SYNTHESIS OF SOME NITROGEN CONTAINING HETEROCYCLIC COMPOUNDS AND THEIR ANTIMICROBIAL ACTIVITIES

A Thesis

Submitted for the Award of Ph. D. Degree of

PACIFIC ACADEMY OF HIGHER EDUCATION AND RESEARCH UNIVERSITY

By

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PREFACE

Nitrogen containing heterocycles have always played a major role in the pharmaceutical and agrochemical industries, because of their potent physiological properties, which have resulted in numerous applications. Pyrimidine and their derivatives are building block for around more than 150 naturally occurring alkaloids isolated from plant kingdom, microorganisms and animals. There has been an enormous increase in the interest among biologists and chemists in the synthesis and bioactivity of pyrimidine derivatives.

The present work planned has been in following manner.

- Detail literature survey will be carried out on research already done in Pyrimidine derivatives.
- Novel chalcones compounds by simple available starting materials will be synthesized.
- The scope of the novel protocol for synthesizing a good library of pyrimidine derivatives will be assessed.
- All the synthesized compounds will be characterized by ^{1}H NMR, ^{13}C, NMR, IR, and MASS spectroscopic techniques.
- Synthesized compounds will be tested for its antimicrobial activity against gram +ve and gram -ve bacteria.

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CONTENTS

CHAPTER – I

INTRODUCTION

CONTENTS

1.1 INTRODUCTION

Pyrimmidines are six membered N bearing heterocycles.They exist in nature throughout in various forms and these are the building blocks of a large number of naturally occurring substances such as liposaccharides, vitamins, antibiotics, DNA, RNA, etc. The commonly used pyrimidine bases are cytosine, thymine or uracil. The source for the name pyrimidine, since past 1884, which was when the name was coined by Pinner by a amalgamation of the word pyridine and amidine. Since these unique investigations, hundreds of pyrimidine-bearing medicines have been detected in biochemistry. The large number of schemes appeared for this scaffold and its connection to important behaviour made it an inspiring field of investigation.

Heterocyclic chemistry is an integral part of the chemical sciences and it constitutes a considerable part of the modern researches. The study of heterocyclic systems is of great interest from both point of views the theoretical and practical. Heterocycles also play an important role in the design and discovery of new pharmacologically active compounds. Nitrogen-containing heteroaromatic and heterocyclic compounds are indispensable structural units for both chemists as well as biochemists.

Heterocyclic compounds consist of cyclic structures, where one or more of the ring atoms are elements other than carbon. The common hetero atoms are nitrogen, oxygen and sulphur. About one third of known organic compounds are heterocycles. They can be divided into alicyclic and aromatic compounds, which possess five or six membered rings. The chemistry of heterocyclic compounds is one of the most complex branches of organic chemistry. It has seen unparalleled progress due to their wide natural occurrence, specific chemical reactivity and widespread utility in the field of therapeutics. It is equally interesting for its theoretical implications, diversity of its synthetic procedures and physiological industrial significance of heterocyclic compounds. Heterocyclic compounds provide convenient building blocks to which biologically active substitutes can be attached. The interesting biological activities of heterocycles have stimulated considerable research work in recent years including their synthetic utility. Most of the natural products obtained from plants and animal origin contain heterocyclic compounds such as alkaloids-nitrogenous bases and glycosides. They have been used since old age as remedial agents. Reserpine alkaloid from Indian

Rauwolfia, febrifuge from ancient Chinese drug changshan, curare alkaloid from arrow poison, codeine, Ψ-tropine and strychnine are all some well-known examples of heterocyclic compounds.

Acharya et al.[1] showed that structures containing benzimidazole are well-known to have a wide range of biological properties. They have commercial applications in various realms of therapy, including anti ulcerative, antihypertensive, antiviral, antifungal, anti-tumour and antihistaminic agents in veterinary medicine.

Somasundaram et al.[2] reported that compounds with imidazole ring systems have many pharmaceutical activities and play important roles in biochemical processes.

Upadhyay et al.[3] indicated that a number of methods are available for synthesis of these compounds. A traditional method for synthesis of benzimidazoles is the reaction between *o*-phenylenediamine and carboxylic acid under harsh dehydrating reaction conditions, for example, in the presence of HCl, PPA (polyphosphoricacid), H_3BO_3, or *p*-toluenesulfonic acid.

Chidella et al.[4] reported that the benzoxazole derivatives are well-known kind of heterocycles that have considerable importance in the field of materials chemistry, in particular due to their fluorescence properties. These electronic states and behaviour are mainly attributed to the planarity and rigidity of the delocalized electronic system. These types of compounds can find a number of different applications such as electronic devices, sensors for metals, as well as photoluminescent dyes.

Zhang et al.[5] indicated that Heterocyclic quinines containing nitrogen atom are known to possess antibacterial, antifungal and cytotoxic activities. The clinical significance of this class of compounds has stimulated the synthesis of new lead compounds retaining the 'core' quinone chromophore. Quinoxaline derivatives are nitrogen containing heterocyclic compounds and their importance has been reported in the literature. They possess well known biological activities including anti-viral. anti-inflammatory, antiprotozoal, anthelmintic, anticancer.

Alyaninezhad et al.[6] reported that quinoxaline derivatives constitute the basis of many insecticides, fungicides and herbicides, as well as it is important as receptor antagonists. Although rarely described in nature, synthetic quinoxaline moiety is a part of number of antibiotics such as echinomycin levomycin and actinomycin which are

known to inhibit the growth of gram-positive bacteria and also active against various transplantable tumours.

Shan et al.[7] predicted that nitrogen containing heterocycles have always played a major role in the pharmaceutical and agrochemical industries because of their often-potent physiological properties, which have resulted in numerous applications.

Ubale et al.[8] showed that quinazolines and condensed quinazolines are reported to possess interesting pharmacological activities such as antihypertensive, antihistaminic, analgesic and anti-inflammatory, anticancer, and anti-HIV activities.

Sanad et al.[9] reported that quinazolinone possess benzimidazole and triazole unit which are important structural motif in medicinal chemistry and these can be found in a number of biologically active molecules.

Pereira et al.[10] showed preparation and degradation of pyrimidines resulted in ring opening or closing. These reactions are known amidohydrolases and they are fraction of a super family bearing a varied set of enzymes that catalyse mainly hydrolysis procedure and few isomerizations. They have several moieties as nucleic acid, amino acids and ester of organophosphate of recognizable amidohydrolases. This member of biocatalyst has a mono or binuclear metal. At the time of synthesis of the amidohydrolase, dehydratase catalyses the ring formation of carbamoyl-L-aspartate. Organisms that utilizes the reduction way for pyrimidine dilapidation uses dihydopyrimidases to open pyrimidine nucleus while organisms that utilize the oxidative pathway use barbiturates.

El-Messery et al.[11] observed that all enzymes share a seemingly common mechanism, using a metal hydroxide as an acid/base. These reactions are generally reversible. One of the best studied enzymes is dihydroorotase from *Escherichia coli*. Recently a less studied pyrimidine utilizing-amidohydrolase is barbiturate.

Poojari et al.[12] prepared that enzyme carries out a function similar to that of the dihydropyrimidases. Preliminary biochemical studies of this enzyme show that the enzyme carried out the conversion of barbiturate to uredo malonic acid, a necessary step in the oxidative catabolism of pyrimidines. This enzyme show that it has relatively low homology to the dihydropyrimidases and dihydroorotases. Barbiturate has been shown to be a tetramer with 4.4 mols of zinc per enzyme, likely a mononuclear zinc amino

hydrolase. This property indicates a slight difference between the mechanism of this amidohydrolase and those of dihydroorotates and dihydropyrimidases, both of which use a binuclear metal centre. Lower metal content for dihydropyrimidase led early researchers to also conclude that it was a mononuclear zinc enzyme. This phenomenon is due to fact that pH playing an important part in the metal binding to amidohydrolases. Both dihydroorotases and dihydropyrimidases require a post-translational carboxylation of an active site lysine to function properly and bind the second metal effectively. This modification and the increase in metal affinity are highly dependent upon pH. Further structural studies or pH-dependent metal titrations of this enzyme provide better insight as to whether this new amidohydrolase family does indeed use a different mechanism than was found for the dihydroorotases and dihydropyrimidase. The ring opening of pyrimidines is also seen in nature without the aid of enzymes. At high temperatures, pyrimidine dihydrouridine, found in modified t-RNA, has been shown to undergo ring opening through hydrolysis. This reaction is accelerated by both heat as well as basic pH, dihydrouracil is thought to be absent in the RNA of thermophiles.

Procedure of drug plan is at length driven by the nature and knowledge of pharmaceutical research scientists. It is often informative to attempt to “imprison” these experiences by analysing the past record in victorious drug design projects of the past. From this analysis, the inferences are haggard which play significant role in shaping our present and future projects. Towards this region, one would like to analyse the structures of a large number of drugs as final product of a victorious drug design attempt. Our objective for this is to begin to deco volute this information in order to be relevant it to design of novel drugs. Nitrogen containing heterocyclic ring such as pyrimidine is a promising structural moiety for drug design. Pyrimidine derivative form a component in different practical drugs and are associated with many biological activities. Pyrimidines have an extended and distinguished history extending from the days of their discovery as significant constituents of more than a few biological molecules such as nucleic acids, cofactors, a variety of toxins, to their present use in the chemotherapy of AIDS. These compounds provide huge assurance for the treatment of retro virus infections in humans.

Chavan et al.[13] showed that first study into the synthesis of pyrimidine nucleus appeared more than a hundred years ago and then more than a few methods for the synthesis of dihydropyridine were reported and their physicochemical properties has been studied.

Ighodaro et al.[14] reported that alloxan is known for its diabetogenic action in a number of animals. Uracil, thymine and cytosine are the three important constituents of nucleic acids. Mahdavi et al.[15] observed that diseases of the arterial tree cause more premature deaths than all other diseases such as cancer. Among the major risk factors for arterial diseases, high blood pressure is the most important one.

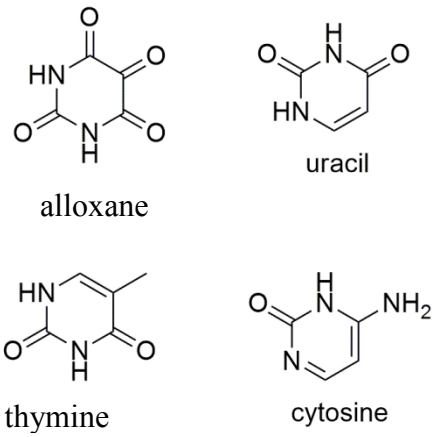

Fig. 1.1: Examples of nucleic acids

The pyrimidine ring is found in vitamins like riboflavin and folic acid.

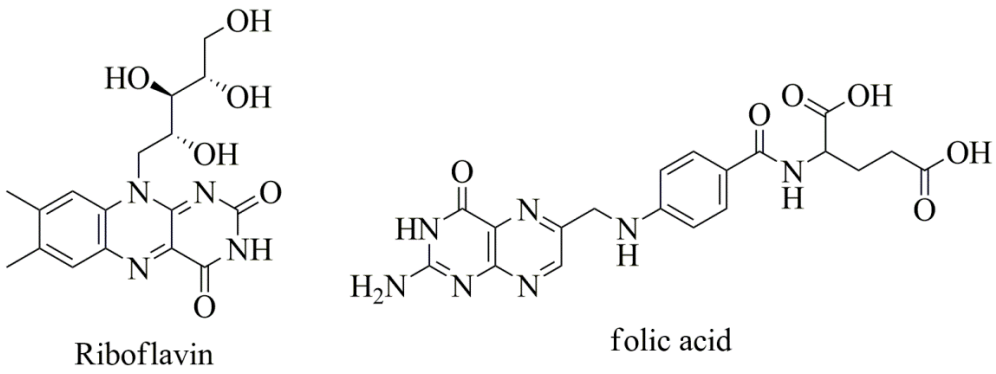

Fig. 1.2: Examples of Vitamines

You et al.[16] reported that sulfadimethoxine was introduced with a half-life of approximately 40 h. The sulfamethoxydiazine also possess good half-life. A new broad-spectrum sulfonamide, sulfamethomidine is comparatively non-toxic and patients do not need extra fluid intake or alkalization. Sulfacytine has been reported to be 3–10 times more potent than sulfaisoxazole and sulfisodimidine**.**

Aggarwal et al.[17] have synthesized 2,7-diamino-3-phenylazo-6-phenylpyrazolo [1,5-a] pyrimidine (PPD) as a new hetero-cyclic ligand, act as a selective Hg^{2+} ion chemosensor.

Finger et al.[18] reported that Pyrimidine represent the valuable scaffold in the discovery of antitubercular agents.

Tabarsaei et al.[19] reported for the synthesis of $Ag/TiO_2/Fe_3O_4$@MWCNTs MNCs as a new heterogeneous organometallic catalyst. XRD, FESEM, EDX and TEM analysis were used for confirming the structure of synthesized nanocatalyst.

