inflammatory activity was studied against carrageen an induced hind paw edema in rats.

Animals

Albino rats of both sex weights ranging from 150-250gm were chosen. The animals were provided with standard pellet diet with free access to water and libitum. The animals were divided in to 14 groups of 6 each.

The Group I Animal served as control & received 10% aqueous tween 80 , Group II animal served as STD and received- Indomethacin 10mg/kg, Group III-XIV animals received ODAZ 01,ODAZ 02, ODAZ 03, ODAZ 04, ODAZ 05, ODAZ 06,PDAZ 01,PDAZ 02, PDAZ 03, PDAZ 04, PDAZ 05, PDAZ 06 [10mg/kg], respectively.

All the Drug were administered by intraperitoneal route, After 30min 0.1ml of 1%(w/v) Carrageenan was injected in the plantar region of the left paw of control as well as drug treated animal. Paw volume of legs was measured for 2hrs at 30min interval. The mean Difference in control and drug treated animal was noted. The statistical analysis was carried out by student t-test.

Anti-Inflammatory Activity

Table No. 8

S.No.	Compound Code	Volume of (Right & Left) paw(ml) after drug administration				
		RP	30min LP	60min LP	90min LP	120min LP
1.	Control Tween 80	0.23±0.021	0.33±0.021	0.35±0.022	0.38±0.017	0.40±0.026
2.	Indomethacin	0.23±0.021	0.29±0.026	0.27±0.031**	0.24±0.034**	0.24±0.022
3.	ODAZ 01	0.25±0.012	0.32±0.021	0.29±0.016	0.27±0.067**	0.26±0.711
4.	ODAZ 02	0.27±0.021	0.34±0.031	0.32±0.022	0.30±0.026**	0.28±0.091
5.	ODAZ 03	0.23±0.013	0.30±0.042	0.27±0.021	0.25±0.021**	0.24±0.018
6.	ODAZ 04	0.29±0.013	0.35±0.021	0.34±0.022	0.31±0.076	0.30±0.073
7.	ODAZ 05	0.30±0.031	0.36±0.051	0.35±0.021	0.33±0.021	0.31±0.021
8.	ODAZ 06	0.26±0.013	0.33±0.021	0.30±0.022	0.29±0.026**	0.28±0.031
9.	PDAZ 01	0.25±0.662	0.32±0.831	0.29±0.826	0.28±0.017**	0.27±0.921
10.	PDAZ 02	0.28±0.041	0.34±0.013	0.33±0.922	0.30±0.806**	0.29±0.961
11.	PDAZ 03	0.24±0.021	0.31±0.031	0.28±0.031	0.26±0.031**	0.25±0.022
12.	PDAZ 04	0.30±0.053	0.35±0.921	0.34±0.662	0.30±0.076	0.30±0.981
13.	PDAZ 05	0.31±0.033	0.37±0.733	0.36±0.021	0.33±0.585	0.31±0.917
14.	PDAZ 06	0.26±0.747	0.33±0.818	0.31±0.033	0.29±0.916**	0.29±0.821

** P < 0 .001 indicates the highly significant difference compared with control.

C. ANTI-NOCICEPTIVE ACTIVITY [108]

Male Albino mice weighing of 25 – 30g were used for this study. The test compounds were administered intraperitoneally with 10% v/v Tween 80 suspension. synthesized compounds ODAZ 01, ODAZ 02, ODAZ 03, ODAZ 04, ODAZ 05, ODAZ 06,PDAZ 01,PDAZ 02, PDAZ 03, PDAZ 04, PDAZ 05, and PDAZ 06 were tested for anti-nociceptive activity by Eddy's hot plate method.

Standard used: Diclofenac sodium 10mg/kg.