Rejinthala et al.[20], a series of new pyrimidine-piperazine hybrid molecules were designed and synthesized as possible antimicrobial agents. The synthesized compounds were characterized using ^{1}H NMR, ^{13}C NMR, MS and elemental analysis and then the activity of the new compounds were compared with that of antibiotics.

Ibrahim et al.[21] showed suitable approach to construct a new annulated systems namely chromeno [3′,2′:5,6] pyrido [2,3-*d*] pyrido [2′,3′:4,5] [1,3] thiazolo [3,2-*a*] pyrimidines.

Badigar et al.[22] described one-pot synthesis of pyrano [2,3-*d*] pyrimidine derivatives using aromatic aldehyde, ethyl cyanoacetate and barbituric or thiobarbituric acid accelerated by microwave irradiation in the presence of agro-waste extract solvent medium with few drops of ethanol as a co-solvent presented. The reaction was optimized by various methods such as magnetic stirring, ultrasound, mechanochemical and microwave irradiation, but the microwave irradiation method excelled product formation faster rate with high yield and purity. The advantages of the present approach are the metal-free, chemical-less, and hazardous solvent-less employed and considered as an eco-friendly protocol for the synthesis of pyrano [2,3-*d*] pyrimidine derivatives developed.

Adel and Abouzid.[23] sought to develop more potent pyrrolopyrimidine surrogates through introduction of fluorine atom at the phenyl moiety near to the urea moiety mimicking regorafenib. They hypothesized that this would improve the compounds potency. Surprisingly, Compound 9e possessed better VEGFR2 inhibitory activity (IC50 = 52.4 nM) compared to standard drug sorafenib, whereas compounds (9b,d and f) showed moderate inhibitory activity. The newly synthesized compounds were tested on 60 human cancer cell lines.

Zarenezhad et al.[24] showed that heterocyclic derivatives as a major group of organic compounds are enormously used for a wide range of pharmaceutical and

industrial applications. They are known for their biological and pharmacological properties including anti-inflammatory, antimicrobial, anticancer, antitumor, and anti-viral activities. The pyrimidine and pyrimidine containing ring have attracted much attention as they are available in the substructures of therapeutic imperative products. The potential therapeutic properties of these heterocycles have encouraged the medicinal chemists to synthesize a large number of novel chemotherapeutic agents.

Bansal et al.[25] reported that Fusion of pyrimidine with different heterocyclics yields a variety of pyrimidine-based scaffolds, which represent a class of privileged structures in chemistry due to their presence in various bioactive agents. Fused-pyrimidine scaffolds are used as templates to develop a diversity of compounds having applications as antiviral, anti-tumor, anti-allergic, antihypertensive, anticancer, antioxidant and hepatoprotective agents.

Ansari and Joshi.[26] summarized the progress of eight-membered heterocycles fused with a pyrimidine ring and their biological properties. Among this fusion class, pyrimidine-fused eight-membered hetero-aromatic ring fused pyrimidines derivatives have not been sufficiently investigated. Despite bioactivity being reported in a handful of studies so far, it has not been explored much. The major reason highlighted for this gap again includes entropic factors, along with transannular interactions and unsatisfactory synthetic procedures. So, it becomes very important to disclose the biological and medicinal properties of eight-membered fused-pyrimidine heterocycles.

1.2 HETEROCYCLIC COMPOUNDS

Heterocyclic compounds are the largest and most diverse group of organic chemicals. After all, any carbocyclic compound, regardless of structure or usefulness, can theoretically be transformed into a collection of heterocyclic analogues by substituting a different element for one or more of the carbon atoms in the ring. Even if we limit ourselves to the most frequent heterocyclic constituents of oxygen, nitrogen, and sulphur, the permutations and combinations of such a replacement are vast. Heterocyclic compounds can be used in a variety of ways. They are the most common sorts of compounds used as medications, agrochemicals, veterinary products, antioxidants, corrosion inhibitors, and other forms of additives. Heterocyclic structures can be found in a variety of dyes and pigments.

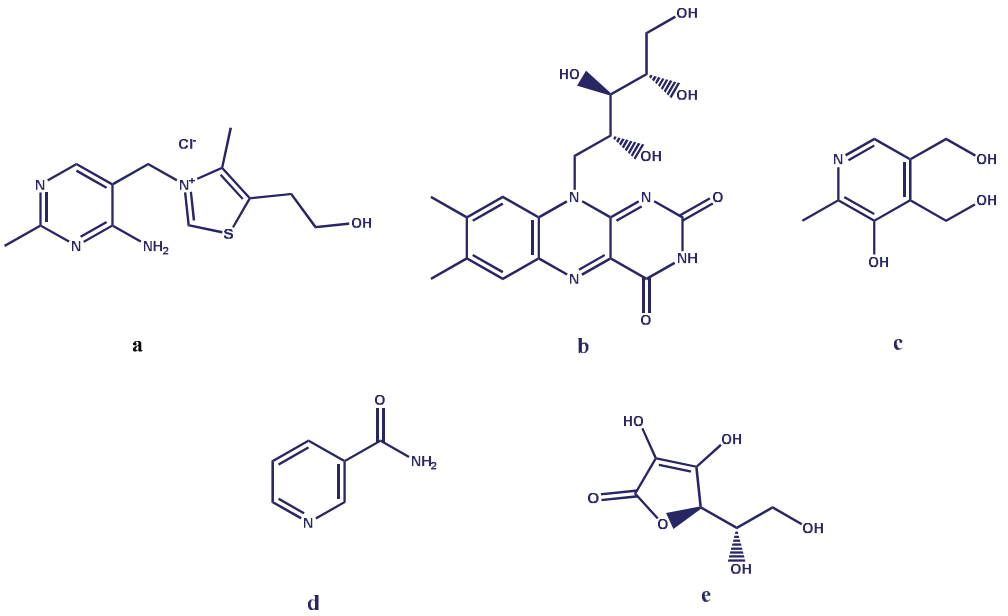

Fig. 1.3: Heterocyclic Compounds

Most biologically active chemicals are heterocyclic organic molecules, which have a ring structure that includes some other atoms than carbon, such as sulphur, oxygen, or nitrogen. Many synthetic heterocyclic compounds have major practical applications, such as dyestuffs, copolymers, solvents, photographic sensitizers, developers, antioxidants, vulcanization accelerators in the rubber sector, and many are useful synthesis intermediates. There are also many pharmacologically active heterocyclic compounds, which are used in clinical practice on a regular basis.

Some heterocyclic compounds, such as pyridines and imidazole have long been employed as metal ligands, but their structure is increasingly being tuned to a specific orientation. Heterocyclic compounds, for example, are now commonly utilised as chiral ligands for transition metals, and the resultant complexes serve as catalysts in a range of asymmetric synthetic reactions. Heterocyclic compounds can be found in abundance in nature. These are important parts of biological processes. Nucleic acid bases, for example, are derivatives of the pyrimidine and purine ring systems and are fundamental to the replication mechanism. The components required for photosynthesis and oxygen transport in higher plants and animals, respectively, are chlorophyll and haeme, both of which are derivatives of the porphyrin ring system. Heterocyclic compounds include thiamine (vitamin B_1), riboflavin (vitamin B_2), pyridoxol (vitamin B_6), nicotinamide (vitamin B_3), and ascorbic acid (vitamin C), which are all found in essential dietary elements.

Over the last few years, medicinal chemistry has introduced various novel strategies to speed up the drug development process, including combinatorial chemistry, microwave-assisted organic synthesis, and high throughput purification. Triazoles, thiazoles, oxadiazoles, pyrimidines, and isoxazoles are nitrogen and sulfur-containing heterocyclic molecules with essential biological activity. As a result, in recent years, the development of novel compounds containing these moieties and known pharmacological characteristics has gained traction. Piperazine has been classed as a favored structure since its nucleus can bind many receptors with high affinity. Some examples of heterocyclic compounds are :

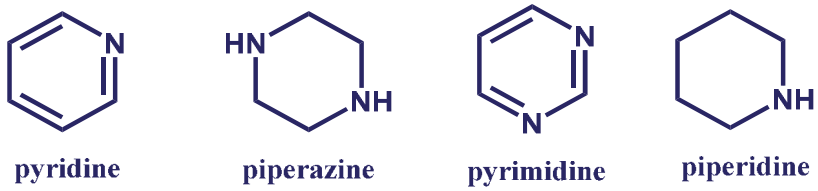

Fig. 1.4: Drug Development Process

Heterocyclic chemistry is a major branch of organic chemistry that accounts for roughly one-third of all recent publications. Heterocyclic compounds make up two-thirds of all organic substances. The carbocyclic compound is a cyclic organic compound with all carbon atoms arranged in a ring configuration. A heterocyclic compound is one in which at least one atom other than carbon is present in the ring structure. Heterocyclic compounds play a vital function in medicinal chemistry, and they are attracting a lot of attention due to their vast scope for synthesizing and processing a wide range of pharmacological activities. Apart from their widespread presence in natural goods, heterocyclic compounds are also important components of biological molecules such as deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Indeed, DNA is the most significant macromolecule in life, and the monomer of RNA and DNA, i.e. nucleotides. The building blocks of our genes are purine and pyrimidine bases derivatives. Chlorophyll, a green pigment that aids in the creation of oxygen by absorbing carbon dioxide in plants, and heme, the non-protein portion of hemoglobin, which is derived from giant porphyrin rings, is the oxygen carrier in animals. On the other hand, synthetic heterocyclic compounds have a wide range of therapeutic applications, including antibacterial, antifungal, analgesic, anti-inflammatory, antimycobacterial, antitubercular, antimalarial, trypanocidal, anti-HIV activity, anticonvulsant, anti-tumoral,

antileishmanial agents, genotoxic etc. They have also been found in a variety of synthetic medications and agro-based chemicals as a significant structural ingredient. Most heterocyclic compounds have essential material science applications, such as fluorescent sensors & dyes, brightening agents, polymers, information storage, and analytical reagents. Many heterocyclic compounds can also be employed in the production of organic conductors, semiconductors, photovoltaic cells, molecular wires, organic light-emitting diodes (LED), light-harvesting systems, optical data carriers, chemically programmable switches, and liquid crystalline compounds. The synthetic value of heterocyclic compounds as synthetic intermediates, chiral auxiliaries, protecting groups, and metal ligands in asymmetric catalysts in organic synthesis is also of great interest. Because of the huge applicability throughout the range of utility, more emphasis has been placed on developing efficient novel methods for synthesizing heterocyclic molecules.

1.3 OXYGEN-BASED HETEROCYCLES

They serve a variety of modulatory and cytoprotective purposes as polyphenolic compounds, which are primarily found in plants. As such, they offer a potential route for the development of novel compounds with a desirable combination of anticancer properties and superior pharmaceutical characteristics for clinical use.

Because they can be used in a wide range of processes, such as the creation of cosmetics, pharmaceuticals, and fragrances, coumarin compounds and their derivatives are crucial in organic chemistry. The benzopyrone family, which includes substances with a benzene ring linked to a pyrone ring, includes coumarin. Manufacturers of pharmaceuticals, cosmetics, and fragrances are just a few industries that employ them. Optical brightening agents, distributed fluorescent dyes, and laser dyes are examples of special applications. The heterocyclic moiety of coumarin (2-oxo-2H-1-benzopyran) is widely regarded as a "privileged" structural motif in a number of natural products and synthetic chemical compounds having pharmacological activity. Insecticides, scents and perfumes, agrochemicals, and food & cosmetic additives all use coumarin derivatives. Optical examples of unique applications include optical brightening agents, distributed fluorescent dyes, fluorescence sensors and laser dyes. Widely regarded as a "privileged" structural motif in many natural products and synthetic chemical compounds with pharmacological activity is the heterocyclic moiety of coumarin (2-oxo-2H-1-

benzopyran). Such molecules include, but are not limited to, fluorescent transthyretin folding sensors, optical brighteners, fluorescent sensors, and molecular photonic devices.

Flavanones, a naturally occurring substance has a wide range of biological properties including potent anticancer activity against human colon, breast, and kidney adenocarcinoma as well as analgesic, antioxidant, and antibacterial properties and minimal toxicity. Surprisingly, the furan rings (oxygen-based rings) derivatives outperformed all other derivatives in terms of anticancer activity across all cell lines. Despite the fact that the exact mechanism of action of this particular derivative is still unknown, furfuraldehyde, a heterocycle flavanone derivative with a furan ring, demonstrated preclinical evidence of being a moderately effective anticancer drug. Like coumarins, flavones could serve as a long-term building block for new and improved anticancer medications.

Similar to coumarins, benzofurans are oxygen-based heterocycle type that can be found in nature and have a variety of biological activities. Recent studies have demonstrated that compounds based on benzofuran are cytotoxic to cancer cell lines.

One with a ring structure that contains both; oxygen and nitrogen is another intriguing heterocycle. The 23 different mefloquine-oxazolidine derivatives, which are cyclic molecules with oxygen and nitrogen, have antiproliferative effects. To better understand the potential therapeutic impact of oxazolidine rings as building blocks for the development of cancer therapies, a number of oxazolidine derivatives have been developed. Surprisingly, it was discovered that substituent groups at the 3 or 4 positions are essential for action, whereas ortho-substituted compounds were ineffective at killing cancer cells. The S isomer exhibited the highest activity, frequently ten times that of the enantiomers.