Eddy's Hot Plate Method:

The animals (albino mice 25 – 30g) were divided into 14 groups of 6 mice each. From this Group I served as control, Group II was treated with standard drug, diclofenac sodium (10mg/kg/) and Group III to Group XIV were treated with the synthesized 1, 3, 4-oxadiazole derivatives (10mg/kg/) respectively. The reaction time was noted for all groups on Eddy's hot plate before and after treatment of standard drug and synthesized compounds at 15min, 30min, 60min, and 120min time interval. All the data (Mean ± SEM) were analyzed statistically by student "t" test and values were tabulated in table no.9

Anti-nociceptive activity:

Table: 9

S. No	Treatment	Basal reaction time(in sec.) before treatment (Mean±SEM)	Basal reaction time (in sec.) after treatment (Mean±SEM)			
			15min	30min	60min	120 min
1.	Control	3.50±0.2236	3.33±0.2108	3.17±0.3073	3.50±0.2236	3.83±0.7528
2.	STD	4.17±0.3073	9.50±0.4282**	13.00±0.3651**	14.17±0.3073**	15.33±0.4216**
3.	ODAZ 01	4.19±0.3173	6.40±0.3651	7.00±0.5774	8.17±0.3073*	9.13±0.4773**
4.	ODAZ 02	4.33±0.3113	7.67±0.4944	8.83±0.4014**	7.17±0.3073	4.83±0.3073
5.	ODAZ 03	4.17±0.4103	7.73±0.5426*	12.97±0.6146**	11.87±0.4216**	9.37±0.3073**
6.	ODAZ 04	4.33±0.4216	7.33±0.4216	8.83±0.4014**	6.17±0.4773	5.00±0.4472
7.	ODAZ 05	4.50±0.4282	7.50±0.5627	8.83±0.3073**	6.33±0.6146	4.83±0.4014
8.	ODAZ 06	4.33±0.2108	5.33±0.3333	6.50±0.4282	6.17±0.3073	5.17±0.3073
9.	PDAZ 01	4.57±0.3563	6.00±0.3651	7.00±0.5774	8.24±0.3073*	9.54±0.4673**
10.	PDAZ 02	4.33±0.3333	7.29±0.3744	8.69±0.4894**	7.42±0.4774	4.33±0.5223
11.	PDAZ 03	4.18±0.4773	7.49±0.4426*	12.62±0.4146**	11.51±0.3276**	9.22±0.4172**
12.	PDAZ 04	4.33±0.4216	7.33±0.4216	8.83±0.4014**	6.17±0.4773	5.00±0.4472
13.	PDAZ 05	4.50±0.4282	7.45±0.5437	8.73±0.3363**	6.41±0.6056	4.72±0.3914
14.	PDAZ 06	4.23±0.1108	5.23±0.4233	6.41±0.3582	6.12±0.2573	5.05±0.3093

** P < 0 .001 indicates the highly significant difference compared with control.

* P < 0 .05 indicates the significant difference compared with control.

D. ANTI-BACTERIAL ACTIVITY [Cup and Plate method] [109]

Standard used: Ciprofloxacin, Control: 0

Procedure:

Preparation of Mueller – Hinton Agar

Beef extract	-	300 gm
Peptone	-	17.5 gm
Starch	-	1.5 gm
Agar	-	17 gm
Cold distilled water	-	up to 1000 ml.