Additionally, studies focus on the anticancer properties of oxazolidine compounds, suggesting that this class of oxygen-based and nitrogen-based heterocycles is a new area of study. These findings demonstrate that the toxicities of many of the oxygen-based heterocycles are currently being investigated in preclinical trials which differ significantly depending on the type of oxygen-based heterocycle, its general structure, ligands, ring size, and aromaticity. Despite this, it is still not clear exactly, how many of these novel heterocycle drugs and scaffolds are effective in treatment of various diseases.

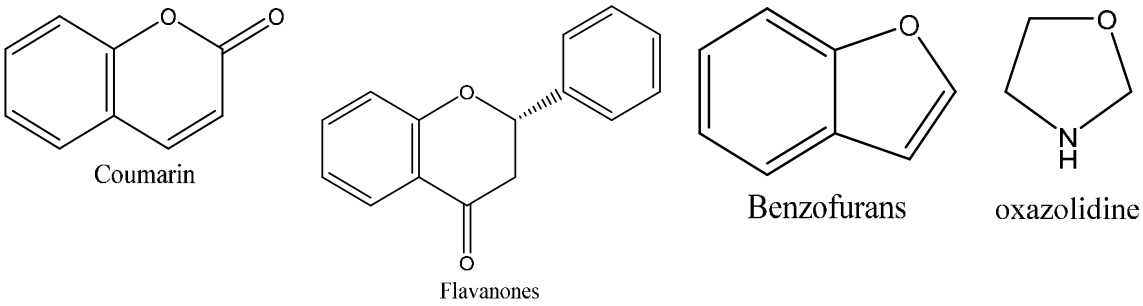

Fig. 1.5: Oxygen Based Heterocycles

1.4 NITROGEN-BASED HETEROCYCLES

In medicinal chemistry, analogues of nitrogen-based heterocycles occupy a special position as a valuable source of pharmaceuticals. More than 75% of drugs that have been FDA-approved and are currently on the market contain heterocyclic moieties with nitrogen as heteroatom. New pharmaceuticals with nitrogen as an active ingredient are likely to make up a much larger portion of the market in the following decades. There have been numerous new nitrogen-based heterocycles synthesized. There are increasingly more novel N-heterocyclic molecules with important physiological traits and potential medicinal chemistry uses. Use of nitrogen-based moieties in drug design and the creation of a number of effective and capable candidates against a variety of diseases have been discussed[27].

The most prevalent pharmacophore system among nitrogen-based compounds is the 1,2,3-triazole moiety, and it is essential for the creation of new biological targets[28]. These three nitrogen heteroatoms can be used to easily assemble these five-membered heterocyclic motives, thanks to "click" chemistry. These substances can interact with a range of biological targets through hydrogen bonding, noncovalent and van der Waals interactions, as well as dipole-dipole bonding interactions[29-32]. Triazoles are weakly acidic and basic, making them more vulnerable to reducing agents. Additionally, the 1,2,3-triazole-based compound carboxyamidotriazole has been successfully used in clinical studies to treat cancer[33]. The triazole unit's strong dipole properties have also increased its value in medicinal chemistry because they allow for highly specific binding to biological targets[34].

One of the most adaptable and frequently used nitrogen-based heterocyclic similar fragments in the preparation of drugs for typical clinical disorders are indoles and

their derivatives[35]. There has been an emphasis on the synthesis of indole derivatives recently because there are practically endless possibilities for architectural design of polycyclic structures by incorporating multiple fused heterocyclic scaffolds in an effort to achieve promising new heterocycles with chemical and biomedical relevance. Due to physicochemical characteristics like hydrogen bond donor-acceptor capability, stacking interactions, coordination bonds with metals as a ligand, van der Waals forces, polarisation, and hydrophobic forces, these fragments are gaining more and more attention. Derivatives can readily bind to a variety of biomolecules, including enzymes and nucleic acids, due to the properties that cause their reactivity[36-39].

Pyrimidines and pyrimidinones have drawn a lot of attention in organic synthesis due to the variety of biological activities[40]. The pyrimidine nucleus is a six-membered 1,3-diazine ring with a ketone unit. Natural products and nucleic acids, among other biologically active substances, contain pyrimidine analogues. Additionally, this type of heterocyclic molecule has several therapeutic uses in medicinal chemistry as a crucial building block of a wide range of drug candidates and nucleic acids due to its structural resemblance to purines. pyrimidine and pyrimidinone derivative-based anticancer medications (ibrutinib, capecitabine, folinic acid, and monastrol). These pyrimidines and their scaffolds are frequently used in drug development studies because of the wide range of bioactivity they exhibit[41-43].

Piperidine and pyridine complexes are two of the heterocyclic elements that are most frequently present in pharmaceuticals. Several N-(piperidine-4-yl) benzamide derivatives were found to have anticancer properties. The structure N-(1-(2, 6-difluorob-benzyl)-piperidine-4-yl)-4-phenoxybenzamide was discovered to be the most effective against a hepatocarcinoma cell line. Other major nitrogen-based scaffolds, their diversity in structure, patterns of substitution, and significance as essential elements are piperidines, pyridines, piperazines, cephems, pyrolidines, pyrazoles, purines, pyrimidines, and others[44].

1.5 SULFUR-BASED HETEROCYCLES

Thiirane, also referred to as ethylene sulphide, is a three-membered heterocycle that contains sulphur. Heterocycles with three atoms are typically very reactive due to ring tension. It has been proved that thiirane and its derivatives have antibacterial, antimicrobial, and anticancer properties. Among the biological effects of steroidal drugs

with the thiirane moiety are peptidase inhibitors, carboxypeptidase A inhibitors, aromatase inhibitors, and metalloproteinase inhibitors. Examples of compounds containing thiirane include natural hydrocarbons, cyclic and acyclic alcohols, natural or semi-synthetic steroids, peptides, and polyethers. Thiirane can be used to synthesise a variety of polymers, drugs, insecticides, herbicides, liquid crystals, and adhesives, according to various publications in the literature.

One sulphate and three carbon atoms make up the four-membered ring saturated chemical known as thietane. Thietane received less attention from researchers than other S and O heterocycles because of ring strain. On the other hand, it has been claimed that oxidized thietane compounds have anticoccidial, anticancer, antidepressant, insecticide, and herbicidal properties. Thietanes have been demonstrated to take part in ring expansion to produce five to seven membered, sulfur-containing heterocyclic compounds using lithium diisopropylamide (LDA) as a catalyst. In addition, they undergo insertions, intramolecular cyclization, ring opening, and isomerization.

Thiophene is a sulfated, five-membered aromatic heterocycle that is present in a variety of natural products, biologically active chemicals, and potential medications. In the field of material sciences, such as the creation of polymer semiconductors and the light-emitting diode, these are also used as building blocks. Thiophenes are colourless liquids with a boiling point that is similar to that of benzene. They also produce an azeotrope when combined with ethanol, just like benzene does. The ability of thiophene and its derivatives, such as benzothiophene and dibenzothiophene to form coordination bonds with metals via sulphur increases with the number of electron-donating substituents in the thiophene. Thiophene and its derivatives have a variety of pharmacological properties, including antibacterial, photoactivated insecticidal, anticancer, anti-inflammatory, anti-leishmanial, antimicrotubule, antioxidant, anti-HIV, and antifungal.

Sulphur heteroatoms replace the ring carbon atom in homocyclic hydrocarbons. There are significant changes in the cyclic molecular structure caused by different electron configurations, unshared pairs of electrons, and ultimately, the electronegativity between heteroatoms and carbon. These changes are give homocyclic hydrocarbons their significance. The physicochemical characteristics and reactivity of heterocycles containing sulphur are strongly influenced by the overall electron configuration as well

as the adaptable chemistry of the sulphur atom itself. The main protein building blocks cysteine and methionine hold sulphur as a key for the overall tertiary structure. Sulfur is a determinant in many biological processes and is known to form metal complexes with metal ions. Other regulatory roles in biological systems include playing significant roles in regulating translation through sulfuration of transfer RNA, as well as being an essential component in many vitamin cofactors, sugars, and nucleic acids.

It is obvious why sulfur-based heterocycle medications should be given importance in biological systems and how well-liked, it is as a regulatory agent. Due to their biological reactivity, thiadiazole and thiazole complexes are also important in the context of sulfur-based heterocycles. The development of medications to treat a wide range of diseases, including cancer, allergies, infectious diseases, neurological disorders, chronic pain, and fungus-related issues, among others, has led to the discovery of these chemicals. Recently, several novel thiazole-based nitrogen mustards significantly inhibit a panel of human cancer cell lines.

Derivatives of benzothiophene acrylonitrile, which resemble natural combretastatins in terms of structure, have also shown promise as scaffolds for the creation of fresh anticancer medications with improved pharmacological profiles.

One of the components of thiopyran, a six-membered heterocyclic compound, has a sulphur heteroatom. Depending on where the double bond is located, the compound thiopyran can be found in two isomeric forms: 2H-thiopyran and 4H-thiopyran. Due to different substitutions on the thiopyran nucleus, this class of S heterocycles has a broad range of pharmacological effects, including antibacterial, anticancer, anti-hyperplasia, anti-inflammatory, anti-viral, anti-bacterial, and anti-glaucoma properties. Additionally, it has been found that the S-oxides and S, S-dioxide thiopyran oxide forms increase the biological activity of the core thiopyran. Thiopyrans have been used in both; synthetic and medicinal chemistry and can be found in a number of natural compounds, including thromoboxanes, serricornin, tetrahydrodicranenone, and cyclopentanoids.

1.6 DIHETEROATOM CONTAINING COMPOUNDS

Heterocyclic compounds based on nitrogen had good properties. Phenazines are a type of heterocylic compound. A wide variety of bacteria produce phenazines, a sizable group of nitrogen-containing heterocyclic compounds. The effects of phenazine derivatives on bacterial interactions and biotechnological procedures are being studied

for both, natural and synthetic forms. Phenazines act as cell signals that control patterns of gene expression, shuttle electrons to different terminal acceptors, alter cellular redox states, support the formation and structure of biofilms, and improve bacterial survival. Phenazines affect eukaryotic hosts and host tissues in a variety of ways, altering a variety of host cellular responses in the process.

Phenazines may also affect plant growth and induce systemic resistance in plants. Phenazines have multiple functions for producing organism and affect behaviour and ecological fitness. The large class of heterocyclic nitrogen-containing compounds known as phenazines has different chemical and physical characteristics depending on the type and location of the functional groups. Over 6,000 compounds with phenazine as a central moiety have been synthesised, and more than 100 different phenazine structural derivatives have been found in nature[44]. The only known source of naturally occurring phenazines is bacteria. However, due to their potential influence on bacterial interactions and biotechnological procedures, natural and synthetic phenazines are of considerable interest. These secondary metabolites are produced by a variety of bacteria, particularly pseudomonads, and have undergone extensive research due to their roles in virulence and broad spectrum antibiotic properties. Physicochemical characteristics of phenazines, such as their oxidation-reduction (redox) properties, bright pigmentation, and capacity to change colour with pH and redox state, are largely responsible for their ongoing biotechnological interest. The use of phenazines is still widespread and includes uses as electron acceptors and donors, building blocks for fuel cells, environmental and biological sensors, and essential parts of antitumor drugs. Phenazines affect cellular redox state, act as electron shuttles that change electron flow patterns, support the formation and architecture of biofilms, act as cell signals that control gene expression patterns, and support producer survival. Phenazines alter a variety of host cellular responses in eukaryotic hosts and host tissues. Phenazines have an impact on plant growth and induce systemic resistance. The observations that bacterial species may produce various and frequently multiple phenazine derivatives, that these derivatives are produced in various proportions, and the question of whether the quantity or proportion of each derivative produced changes during growth or in response to environmental factors are of particular interest in defining their functional impact.

A five-membered aromatic ring called, isothiazole is also called a 1,2-thiazole, containing three carbon atoms, one nitrogen atom, and one sulphur atom. Isothiazoles

interact with other heteroaromatic chemicals exhibiting aromatic properties. Particular focus is placed on isothiazole ring opening and modifications that lead to functionalized alkenes or other heterocyclic compounds. Particularly appealing isothiazole addition processes produce novel bisheterocyclic compounds with an isothiazole fragment. Reactive dioxides, which are of great interest, are also produced, when the sulphate atom of the isothiazole ring is oxidised. The preferred heterocyclic frameworks are isothiazole (1,2-thiazole) and its benzo counterparts, which can be found in a variety of chemicals with various biological profiles.

Antibacterial drug sulfamethyzole and neuroleptics are ziprasidone and perospirone. In the presence of adogen, it is simple to produce the pale greenish solid dithiazole from chloroacetonitrile and sulphur monochloride. An important class of molecules in medicine chemistry are nitrogen-containing heterocycles with sulphur atoms, such as 1,2,3-dithiazole, a five-membered sulfur-nitrogen heterocycle. It is viewed as a potential scaffold for medicinal chemistry because of its biological activity, unexpected chemical changes, and intriguing physical properties. The design and synthesis of stable neutral and negatively charged radicals, can be used as actual or potential building blocks for molecules-based conductive and/or magnetic functional materials, have been successfully accomplished using the 1,2,3-dithiazole scaffold. The intriguing properties of neutral 1,2,3-dithiazoles have been studied against bacteria, fungi, and herbs.