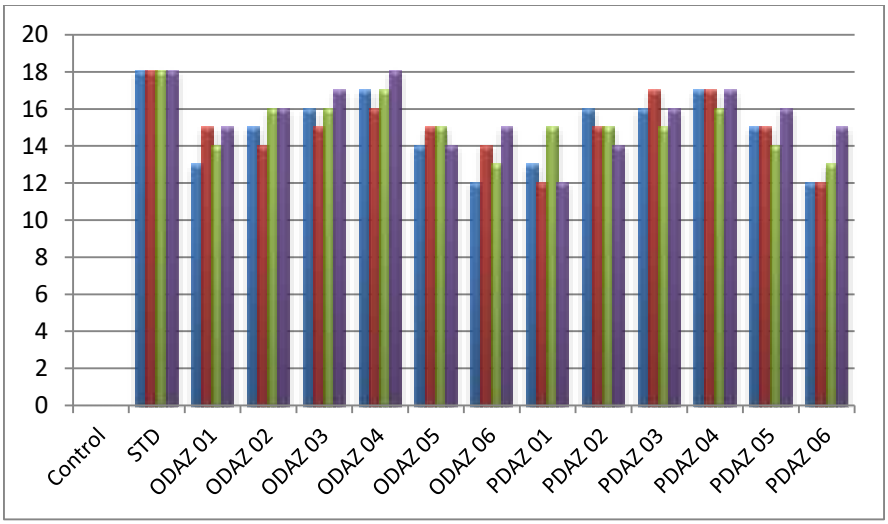
Method

All the ingredients were weighed and suspended in 1000 ml of cold distilled water and heated to boiling. The pH of the media was adjusted to 7.4 with 5 M sodium hydroxide solution. Then 25 – 30 ml of this agar medium was transferred into each boiling tube and plugged with non- absorbent cotton. The tube containing agar medium was sterilized by pressure controlled heat sterilizations technique using an autoclave at 15 lbs at 121^{o}C for 20 minutes. After sterilization the agar medium was cooled up to 45-50^{0}C and inoculated with G (+ ve) organisms like *Streptococcus pyogenes* and *Staphylococcus aureus,* G (- ve) organisms like *Escherichia coli* and *Psuedomonus auruginosa* and poured into sterile Petri dish to get a uniform thickness of 5 – 6 mm. Cups were made out in the other plate using sterile cork borer (6 dm).Then the cups were charged with appropriate concentration of the standard such as ciprofloxacin (0.1ml of 100 µg/ml) likewise the cups were also charged with the series of synthesized oxadiazole derivatives (0.1ml of 100 µg/ml) and incubated at 37^{o}C for 24 hours. The diameters of zone of inhibition around the cups were measured tabulated in the following Table No.10.

Anti-bacterial activity data for synthesized compounds

Table No: 10

S.No.	Compound code	Zone of inhibition (dm in mm)			
		G(+ve) Organism		G (-ve) Organism	
		S.pyrosenes	*S.aureus*	*E.coli*	*P.auruginosa*
1.	STD	18	18	18	18
2.	ODAZ 01	13	15	14	15
3.	ODAZ 02	15	14	16	16
4.	ODAZ 03	16	15	16	17
5.	ODAZ 04	17	16	17	18
6.	ODAZ 05	14	15	15	14
7.	ODAZ 06	12	14	13	15
8.	PDAZ 01	13	12	15	12
9.	PDAZ 02	16	15	15	14
10.	PDAZ 03	16	17	15	16
11.	PDAZ 04	17	17	16	17
12.	PDAZ 05	15	15	14	16
13.	PDAZ 06	12	12	13	15



E. ANTIFUNGAL ACTIVITY [cup and plate method]

Standard used: Ketoconazole, Control: 0

Procedure

Preparation of Mueller – Hinton Agar

Beef extract	-	300 gm
Peptone	-	17.5 gm
Starch	-	1.5 gm
Agar	-	17 gm
Cold distilled water	-	up to 1000 ml.

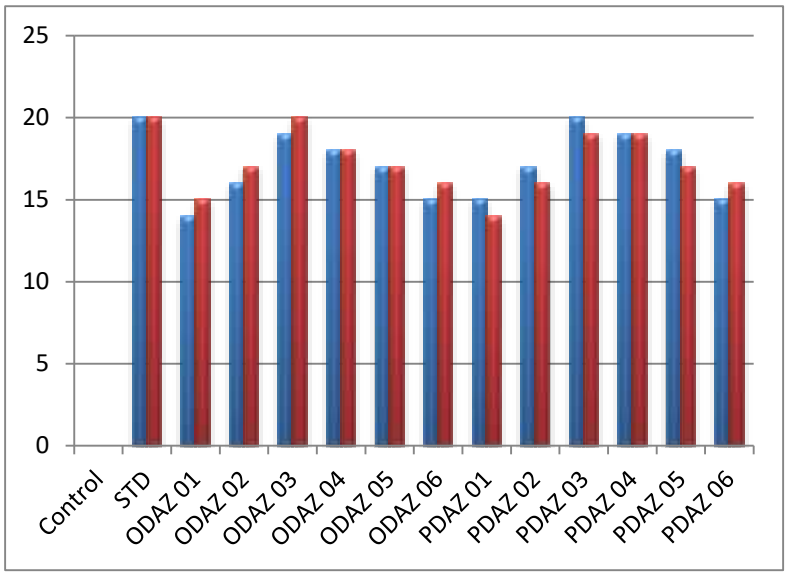
Method

All the ingredients were weighed and suspended in 1000 ml of cold distilled water and heated to boiling. The pH of the media was adjusted to 7.4 with 5 M sodium hydroxide solution. Then 5 – 20 ml of this agar medium was transferred into each boiling tube and plugged with non- absorbent cotton. The tube containing agar medium was sterilized by pressure controlled heat sterilizations technique using an autoclave at 15 lbs at 121^{o}C for 20 minutes. After sterilization the agar medium was cooled up to 45-50^{0}C and inoculated with fungus such as *Candida albicans*, *Aspargillus nigar* and poured into sterile Petri dish to get a uniform thickness of 5 – 6 mm. Cups were made out in the other plate using sterile cork borer (6 dm).Then the cups were charged with control, appropriate standard ketoconazole (100 µg/ml) likewise the cups were also charged with the series of synthesized oxadiazole derivatives (100 µg/ml) and incubated at 37^{o}C for 24 hours. The diameter of zone of inhibition around the cups were measured and tabulated in the following Table No.11

Anti-fungal activity data for synthesized compounds

Table No: 11

S.No.	Compound code	Zone of inhibition(dm in mm)	
		Candida albicans	*Aspargillus nigar*
1.	STD	20	20
2.	ODAZ 01	14	15
3.	ODAZ 02	16	17
4.	ODAZ 03	19	20
5.	ODAZ 04	18	18
6.	ODAZ 05	17	17
7.	ODAZ 06	15	16
8.	PDAZ 01	15	14
9.	PDAZ 02	17	16
10.	PDAZ 03	20	19
11.	PDAZ 04	19	19
12.	PDAZ 05	18	17
13.	PDAZ 06	15	16



F. Minimum Inhibitory Concentration (MIC)[110]

Nutrient agar was prepared, sterilized, and cooled to 45°C with gentle shaking to bring about uniform cooling. It was inoculated with 0.5-0.6 ml of culture and mixed well by gentle shaking before pouring into the sterilized petridishes. The poured materials were allowed to set and thereafter the cups were made by punching into the agar surface with sterile cork borer and scooping out the punched part of the agar. 0.1 ml of each test compounds was added into the cups with the help of sterile syringe. Twofold diluted solutions of the compounds and reference drugs were used (6.25, 12.5, 25, 50, 100 µg/mL). The drug solutions were allowed to diffuse for some time into the medium. The plates were incubated at 30–35°C for 24–48 hours. The incubation chamber was kept sufficiently humid. MIC values were determined at the end of the incubation period.MIC of synthesized 1, 3, 4-oxadiazole derivatives and standard drugs against gram negative and gram positive bacterial strains and fungus are given in Table No: 12, respectively.

Minimum inhibitory concentrations (MIC)

Table No: 12

S.NO	Compound	MIC (µg/ml)					
		S.pyrosenes	*S.aureus*	*E.coli*	*P.auruginosa*	*Candida albicans*	*Aspargillus nigar*
1.	ODAZ 01	50	12.5	25	12.5	100	50
2.	ODAZ 02	12.5	25	12.5	12.5	25	12.5
3.	ODAZ 03	12.5	12.5	12.5	6.25	6.25	6.25
4.	ODAZ 04	6.25	12.5	6.25	6.25	12.5	12.5
5.	ODAZ 05	25	12.5	12.5	25	12.5	12.5
6.	ODAZ 06	100	25	50	12.5	50	25
7.	PDAZ 01	50	100	12.5	100	50	100
8.	PDAZ 02	12.5	12.5	12.5	25	12.5	25
9.	PDAZ 03	12.5	6.25	12.5	12.5	6.25	6.25
10.	PDAZ 04	6.25	6.25	12.5	6.25	6.25	6.25
11.	PDAZ 05	12.5	12.5	25	12.5	12.5	12.5
12.	PDAZ 06	100	100	50	12.5	50	25
13.	Cefixime	6.25	6.25	6.25	6.25	-	-
14.	Fluconazole	-	-	-	-	6.25	6.25

G. ANTHELMINTIC ACTIVITY[111]

Worm: *Pheritima posthuma*

PROCEDURE:

The method described by Dashetal was employed for evaluating anthelmintic activity. *Pheritima posthuma* (obtained from horticulture department, Madurai, Tamilnadu, India) of approximately equal size (15 cm) was divided into 37 groups. Each group consists of six earth worms of same type and treated with any of the following. Fifty milliliter of test solution containing 20, 50 and 100 mg /ml of test solution and Piperazine citrate (10mg/kg).The Mean time of paralysis and death was recorded in minutes. The paralysis time was recorded when no movement of any sort could be observed except when the worms were shaken vigorously. Time for death of worms was recorded, when worms were neither moved while shaken vigorously, nor when dipped in warm water (50ºC).