The five-membered ring of thiazolidine, the sulphur counterpart of oxazolidine, has S and N at positions 1 and 3, respectively. Thiazolidine-2,4-diones have anti-tubercular, antibacterial, anti-diabetic, anti-inflammatory, anti-oxidant, anticonvulsant, antifungal, and anticancer properties.

Thiazole is a sulphur and nitrogen-containing five-membered heterocyclic molecule with the chemical formula C_3H_3NS. It is also known as 1, 3-thiazole because nitrogen and sulphur are located in the first and third positions, respectively. Thiazole is a flexible nucleus that is present in many bioactive molecules, including natural chemicals, and has pharmacological effects that include anti-cancer, anti-microbial, anti-inflammatory, anticonvulsant, antiviral, and anti-tubercular. An important class of S heterocycles with a large number of commercially available drugs are thiazoles. New

biologically active compounds have been developed by combining the thiazole moiety with various heterocyclic rings.

The seven-membered heterocyclic ring structure is thiazepine, which contains nitrogen and sulphur atoms. Depending on where the nitrogen and sulphur atoms are located in the ring, these are either 1,3-thiazepine or 1,4-thiazepine. Thiazepines come in two reduced forms: Thiazapanes, which are completely reduced, and dihydrothiazepines, tetrahydrothiazepines, which are only partially reduced. The 1,4-thiazepine isomer is the more significant one, because it has structural characteristics that make it possible to design and synthesise new bioactive compounds with significant pharmacological activity. Additionally, the benzo- and dibenzo-fused derivatives of these compounds are an important class of scaffolds for numerous drugs and medications.

S-Heterocycles are more in demand in the pharmaceutical industry due to their greater therapeutic potential. In addition, the accessibility of S-heterocycles has increased as a result of recent advancements in their synthesis feasibility. They are a well-known group of heterocyclic chemicals that have a variety of biological effects, such as antiviral, anticancer, antidiabetic, antibacterial, antifungal, anti-inflammatory, and antiviral properties. There is still a need to research new S heterocycles to address various failures and obstacles, such as the increased risk of toxicity via S-heterocycles containing pharmaceuticals, against various pathogenic targets, despite many advancements and diverse techniques in the field of sulphur chemistry. Sulfur-containing pharmaceutically active molecules have been synthesized using more environmentally friendly techniques. Molecules based on S-heterocycles, can serve as a guiding reservoir for researchers in almost every pathological condition, aiding them in the creation of new drugs.

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CHAPTER – II

REVIEW OF LITERATURE

CONTENTS

2.1 CHEMISTRY OF CHALCONES

Sahu et al.[1] showed that Chalcones (1,3-diaryl-2-propen-1-ones) and their heterocyclic analogues, belong to the flavonoid family, which possess a number of interesting biological properties such as antioxidant, cytotoxic, anticancer, antimicrobial, antiprotozoal, antiulcer, antihistaminic and anti-inflammatory activities.

Both functional groups properties are shared by molecules having a carbon-oxygen double bond and a carbon-carbon double bond. In unsaturated carbonyl compounds, the oxygen-carbon double bond and the carbon-carbon double bond are separated only by one carbon-carbon single bond, and both double bonds are conjugated. Chalcones are unsaturated ketones comprised of two aromatic rings with different substituents, [A] and [B]**.** These two rings are joined by a remarkably electrophilic three-carbon unsaturated carbonyl system, creating a nearly planar or linear structure. (Fig.2.1) . Zhu et al.[2] reported the design and synthesis and evaluation of performance towards anti-lung cancer by inducing reactive oxygen species.

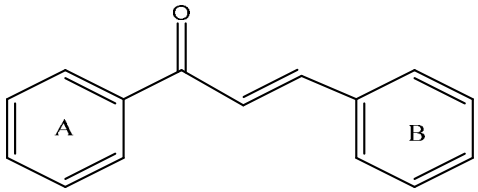


Fig. 2.1: Chalcone Structure

Unsaturated carbonyl systems are a particular class of biologically active chemicals that are mostly used as a building block for the creation of heterocyclic and biodynamic systems. Additionally, it's critical to synthetic and medical organic chemistry. Lin et al.[3] Studied the anti-tuberculosis activity of chalcones.The chalcone is a bichromophoric molecules, which are separated by a keto-vinyl chain and at is a significant group of naturally occurring flavonoids with a wide range of biological roles. Their reactivity is due to presence of a unsaturated keto functional group, which gives them their activity. Chalcones are abundant in nature, particularly in vibrant flowers. Ebenezer at al.[4] reported the Benzimidazole and its derivatives as potent-bioactive substances.

Pyrimidines have intriguing potential as bioactive molecules, heterocyclic compounds containing nitrogen, oxygen, and sulphur have recently received a lot of

attention. Examples of substances with these qualities include pyrazole, benzimidazole, and triazole, which have been shown to have antiproliferative, anti-inflammatory, kinase inhibitory, antibacterial, and anticancer effects. Meanwhile, because of their potential for use as antitubercular, antibacterial, antioxidant, cytotoxic, and anticancer medications, heterocycles containing oxygen as well as sulphur, such benzofuran, benzopyran, and benzothiophene derivatives, have attracted the attention of medicinal chemists. Numerous researchers have concentrated their research on the synthesis of chalcone derivatives using heterocyclic scaffolds due to the broad benefits of organic molecules containing these moieties. With the presence of a heterocyclic ring in the structure, several bioactive chalcones are produced. Due to their remarkable biological activities, these compounds have recently undergone significant development.

In the field of naturally occurring compounds, vibrant compounds are known as Chalcones, Kotahecki and Tambor[5] presented groundbreaking findings. The Greek word "chalcos," which means "bronze," from where this term "Chalcone" originated. Syahri et al.[6] reported a group of naturally occurring compounds known as chalcones has a wide range of characteristics and biological activity.

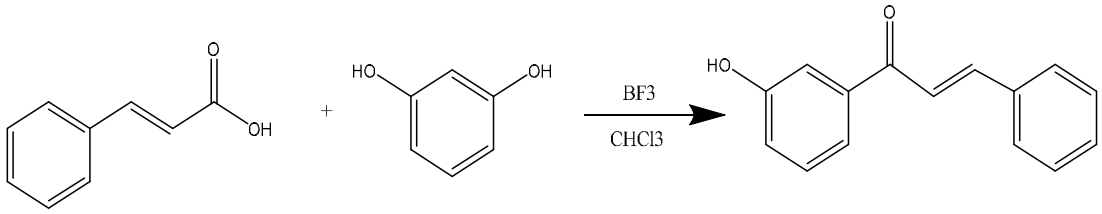
Chalcones are one of the most important classes of natural products existing in many plant species. In nature, they serve as precursors for flavonoids and isoflavonoids biosynthesis. They are 1,3-diphenyl-2-propen- 1-ones (two aromatic rings connected with a carbonyl moiety). According to Shalaby et al.[7], chalcones are crucial flavonoid and isoflavonoid precursors. Many chalcones are prepared by Claisen-Schmidt condensation of methyl ketones with aldehydes in a basic environment[8]. These substances exhibit antimalarial action against variants of plasmodium that are both; chloroquine-sensitive and chloroquine-resistant falsciparum[6]. The synthesis of chalcones was recently reported utilising acetic acid and perchloric acid under acidic conditions[9,10]. Numerous chalcones have been identified as potent tyrosinases as new depigmenting agents since they act as antioxidants and inhibitors[8,11].

All of the chalcones turn pink, when exposed to concentrated H_2SO_4 (a positive Wilson test), and turn violet, when exposed to an alcoholic ferric chloride solution. Chalcones with traces of iodine are heated for two hours in

dimethylsulphoxide (DMSO) produced matching flavones. Chalcones are oxidized with hydrogen peroxide in a methanolic sodium hydroxide solution. These were converted to flavonols, and these flavonols fluoresced conspicuously in ethanolic solution. and concentrated sulfuric acid. Hsueh et al.[12] reported the formation of sulfonyl dihydrobenzo[c] xanthen -7- ones core using double cyclocondensation.

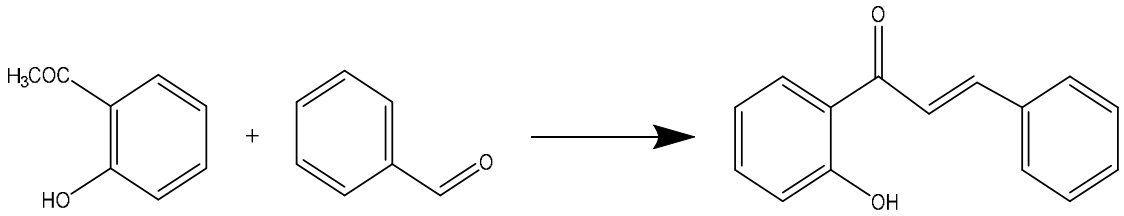
2.2 SYNTHESIS OF CHALCONES

When cinnamic acid and resorcinol are condensed in chloroform in the presence of boron trifluoride (Scheme-2.1)[13,14], chalcone is obtained.



Scheme 2.1

Chalcones play a crucial role as intermediates in the synthesis of pyrazoles, isoxazoles, and pyrimidines. They are created through the catalytic aldol condensation of 2-hydroxyacetophenones with benzaldehydes[15-17]. The 2-hydroxyacetophenone and benzaldehyde can react to afford chalcone in the presence of 0.1 M NaOH (Scheme-2.2)[18,19].



Scheme 2.2

2.3 MEDICINAL IMPORTANCE OF CHALCONES

The 3,4-methylenedioxychalcones have anticonvulsant activity[20], while halosubstituted methylenedioxychalcones have uterotropic, estrogenic, and anti-fertility properties[21]. The 3,4-dimethoxychaleones and its derivatives exhibited antibacterial action[22]. Chalcones with halo, nitro, or amino groups exhibited antibacterial[23], antiviral[24], antifungal[25,26], and anti-allergic activities. Their activity is

increased by the number of hydroxyl substitutions on both rings[27], specifically at positions 2 and 2' or 4 and 4' in chalcones.

The main component of a Chinese medication (the root of *Sophara subprotstrata)*, isoprenyl chalcone sophradin, and its synthesised analogues were found to be efficient anti-ulcer agents[28]. The 2',4'-dihydroxy-3'-methoxychalcone promoted *Pitysaranima calomelaons* spore germination at lower doses and reduced it at higher concentrations[29]. A benzofuranylehalcone called mecinarone has vascular and cardiac effects[30]. While 2',4'-dihydroxy-3',6'-dimethoxy chalcone, isolated from *Polygonum senegalense*, exhibited molluscicidal activity[31].

Certain 2',4'-dihydroxychalcones have been found to have anthelmintic activity also[32]**.** The 3, 4, 2', 6'-tetrahydroxychalcones and their methoxy derivatives have lower capillary fragility[33]. Dihydrochalcones have antimicrobial properties and these can be used to treat coronary insufficiency and cardiac arrhythmia[34,35]. It was revealed that naphthylchalcones have a germicidal effect[36]. Dihydrochalcones have been found to hinder plant growth[37]. The chalcones (flavokawains) isolated from pepper (*P. methysticum*) have been found to exhibit amoebic activity[38]**.** It has been proved that 7, 8-dihydrochalcones have antithyroid effects. The 2,4,4'-trihydroxy and 2,4,4',6-tetrahydroxychalcones have demonstrated effective antitumor activity[39].

A number of novel iodochalcones, flavones, and other chemicals were synthesised by Mokle et al.[33]. Research on flavonols' *in vivo* antibacterial activity is little encouraging. It was shown that a number of substances were more effective than tetracycline. A variety of hydroxychalcones were synthesized and evaluated by Sabzevari et al.[34] for a capacity to combat cancer. Every hydroxychalcone breaks down the mitochondrial membrane by reducing hepatocyte GSH and oxidizing it to GSSG with improved potential and absorption of oxygen. A variety of aryloxypropanolamines were synthesized by Pratap et al.[35]. Chalcones were investigated for antihyperglycemic effectiveness in mice that were either sucrose-laden (SLM) or not (NSL). Streptozotocin was used to create diabetes in the animal (STZ).

The antibacterial activity of various 4-hydroxychalcones and 4-carboxychaIcones was investigated by Kromann et al.[36] who discovered that the carboxychalcones have more antibacterial activity than the parent phenol molecule

(due to their greater aqueous solubility). Lin et al.[37] synthesized a number of chalcones using the Claisen-Schmidt condensation method and tested them for anticancer and anti-inflammatory properties. Strong cytotoxic and anti-inflammatory activities were reported to be present in 2-hydroxychalcones and 2',5'-dihydroxychalcones.

Numerous tetrahydroxychalcones were prepared by Khatib et al.[38] and tested for their capacity to inhibit tyrosinase. It was discovered that two chalcones, 2,3,3',4'-tetrahydroxychalcone and 2,4,2',4'-tetrahydroxychalcone, significantly inhibited tyrosinase. Churkin et al.[39] showed biologically active thiophene derivatives. IV. Synthesis and antiviral activity of unsaturated ketones of the thiophene series. Choudhury et al.[40] identified eight chalcones, dihydrochalcones, and flavones from *Flemingia chappar*. The maximum antifungal activity of 2',4'-dihydroxy-dihydrochalcone was seen *in vitro* against *Curvularia lunata, Atlemaria solani*, and *Helminthosporiim oryzae*.

Several chalcone compounds, with anti-inflammatory and capillary strengthening activities were synthesized by Oganesyan et al.[41]. A class of anti-seborrheic chalcones was prepared by Hinrich et al.[42]. Chalcones stop neutrophils from releasing lysosomal p-glucuronidase[43].

The antibacterial and antifungal activity of several chalcones and flavones was examined by Vibhute and Wadje[44], who discovered that every chalcone and flavone tested was both antibacterial (against *Xanthomonas oryzae* and *Xanthomonas citri*) and antifungal (against *Altemaria tenuis* and *Curvularia lunata*). It was discovered that hydroxy derivatives effectively inhibited bacteria and fungi both. Herbicide chalcone compounds containing triazolyl or imidazolyl substituents were prepared by Lewis et al.[45]. Five of the thirteen phenanthryl and naphthylchalcones were produced by Misra et al.[46] were germicidal. Chalcones inhibited the development of *Diplodia maydis* in liquid cultures has been reported by Ray et al.[47]. Two chalcones counteract ascorbic acid's effects on suppressing hypocotyl growth in *Amaranthus caudatus* seedlings[48]**.** The cytosolic epoxide hydrolase enzyme was successfully inhibited by chalcone oxide derivatives that had a single p-substituent on either phenyl ring[49].

Iwata et al.[50] reported that 3-hydroxy chalcones with a methyl group in the 3',4',2'-positions and isoliquiritigenin homologs had strong inhibitory activities in

phosphorylation which implied antitumorigenic characteristics. Almeida et al.[51] showed identification of a chalcone molecule with best binding energy after molecular docking calculations.

Iwata et al.[52] reported that some chalcones are capable of phototransforming in solution from ferrous to cis isomers. The isomerization of 3-hydroxy-3'-methyl chalcone from trans to cis was found to occur under the influence of daylight in a methanolic solution. The presence of a hydroxy group in the 2- or 4- position of the trans chalcone structure prevents phototransformation into the cis-isomer. The phototransformed cis-3-hydroxy-3'-methyl chalcone had greater antitumorigenic activity than the original trans form. Nielsen et al.[53] synthesized a large number of substituted chalcones and tested them for their ability to inhibit lymphocytes and fight leishmaniasis and found that the steric interactions between the chalcones and the target are essential for compound potency. Chalcone derivatives inhibited the synthesis of denovo inducible nitric oxide synthase and cylcooxygenase-2, suggesting that they may be used to treat inflammatory diseases[54]. It has also been demonstrated that several chalcone chemicals inhibit famesyl protein transferase.

Chalcones can obstruct the development and function of effector cytotoxic T lymphocytes[55]. A chalcone derivative having a 3,4-dihydroxycinnamoyl structure is 3,4-dihydroxychalcone. The 3,4,2'-trihydroxychalcone, 3,4,2-dihydroxychalcone, and 3,4,2',4'-tetrahydroxychalcone were ten times more effective than cyclo-oxygenase activity at suppressing epidermal 12-lipoxygenase activity. Both enzyme activities were minimal or not at all affected by the chalcone derivatives with a cinnamoyl or 4-hydroxycinnamoyl structure in the molecule. Chalcone oxides block the activities of glutathione 5-transferase and cytosolic epoxide hydrolase by binding to an active location where the chalcone's carbonyl group interacts with an acidic area known to be crucial for initiating epoxide hydrolysis[55,56].

Chalcones are useful probes for comparing secretory events because they restrict the release of histamine by human basophils, when they are triggered by various stimuli. At doses, larger than 0.5 mM, chalcone and its derivatives, in particular 4-hydroxychalcone, hindered the mitochondrial electron transport system as powerful uncouplers of oxidative phosphorylation. Analogues of chalcone thiophene had only moderate antiviral activity. Adenosine-3',5'-cylcic monophosphate

phosphodiesterase was inhibited by prenyl chalcones and Diels-Alder adducts of mulberry tree chalcones in medicinal plants[40]. The cytosolic epoxide hydrolase activity in the liver is suppressed by chalcones, p-naphthoflavones, and a-naphthoflavones. Chalcone, quercetin, and fisetin were the most effective and membrane-permeable inhibitors of histamine release from human basophils. A variety of chalcones were developed by Oganesyan et al.[41]. They also investigated the relationship between anti-inflammatory and hypoglycemic actions.

Chalcones have been demonstrated to inhibit thyroxine-5'-deiodinase, causing them to have anticancer effects[56]. The virus is rendered inactive by a chalcone that has been found to be specifically active against human rhinoviruses[57] by binding with a particular region on the viral capsid protein. The molluscicidal activity of 24 chalcones and 12 chalcone epoxides was examined by Adewunmi et al.[58]. The epoxides had little impact compared to the chalcones, which were extremely powerful against Biomphalaria glabrata.

Two active chalcones from *Glycerrhiza uralensis*, liqueritigenin and isoliquiritigenin inhibited rat liver mitochondrial monoamine oxidase[59] (MAO). The reason is that the second molecule was more effective than the first, MAO inhibition was substrate-competitive. In mouse and rat liver, 4-phenylchalcones, chalconeoxides, and related compounds were made and tested for their ability to inhibit GST and cytosolic epoxide hydrolase, which resulted in a concentration-dependent decrease in tumor-promoter-induced histamine release[60]. The cytosolic epoxide hydrolase was inhibited by a number of substances more effectively than the parent chemical, 4'-phenylchalconeoxide, although the inhibition was decreased by the presence of bulky substituents in the 4th and 2nd positions. While chaleones were found to be inhibitors of cytosolic GST acting on cw-stilbene oxide, chalcone oxides were revealed to be selective inhibitors of cytosolic epoxide hydrolase acting on mms-stilbene oxide.

A group of chalcone compounds were prepared by Mehta et al.[61], a new class of antimitotic medications that can be used to treat gout. Chaleones antiviral action was shown by their ability to bind to the hydrophobic pocket-corresponding region of the viral protein VPI P-baorel of HRV[62]. The antifeedent activity of chaleones from the genera *Lonchocarpus* and *Tephrosia* against larvae of Spodoptera littoralis and

Spodoptera exempt was examined by Simmonds et al.[63], and reported a link between the activity and the molecular structure of the compounds was.

The possible conversion of flavones to 2'-hydroxychalcones was associated with the antiallergic effect of 2'-hydroxychalcones[64]. Several chalcones inhibited the gastric H*, K+ - ATP ase and Na+, K+ - ATP ase enzymes in comparison to the inhibition brought on by sophradin and sofalcone[65]. It was reported that chalcones prevented 74% of the liver damage caused by galactosamine[66] even at higher doses (5000 mgKg-1). Nematollahi et al.[67] reported recent advancements pertaining to the antibacterial, antiviral, antiparasitic, and antifungal activities of chalcones and their derivatives are deliberated, focusing on the relevant mechanisms of action, crucial challenges, and future prospects. Collins-Burow et al.[68] suggestsed that phytochemicals affect multiple signaling pathways that converge at the level of transcriptional regulation. The ability of flavonoids to regulate MAPK-responsive pathways in a selective manner indicates a mechanism by which phytochemicals may influence human health and disease. Liu et al.[69], assessed the responses of the flavonoid pathway to UV-B radiation treatments and its correlation to the lipid peroxide and antioxidant systems in C. mongolica. In UV-B radiation experiments, plants were exposed to UV-B radiation treatments with a intensity of 30 J/s for 1, 4 and 24 h, respectively

Licochalcone, which was obtained from an ethanol extract of dried Chinese licorice roots, inhibited Leishmania major's development both in vitro and in vivo by alkylating the thiol group in N-acetyl-L-cysteine. The 2-hydroxychalcone inhibited glutathione-S-transferase isoforms, and this inhibition is reversible. Chaleones decreased the amount of reactive oxygen species that human neutrophils released by interfering with the membrane N-iMet Leu Phe (FMLP) receptor[70]. Yuan et al.[71] represented the first report of the natural phenylpropanoid-dihydrochalcone hybrid compound, and lays foundation for the study on the bioactive principles of the ethnic hypoglycemic medicinal plant. Janković et al.[72], studied to test antioxidative potency of chalcones in *in vitro* model in serum (native conditions), so as with exogenously induced oxidative stress. Tao et al.[73], studied that pyrene based chalcone derivatives possess the potential for optical data storage and optical limiting. Moreover, our study further proved the superiority of ISRE on enhancing the TPA of nonlinear materials.

Phrutivorapongkul et al.[74] found novel chalcone derivatives from the stem bark of *Millettia leucantha* (leguminosae), where dihydrochalcones showed only minor anti-herpes simplex virus (HSV) activity. Numerous chalcones were prepared by Climent et al.[75] and it was found that they exhibit anti-inflammatory, anti-cancer, and diuretic characteristics. Chalcones were synthesised by Lunardi et al.[76] and found to be leishmanicidal and trypanocidal *Leishmania brasiliensis* and *Trypanosoma cruzi's in vitro* growth were suppressed by all these compounds, where tested at various concentrations with no discernible harm to host macrophages.

A new enaminone synthon was employed to prepared a number of retinoid-like chalcones[77-81] as well as other licochalcone A derivatives. These new compounds have been tested *in vitro* as potential antimalarial medications. They exhibited a potent and consistent inhibitory action on the *in vitro* growth of *Plasmadium falciparum*. Several analogues trapped in the Z- or E- state were examined for anti-plasmodial action[82-85]. Kidwai et al.[86] synthesized base catalysed pyrimidine using microwave. Jagir, Mukut et al.[87], a facial microwave-induced one-pot synthesis of novel pyrimido [4,5-d] pyrimidines and pyrido [2,3- d] pyrimidines under solvent-free conditions. Nagaraj et al.[88], a series of novel bis-chalcones 3 were prepared by the reaction of 5,5′-methylene-bis-salicylaldehyde 2 with various acetophenones, subsequent treatment of 3 with thiourea or guanidine resulted to the corresponding bis-thiazines or bispyrimidines in good yields. All the new compounds have been characterized by IR, ^{1}H NMR, MS and elemental analysis. The antibacterial, antifungal and anti-inflammatory activities of the compounds have also been evaluated. Adib et al.[89], a simple and efficient synthesis of 2,4,6-triarylpyridines is described from a novel reaction between chalcones and ammonium acetate under solvent-free conditions in excellent yields. Wu et al.[90] showed the silica gel-catalyzed synthesis of 5-amino-2-aryl-3H-chromeno [4,3,2-de][1,6] naphthyridine-4-carbonitriles and 5-amino-2-aryl-3H-quinolino [4,3,2-de][1,6]naphthyridine-4-carbonitriles were simply achieved upon the one-pot cascade reaction of malononitrile with substituted 2-hydroxyacetophenone (or 2-aminoacetophenone) and aromatic aldehyde in aqueous media.). Ramesh et al.[91] showed to select substituents by using Topliss modified approach to synthesize new 1,3 oxazines with antimicrobial effect. In the series of 6-[4-substitutedphenyl]-4-phenyl-6H-1,3-oxazin-2-amines and N-[6-(4-substitutedphenyl)-4-phenyl-6H-1,3-oxazinyl] acetamides, substituents at fourth

position of the phenyl ring were selected according to the Topliss modified approach and the initial set of compounds was synthesized. The antimicrobial screening revealed that compounds with methoxy substituent having negative sigma (-0.04) and negative pi (-0.27) values are good antimicrobial agents showing low minimum inhibitory concentration (MIC). Mamoru et al.[92], various 2-alkylthio-1,3-thiazine derivatives were synthesized by the reactions of S-alkylthiocarbamates with α,β-unsaturated ketones in the presence of BF 3· Et 2 O. The thiazine was converted into two isomeric dehydrated products in the presence of a Lewis acid. Waterinckx et al.[93], new, efficient, and straightforward synthesis of 3-arylmethyl-4-chloromethyl-2-imino-1,3-thiazolidines and 2-(N-acylimino)-3-arylmethyl-4-chloromethyl-1,3-thiazolidines has been developed by ring transformation of 1-arylmethyl-2-(thiocyanomethyl) aziridines upon treatment with a catalytic amount of titanium(IV) chloride in dichloromethane. Van Allan et al.[94], prepared a certain pyrylium salts by using chalcone and boron trifluoride etherate. Mcnaught[95], the systematic name of a compound is designed so that one may deduce from it, the molecular structure of the compound, as indicated by its graphic formula. In other words, it is essentially a verbal substitute for the graphic formula and, in its most elaborate form, provides precisely the same structural information. This chapter provides a guide to the nomenclature of heterocyclic compounds. Houben-Weyl Methods of Molecular Transformations. Hetarenes and related ring systems: Six- Membered Hetarenes with two identical Heteroatoms covering research of Peptide and peptidomimetic,five membered hetarenes with one chalcogen and one heteroatom. Ullmann's Encyclopedia of Industrial Chemistry is the benchmark reference in chemistry and chemical and life science engineering, covering inorganic and organic chemicals, advanced materials, pharmaceuticals. Heterocyclic compounds play a vital role in the metabolism of living cells. Their practical applications range from extensive clinical use to fields as diverse as agriculture, photography, biocide formulation and polymer science. Modern heterocyclic chemistry covering heterocyclic compounds synthesis, structure and chemical and physical properties.[96-102]

2.4 INTRODUCTION TO PYRIMIDINE

The 6-membered heterocyclic compounds with two hetero atoms containing two or more fused rings are of our main concern because of their wide applications.