ANTHELMINTIC ACTIVITY

Table No: 13

Category	Dose	Time of paralysis Mean ± S.E.M (min)	Time of death Mean ± S.E.M (min)
Piperazine citrate	10 mg/ml	22±0.04*	41±0.29*
ODAZ 01	20 mg/ml	51±0.91	56±0.37
	50 mg/ml	50±0.93*	55±0.36*
	100 mg/ml	48±0.75*	54±0.90*
ODAZ 02	20 mg/ml	51±1.09	56±1.35
	50 mg/ml	49±1.70*	47±1.03
	100 mg/ml	45±0.86*	46±0.42*
ODAZ 03	20 mg/ml	42±1.71	48±0.65
	50 mg/ml	41±1.63	46±0.54*
	100 mg/ml	39±0.53*	44±0.32*

ODAZ 04	20 mg/ml	33±1.26	38±0.75
	50 mg/ml	31±1.52	37±0.41*
	100 mg/ml	29±0.62*	32±0.32*
ODAZ 05	20 mg/ml	27±1.31	31±0.45
	50 mg/ml	24±1.53	29±0.64*
	100 mg/ml	23±0.48*	28±0.52*
ODAZ 06	20 mg/ml	61±1.65	68±0.25
	50 mg/ml	56±1.53	62±0.14*
	100 mg/ml	46±0.54*	58±0.62*
PDAZ 01	20 mg/ml	51±0.91	57±0.57
	50 mg/ml	50±0.73*	54±0.56*
	100 mg/ml	49±0.55*	53±0.60*
PDAZ 02	20 mg/ml	52±1.79	55±1.75
	50 mg/ml	45±1.70*	47±1.63
	100 mg/ml	41±0.76*	44±0.52*
PDAZ 03	20 mg/ml	43±1.51	46±0.65
	50 mg/ml	41±1.83	44±0.54*
	100 mg/ml	40±0.33*	43±0.42*
PDAZ 04	20 mg/ml	34±1.36	39±0.75
	50 mg/ml	32±1.72	35±0.61*
	100 mg/ml	30±0.92*	33±0.72*
PDAZ 05	20 mg/ml	31±0.58*	35±0.55
	50 mg/ml	29±1.53	34±0.74*
	100 mg/ml	28±1.31	32±0.42*
PDAZ 06	20 mg/ml	62±1.75	67±0.35
	50 mg/ml	55±1.53	61±0.64*
	100 mg/ml	41±0.64*	55±0.72*

* P < 0 .001 indicates the highly significant difference compared with control.

RESULTS AND DISCUSSION

SYNTHETIC METHODOLOGY

Substituted oxadiazole, 5-(2-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione was synthesized by reacting salicylic acid with ethanol in presence of sulphuric acid followed by reacting with hydrazine hydrate carbon disulphide and alkali.

The titled oxadiazole derivatives were synthesized by making substitution at free N-(3H) position of 5-(2-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione through mannich condensation with formaldehyde and series of primary and secondary amines Substituted oxadiazole, 5-(4-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione was synthesized by reacting p-hydroxy benzoic acid with ethanol in presence of sulphuric acid followed by reacting with hydrazine hydrate carbon disulphide and alkali.

The titled oxadiazole derivatives were synthesized by making substitution at free N-(3H) position of 5-(4-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione through mannich condensation with formaldehyde and series of primary and secondary amines

CHARACTERISATION OF SYNTHESISED COMPOUNDS

MELTING POINT AND Rf VALUE

The melting point and Rf values of synthesized compounds were calculated and it was given in table no 3&4.

INFRARED SPECTROSCOPY

The all spectrum of IR were well seen in the spectra of the respective compounds.

NUCLEAR MAGNETIC RESONANCE SPECTRA

All relevant peaks were observed in 1H NMR, 13C NMR and its data's given in the tables, which agree with the expected structural feature.

BIOLOGICAL EVALUATION

PHARMACOLOGICAL EVALUATION

Anti convulsant activity

The new synthesized compounds ODAZ 01,ODAZ 02, ODAZ 03, ODAZ 04, ODAZ 05, ODAZ 06,PDAZ 01,PDAZ 02, PDAZ 03, PDAZ 04, PDAZ 05, PDAZ 06 were screened for anti convulsant activity by using maximal electroshock induced convulsions method at the dose of 20mg/kg.

The compounds which shown highly significant reduction in the extensor phase are ODAZ 06, PDAZ 06, ODAZ 05, PDAZ 05, ODAZ 03, and PDAZ 03. The compounds ODAZ 01, ODAZ 02 PDAZ 01, PDAZ 02, PDAZ 04,ODAZ 04 shown significant activity.

In comparison to Phenytoin, Valproic acid, all the test compounds showed comparable anti convulsant activity. Mannich base (ODAZ O6, PDAZ 06) displayed the highest anti convulsant activity among the set of compounds tested in the present study. The anti convulsant activity showed that the compounds having morpholine group (06) and methylpiperazine (05) possess highest activity. Replacement of (06, 05) by dimethyl amine derivative resulted in decrease of activity.this further evidenced by optimum log P value that ensure lipophilicity required by the compounds. Although the drug levels in cerebrospinal fluid (CSF) or in brain optimum log p value for the potent molecules suggest that there is a correlation between anti convulsant and lipophilicity. The results shown in the anti convulsant activity report which coincides with the results obtained in the BBB predictor.

Anti-inflammatory activity

The new synthesized compounds ODAZ 01,ODAZ 02, ODAZ 03, ODAZ 04, ODAZ 05, ODAZ 06,PDAZ 01,PDAZ 02, PDAZ 03, PDAZ 04, PDAZ 05, PDAZ 06 were screened for anti-inflammatory activity against carrageen induced hind paw edema in rats at the dose of 10mg/kg.

The compounds ODAZ 03, PDAZ 03, ODAZ 01, PDAZ 01 ODAZ 06, PDAZ 06 shown significant anti-inflammatory activity at 90 mins.

The structure reactivity relationship point of view, the 5-(2-hydroxyphenyl)-3-[(piperidin-1-yl) methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione, 5-(4-hydroxyphenyl)-3-[(piperidin-1-yl) methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione has the strongest anti-

inflammatory activity. Replacement of the piperidine group by either methyl or other group in compound decreased the anti-inflammatory activity of the oxadiazole moiety.

Anti-nociceptive activity

The new synthesized compounds ODAZ 01, ODAZ 02, ODAZ 03, ODAZ 04, ODAZ 05, ODAZ 06, PDAZ 01, PDAZ 02, PDAZ 03, PDAZ 04, PDAZ 05 and PDAZ 06 were screened for anti-nociceptive activity by Eddy's hot plate method at dose of 10mg/kg.

Among these compound ODAZ 03 posses highly significant anti-nociceptive activity when compare with standard, Diclofenac sodium 10 mg/kg and compounds ODAZ 01, ODAZ 02, ODAZ 04, ODAZ 05, ODAZ 06, PDAZ 01, PDAZ 02, PDAZ 03, PDAZ 04, PDAZ 05 and PDAZ 06 shown significant activity.

ANTI-MICROBIAL SCREENING

Anti-bacterial activity

All compounds were screened for anti-bacterial activity against *Streptococcus pyogenes* and *Staphylococcus aureus, Escherichia coli* and *Psuedomonus auruginosa* at 100mcg/ml.

The synthesized compounds ODAZ 04, PDAZ 04, ODAZ 03, PDAZ 03, ODAZ 02, PDAZ 02 shown significant anti-bacterial activity of gram positive and gram negative bacteria and compounds ODAZ 05, PDAZ 05, ODAZ 01, PDAZ 01, ODAZ 06, PDAZ 06 shown moderate anti-bacterial activity.