Pyrimidines are 6-membered heterocyclic compounds, containing two nitrogen atoms at positions 1 and 3 of the six membered rings.

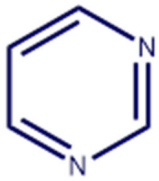


Fig. 2.2

It has a formula molecular $C_4H_4N_2$and its molecular weight is 80.088 g mol^{-1}. It is a colourless compound, having melting point 20- 22.5°C and boiling point 123-124°C. It is weak base (pKa = 1.23) that forms a number of solid derivatives such as hydrochloride, methiodide and its λ_{max} value is 240 nm.

The reactivity of pyrimidine ring is approximately equivalent to that of 3-nitropyridine. The electrophilic substitution reactions are difficult as compared to nucleophilic substitutions. Because of weak basicity of nitrogen, the electrophilic reagent attack is more difficult on pyrimidine ring but in presence of activating groups, the electrophilic attack becomes feasible and takes place at 5^{th} position of the ring. The unsubstituted pyrimidine undergoes 5-halogenation under vigorous conditions, but it becomes easier, when one or more activating substituent are present.

2.5 SOME IMPORTANT NATURALLY OCCURRING DERIVATIVES OF PYRIMIDINE

Pyrimidines are essential for any form of life because it is an important pharmacore. Being integral part of DNA and RNA, it interacts with the synthesis and functions of nucleic acids. Ortic acid, is thought to be the key precursor in the biosynthesis of all naturally occurring pyrimidines. It has been used in combination with 4-amino-5-imidazole carboxamide for the treatment of liver disease. Uracil, is a constituent of nucleic acid and widely distributed in nature. It is excellent starting material for the preparation of pyrimidines, pteridines and purines. Thymine, is not found in ribonucleic acid but present in deoxyribonucleic acid. Alloxan, induces permanent diabetes in many animals, but not in humans. Cytosine, is widely distributed in nature being a constituent of nucleic acid and it can be isolated by hydrolyzing thymus nucleic acids.

Thiamine, (vitamin B_1), is a water-soluble vitamin of the B-complex family. Its structure consists of aminopyrimidine and a thiazole ring linked by a methylene bridge. The thiazole is substituted with methyl and hydroxyethyl side chains. All living organisms use thiamine, but it is synthesized only in bacteria, fungi and plants. Adenine, is a nucleobase and chemical component of DNA and RNA. The shape of adenine is complementary to either thymine in DNA or uracil in RNA. Uric acid, is the product of the metabolic breakdown of purine nucleotides. Guanine is one of the four main nucleobases found in the nucleic acids and derivative of purine consisting of fused pyrimidine-imidazole ring system with conjugated double bonds.

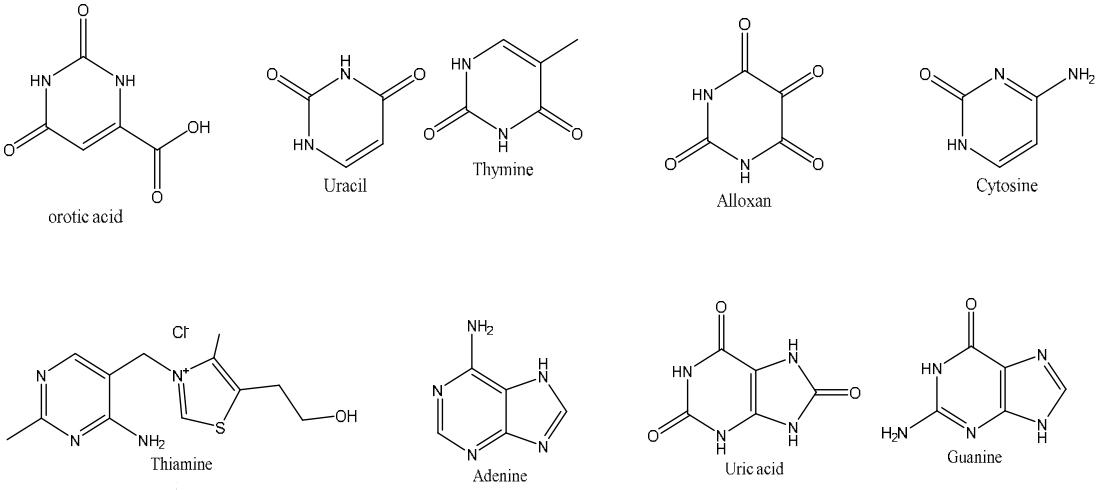


Fig. 2.3

Certain pyrimidine derivatives are also used as agrochemical and dyes industries. In agrochemical, such as bensulfuron- methyl is used as systemic herbicides that inhibit biosynthesis of the essential amino acids valine and isoleucine; Nuarimol is systemic fungicide that acts by inhibiting ergosterol biosynthesis and it is used to control a wide range of pathogenic fungi, such as powdery mildews on fruit. Pyrimidine is also used in dye industries as isoindoline pigments (Pigment yellow) for the coloration of paints and plastics.

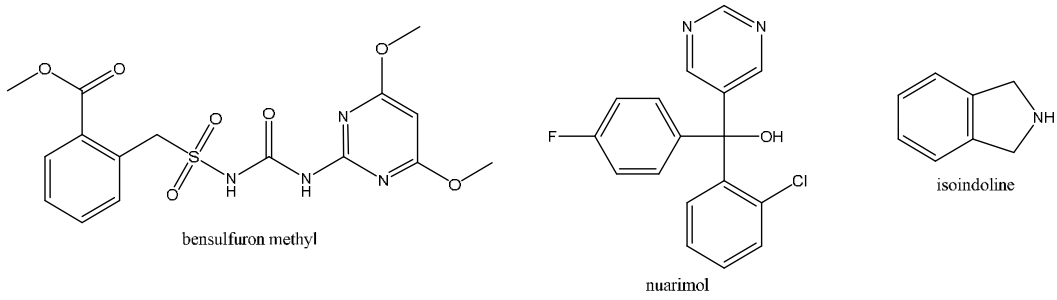


Fig. 2.4

Heterocyclic compounds, pyrimidines are one of the most important heterocycles with remarkable pharmacological activities because it is an essential constituent of all cells and thus all living matters. Pyrimidines have occupied a unique place and remarkably contributed to medicinal chemistry. There are very important class of pharmaceutical compounds. The various compounds such as alkaloids, essential amino acids, vitamins, haemoglobin, hormones, large number of synthetic drugs and dyes contain pyrimidine heterocyclic ring systems. The presence of pyrimidine nucleus in the compounds enhances their medicinal and biological activities. The several pyrimidine nucleoside analogues have been developed as antiviral agents: AZT is the most widely used anti-AIDS drug; stavudine, which is effective in the treatment of HIV infections and AIDS and lamivudine, which is used to treat both hepatitis B and AIDS.

2.6 BIOLOGICAL ACTIVITY OF PYRIMIDINE BASED COMPOUNDS

Because of their biological relevance, pyrimidines is the topic of a lot of synthetic activity. The pyrimidine nucleus can be found in a variety of natural products that are essential to biological processes and living creatures. Pyrimidine derivatives have a long history in medicinal chemistry because of their therapeutic potential. Several pyrimidine derivatives have been created as chemotherapeutic medicines over the last three decades and have found widespread clinical use. Some biologically important pyrimidine-based derivatives are;

2.6.1 ANTIMICROBIAL ACTIVITY

Abdel-Gawad et al.[103] synthesised various novel pyrazolo [3,4-d] pyrimidines and tested their antibacterial and antifungal properties *in vitro* at 100 pg mL^{-1} using

ampicillin and elaforam as reference compounds. Ismail[104] synthesised certain sulfur-containing pyrazolo [3,4-d] pyrimidines, and some of these compounds exhibited antimicrobial action, when compared to typical antibacterial and antifungal agents, chloramphenicol and terbinafine.

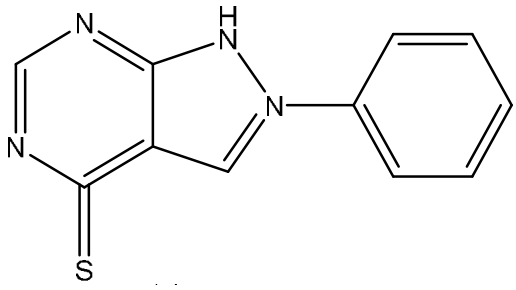


Fig. 2.5

Condensed pyrimidine derivatives were produced by Ashok et al.[105], *S. aureus*, *S. typhi*, *E. coli*, *B. subtilis*, and *S. cervisiae* were all evaluated with these chemicals.

Khatri et al.[106] produced various new amino pyrimidines and tested their antibacterial efficacy against gramme positive, gramme negative, and antifungal organisms such as *Aspergillus niger*.

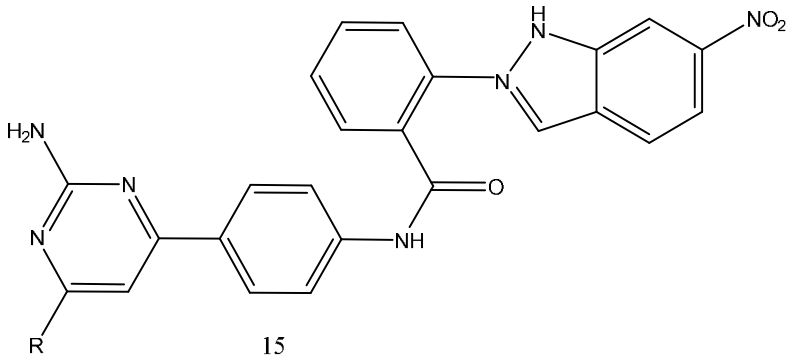


Fig. 2.6

Oyama and Ito[107,] electrophilic cyclization via the boronate complex between various homoallylic boronates and Selectfluor is reported. This reaction provided a fluoromethylated cyclopropane ring that was difficult to synthesize by previous methods. The use of phenyl lithium, which activated the homoallylic boronate, was important for the reaction.

Bodke et al.[108] prepared some novel benzofuro [3,2-d] pyrimidines, which were tested for their antibacterial and antifungal properties. Nimavat et al.[109] synthesised a series of 1,6 dihydro-2-mercapto-4-aryl-6-(3'-bromophenyl)-pyrimidines, all of which exhibited significant antibacterial action.

Some 5H-pyrazolo [3',4':4,5] thiazo[3,2-a] pyrimidines were synthesised by Sherif et al.[110] and some of these compounds demonstrated antibacterial action. antibacterial thienopyrimidine compounds were prepared by Shah et al.[111]. Thakral et al.[112] synthesised pyrido [2,3-d] pyrimidines. Their antibacterial and antifungal activity was tested which was found to be modest.

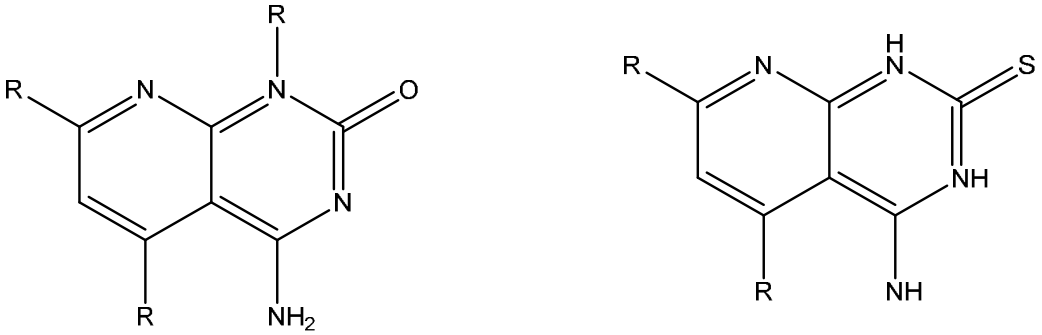


Fig. 2.7

New pyrimidine derivatives were synthesised by Dhokale et al.[113]. The antibacterial activity of the compounds created was moderate.