The antibacterial screening revealed that some of the tested compounds showed good inhibition at 10 mg/ml concentration. The antibacterial screening indicated that among the tested compounds, 5-(2-hydroxyphenyl)-3-[(piperazin-1-yl) methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione & 5-(4-hydroxyphenyl)-3-[(piperazin-1-yl) methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione substitution exhibited excellent activity against all the tested bacterial strains, namely *Streptococcus pyogenes* and *Staphylococcus aureus, Escherichia coli* and *Psuedomonus auruginosa* at 100mcg/ml.

Anti-fungal activity

All compounds were screened for anti-fungal activity against *Candida albicans, Aspargillus nigar* at 100mcg/ml.

The synthesized compounds ODAZ 03, PDAZ 03, ODAZ 04, PDAZ 04, ODAZ 05 & PDAZ 05 shown significant anti-fungal activity and compounds ODAZ 02, PDAZ 02, ODAZ 06, PDAZ 06, ODAZ 01 & PDAZ 01 shown moderate anti-fungal activity.

The antifungal screening revealed that among the tested compounds, 5-(2-hydroxyphenyl)-3-[(piperidin-1-yl) methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione and 5-(4-hydroxyphenyl)-3-[(piperidin-1-yl) methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione showed excellent activity against all the tested fungal strains similarly.

Minimum Inhibitory Concentration (MIC)

Minimum Inhibitory Concentration values are synthesized compounds against various organism are tabulated are titled compounds were graded as highly active with MIC>6.25 to 12.5 moderately active with MIC value 50-100ug.The compound 5-(2-hydroxyphenyl)-3-[(piperazin-1-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione and 5-(4-hydroxyphenyl)-3-[(piperazin-1-yl)methyl]-1, 3, 4-oxadiazole-2(3*H*)-thione was found to be highly active against all the test organism.broad spectrum activity ODAZ O4,PDAZ 04 gram positive and negative and the fungi may be due to the piperazine moiety which place a crucial role in enhancing the observed activity.

Anthelmintic Activity

All oxadiazole showed moderate to good anthelmintic activity. Comparison of anthelmintic data revealed that methyl piperazine derivative is more active than other compounds. The anthelmintic activities of synthesized compounds were decreased in the following order:

ODAZ 05≥PDAZ 05≥ODAZ 04≥PDAZ 04≥ODAZ 03≥ PDAZ 03≥ODAZ 01≥PDAZ 01≥ODAZ 02≥PDAZ 02≥ODAZ 06≥PDAZ 06

CONCLUSION

- Substituted oxadiazole, 5-(2-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione was synthesized from salicylic acid.
- The titled oxadiazole derivatives were synthesized by making substitution at free N-(3H) position of 5-(2-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione through mannich condensation.
- Substituted oxadiazole, 5-(4-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione was synthesized from p-hydroxy benzoic acid.
- The titled oxadiazole derivatives were synthesized by making substitution at free N-(3H) position of 5-(4-hydroxyphenyl)-1, 3, 4-oxadiazole-2(3*H*)-thione through mannich condensation.
- The synthesized compounds were characterized by melting point and solubility and subjected to various analytical techniques like Thin Layer Chromatography, IR and NMR spectral studies.
- Synthesized compounds ODAZ 06, PDAZ 06, ODAZ 05, PDAZ 05, ODAZ 03, and PDAZ 03 compounds posses highly significant anti-convulsant activity.
- The synthesized compounds ODAZ 03, PDAZ 03, ODAZ 01, PDAZ 01 ODAZ 06, and PDAZ 06 possess significant anti-inflammatory activity at 90 mins.
- The synthesized compound ODAZ 03 possesses highly significant anti-nociceptive activity.
- The synthesized compounds Compound, ODAZ 04, PDAZ 04, ODAZ 03, PDAZ 03, ODAZ 02, PDAZ 02 posses significant anti-bacterial activity against both G(+ve) and G(-ve) organisms.
- The synthesized compounds Compound, ODAZ 03, PDAZ 03, ODAZ 04, PDAZ 04, ODAZ 05, PDAZ 05 posses significant anti-fungal activity against *Candida albicans, Aspargillus nigar*
- The synthesized compounds Compound, ODAZ,ODAZ 05, PDAZ 05, ODAZ 04, PDAZ 04, ODAZ 03, PDAZ 03 posses significant anthelmintic activity against *pheritima posthuma*

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