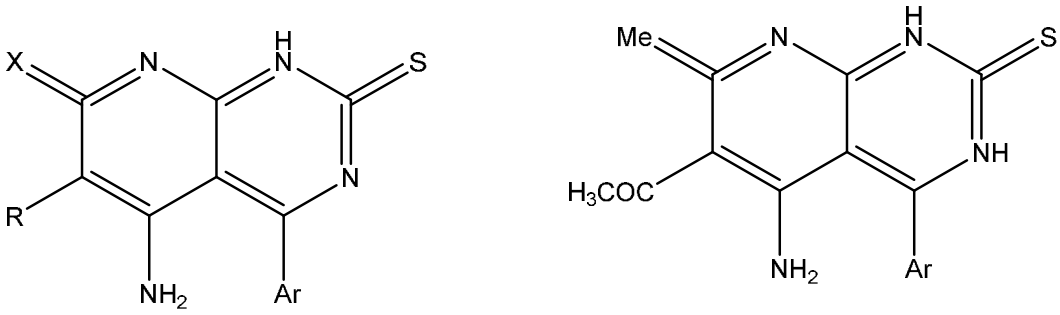


Fig. 2.8

Some pyrido [2,3-d] pyrimidines were synthesised by Bedarir et al.[114]. Some of these compounds were shown to have antibacterial properties. Novel thiazolo [4,5-d] pyrimidines were synthesised by Balkan et al.[115]. The microdilution method was used to test them against bacteria and yeasts. New pyrimidine and pyrazolo [3,4-d]

pyrimidine derivatives were synthesised by Zhang et al.[116]. The antibacterial activity of all of these produced compounds was evaluated *in vitro*.

Eissa et al.[117] prepared a novel class of tetrahydro benzothieno pyrimidines and C albicans was used to evaluate activity of synthesised compounds, as well as against a variety of gram-positive and gram-negative bacteria. Their MIC was found. Ibrahim et al.[118] prepared thiazolo [4,5-c] pyrido [1,2-a] pyrimidines with potent antibacterial properties. Innocenti et al.[119], Fused pyrimidine cores are privileged kinase scaffolds, yet few examples of the 2-amino-pyrido[3,4-d]pyrimidine chemotype have been disclosed in the context of kinase inhibitor programs. Furthermore, no general synthetic route has been reported to access 2-amino-pyrido[3,4-d]pyrimidine derivatives and reported a versatile and efficient chemical approach to this class of molecules. Strategy involvesed the concise preparation of 8-chloro-2-(methylthio)pyrido[3,4-d]pyrimidine intermediates and their efficient derivatisation to give novel compounds with potential as kinase inhibitors.

Patel and Mehta[120] synthesized 2-amino-4-substituted-phenyl-6-(8-quinolinol-5-yl) pyrimidines with moderate to powerful antibacterial activity.

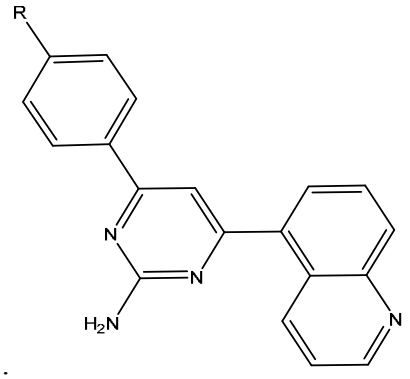


Fig. 2.9

New pyrimidine derivatives with antibacterial action were synthesised by Verma et al.[121].

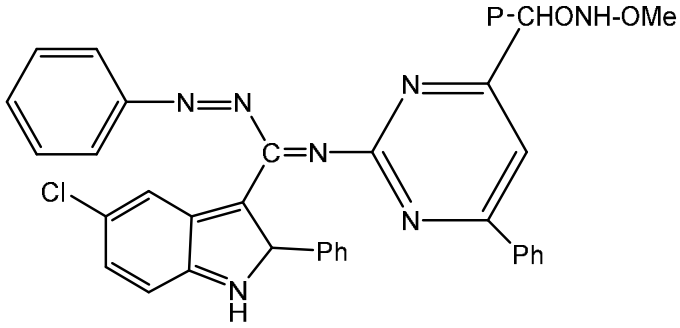


Fig. 2.10

2.6.2 ANTICANCER ACTIVITY

Some 5H-pyrimido [3',2':5,6] thipyrano [4,3-d] pyrimidines were synthesised by Primofiore et al.[122]. An *in vitro* assay on human tumour cell lines was used to investigate the antiproliferative efficacy of these drugs (HL-60 andHelA). These fluorinated thiazolo [4,5-d] pyrimidines were synthesised by Fahmy et al.[123]. The chemicals were found to be active on 60 human cell lines.

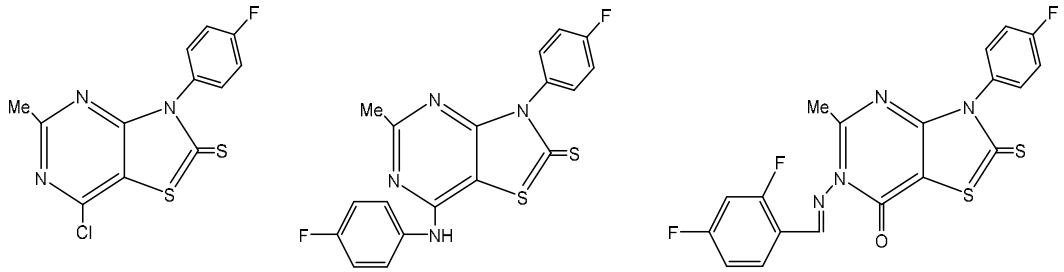


Fig. 2.11

Some 3,4-dihydro-lH-pyrimidine-2-ones were synthesised by Schroeder[124] **.** They showed dual FGFR/VEGFR tyrosine kinase inhibition capability. A series of pyrido [2,3-d] pyrimidines were synthesised by Veanch et al.[125]. These have substantially stronger anticancer properties. Donkor et al.[126] prepared a new class of 6-substituted-2,4-diaminothieno[2,3-d]pyrimidines and listed for *P. carinii*, *T. gondii*, and *M. avium*. These drugs were found to block dihydrofolate reductase.

Some pyrazolo [3,4-d] pyrimidines were synthesised by Kim et al.[127]. The anilino compounds outperformed 4-benzyl compounds in terms of inhibitory efficacy in this series. The 2,4-diamino pyrrolo[2,3-d]pyrimidine derivatives were synthesised by Rosowsky et al.[128]. They are dihydrofolate reductase inhibitors in *P. carinii*, *T. gondii*, and *M avium*. Burchat et al.[129] synthesized pyrazolo [3,4-d] pyrimidines and pyrrolo[2,3-d]pyrimidines. These chemicals are strong kinase inhibitors. Fluorinated

thiazolo [4,5-d] pyrimidines were synthesised by Fahmy et al.[130]. The NCI selected nine of these newly produced drugs for *in vitro* anticancer testing.

Babu et al.[131] prepared new substituted pyrimidines containing benzofurans, all of which had anticancer action.

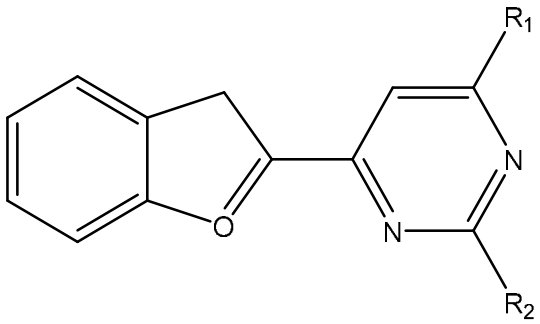


Fig. 2.12

Some 2-anilino-4-(lH-pyrrol-3-yl) pyrimidines were produced by Wang et al.[132] shown anti-cancer action.

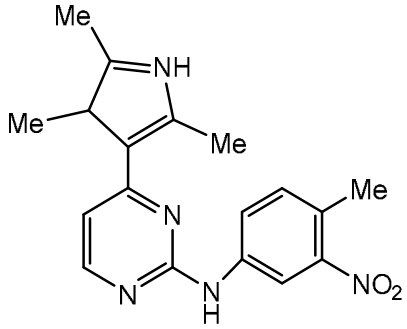


Fig. 2.13

Deasi et al.[133] reported a series of pyrimidino [2,l-c][l,2,4] triazin-8-ones and l,2,4-triazolo[4,3-a]pyrimidine-7-ones. These two compounds were found to have potent anticancer properties.

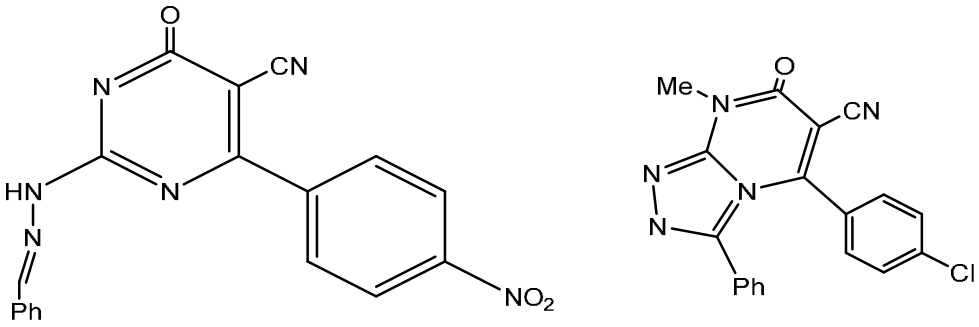


Fig. 2.14

2.6.3 ANTI-TUBERCULAR ACTIVITY:

Moukha-chafiq et al.[134] prepared 4-substituted l-[l-(2,3-dihydroxy-lpropoxy) methyl-1,2,3- triazol- (4 and 5)-yl-methyl] l-[l-(2,3-dihydroxy-lpropoxy) methyl-1,2,3- triazol- (4 and 5)-yl-methyl]. The anti-tubercular action of -lH-pyrazolo [3,4-d] pyrimidines was found to be modest.

Nimavat et al.[135] synthesized and tested 2-amino-4(31-bromophenyl)-6-arylpyximidines for anti-tubercular action. Pathak et al.[136] prepared and tested 2-thiosubstituted pyrimidines against different Mycobacteria TB strains. Some 2-amino-4,6-substituted pyrimidines and 2-mercapto-4,6-disubstituted pyrimidines were synthesised by Abd EI-Fatah et al[137]. These have a negligible anti-tubercular effect. The N-,S-, and o-mononitro- and dinitro benzyl derivatives of nitrogen heterocycles were produced and tested against *Mycobacterium tuberculosis* by Koci et al.[138].

Pasha et al.[139] prepared antitubercular 2,6-disubstituted pyrimidine-2-thiones and 2- amino-4,6-disubstituted pyrimidines.

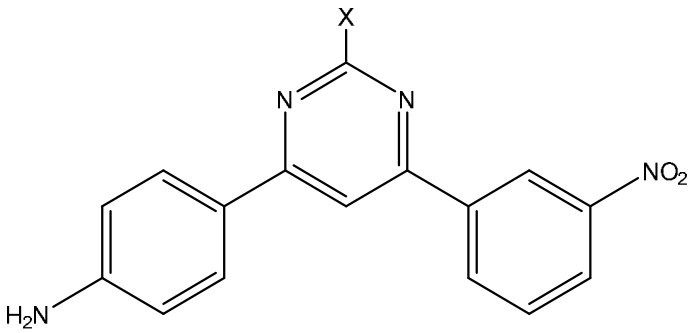


Fig. 2.15

Sixteen, out of thirty 6-aryl-2-substituted pyrimidine-4-yl phenols synthesized by Agarwal et al.[140] demonstrated anti-mycobacterial action.

2.6.4 ANTIVIRAL ACTIVITY:

Rostom et al.[141] prepared 2-(benzoxazol-2-ylamino)-3H-4-oxo pyrimidines and tested them for anti-HIV efficacy *in vitro*.

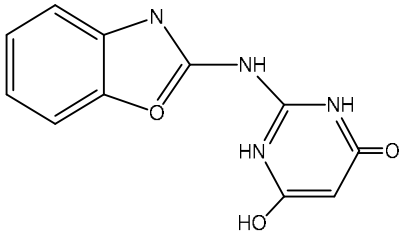


Fig. 2.16

Phaditare et al.[142] observed that 1-[(hydroxy methyl) phenyl methyl] thiophenyl pyrimidines are effective HIV-RT inhibitors. Jeong et al.[143] prepared 2'-azido-2',3'-deoxy arabinofuranosyl pyrimidines and tested them against HIV-1, HSV-1, HSV-2, and HBY viruses.

Zhou et al.[144] synthesized (Z)- and (E)-[2-fluoro-2-(hydroxyl methyl) cyclopropylidiene] methyl pyrimidines that are methylene cyclopropane nucleoside analogues.

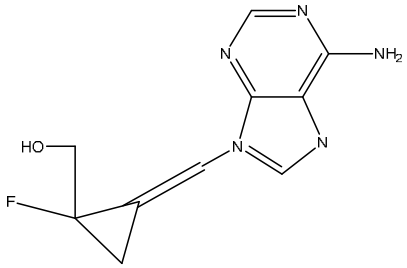


Fig. 2.17

The 2,4-diamino-5(2',5'-substituted benzyl)pyrimidines were synthesised by Rosowsky et al.[145], and these are prospective medications against opportunistic infections of AIDS and other immunological diseases. Chern et al.[146] prepared pyrazolo [3,4-d] pyrimidines, which are highly specific for human enteroviruses, especially coxsackie viruses.

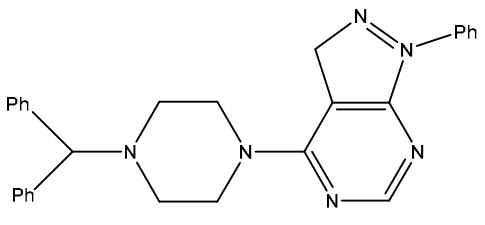


Fig. 2.18

El Otmani et al.[147] synthesised some pyrazolyl (isoxazolyl) pyrido [l,2-a] pyrimidines having anti-HIV activity. Warmstaedt et al.[148] synthesised some acyclic nucleoside phosphonates and tested against HSV-1, HSV-2 and HIV-1. They showed weak antiviral activity.

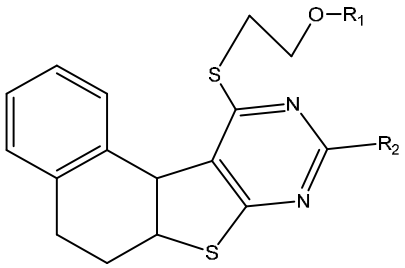


Fig. 2.19

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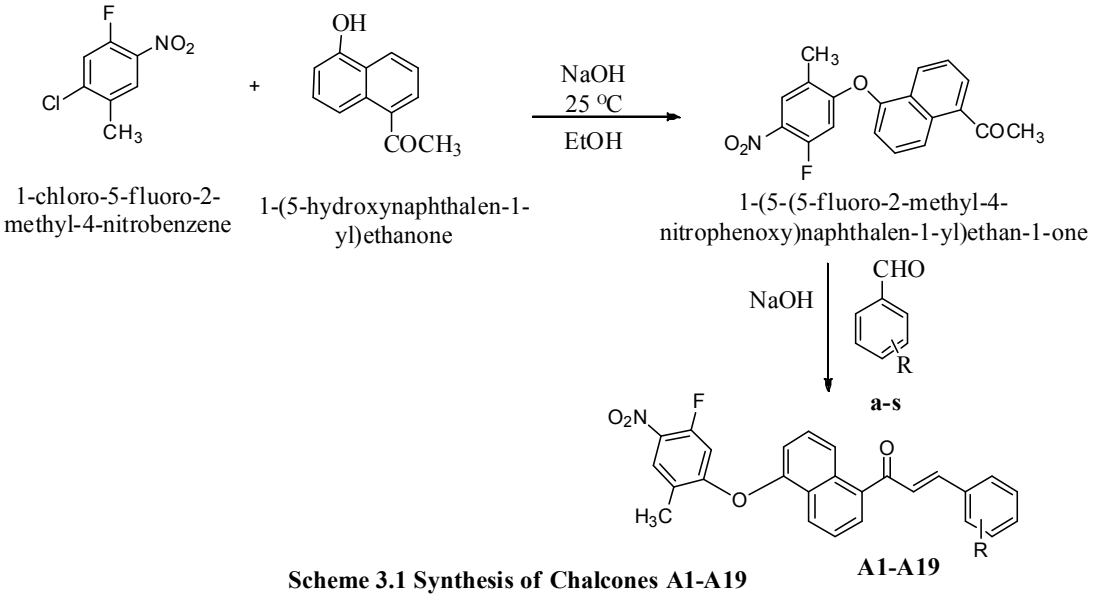
CHAPTER – III

SYNTHESIS AND CHARACTERIZATION OF CHALCONES

CONTENTS

3.1 REACTION SCHEME

Some chalcones [**A1-A19]** were prepared by reaction between 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in the presence of NaOH under ethanol as solvent followed by reaction with aromatic aldehyde (**Scheme 3.1**).



1-chloro-5-fluoro-2-methyl-4-nitrobenzene

1-(5-hydroxynaphthalen-1-yl)ethanone

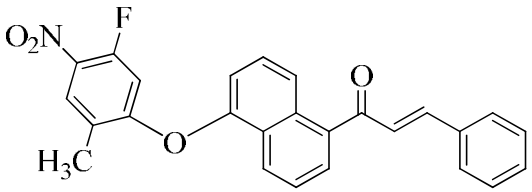
1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)ethan-1-one

A1-A19

Scheme 3.1 Synthesis of Chalcones A1-A19

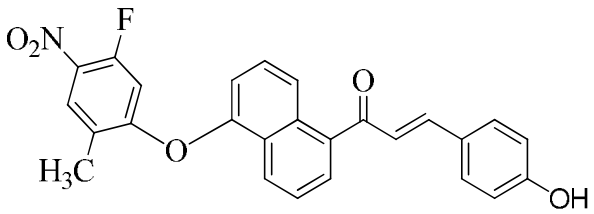
3.2 STRUCTURE OF COMPOUNDS A1 TO A19

Compound A1:



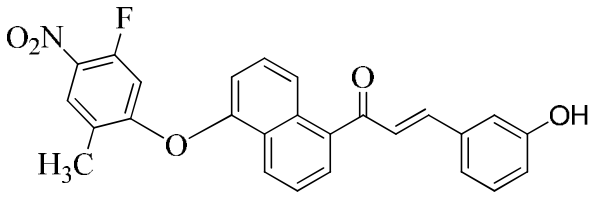
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-phenylprop-2-en-1-one

Compound A2:



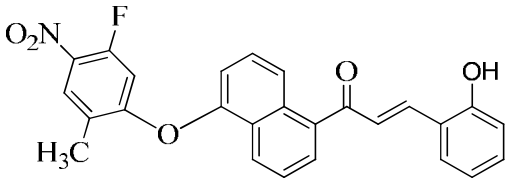
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(4-hydroxyphenyl)prop-2-en-1-one

Compound A3:



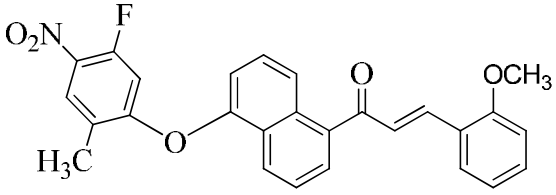
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(3-hydroxyphenyl)prop-2-en-1-one

Compound A4:



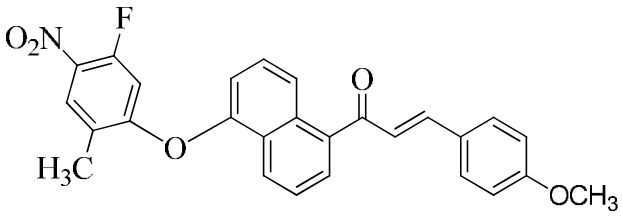
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(3-hydroxyphenyl)prop-2-en-1-one

Compound A5:



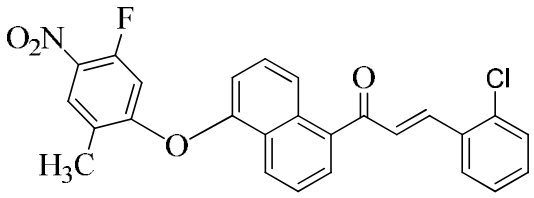
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(2-methoxyphenyl)prop-2-en-1-one

Compound A6:



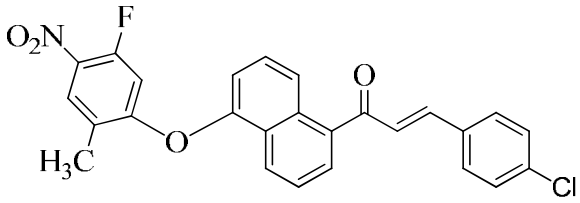
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(4-methoxyphenyl)prop-2-en-1-one

Compound A7:



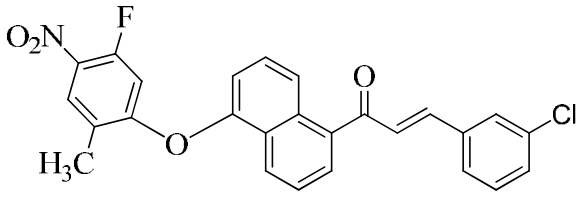
(*E*)-3-(2-chlorophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

Compound A8:



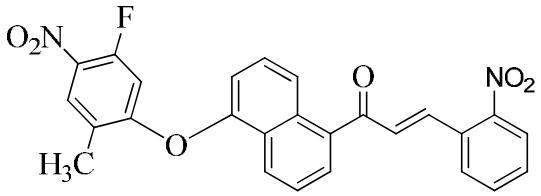
(*E*)-3-(4-chlorophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

Compound A9:



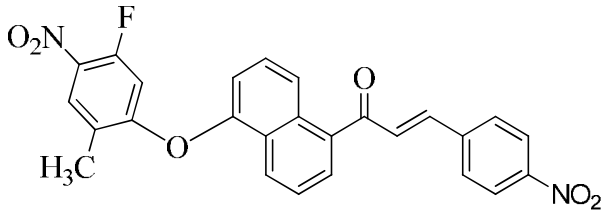
(*E*)-3-(3-chlorophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

Compound A10:



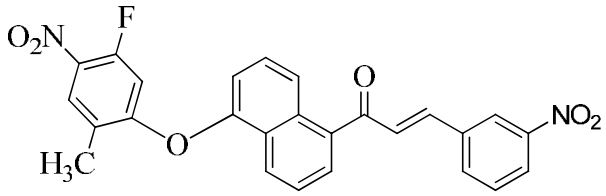
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(2-nitrophenyl)prop-2-en-1-one

Compound A11:



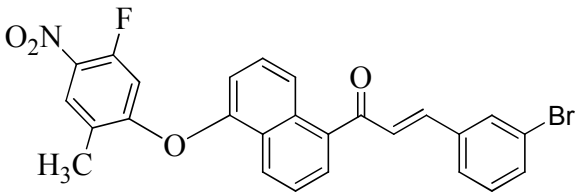
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(4-nitrophenyl)prop-2-en-1-one

Compound A12:



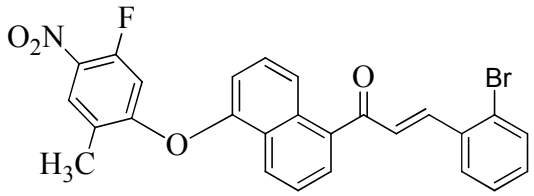
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(3-nitrophenyl)prop-2-en-1-one

Compound A13:



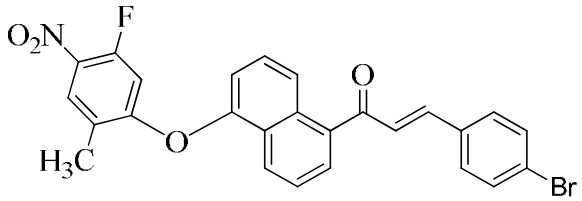
(*E*)-3-(3-bromophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

Compound A14:



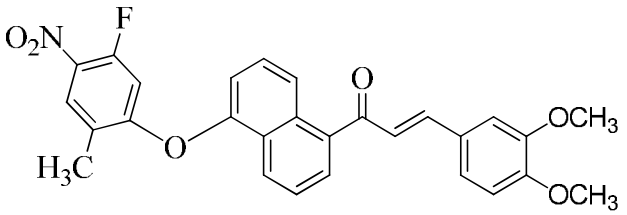
(*E*)-3-(2-bromophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

Compound A15:



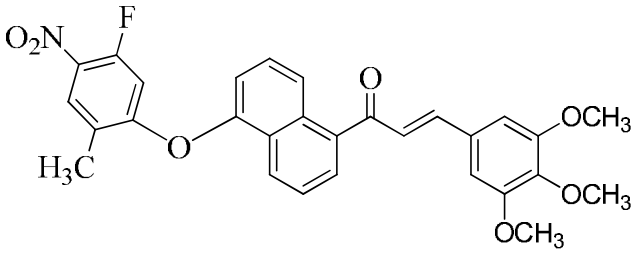
(*E*)-3-(4-bromophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

Compound A16:



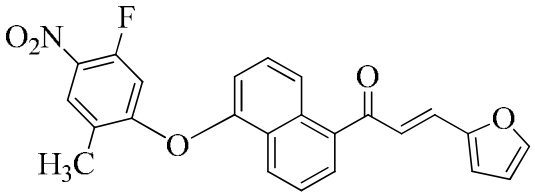
(*E*)-3-(3,4-dimethoxyphenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

Compound A17:



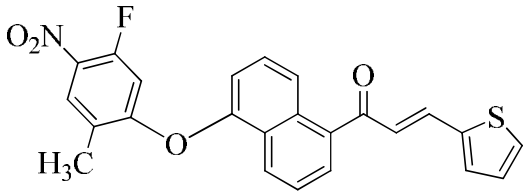
(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one

Compound A18:



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(furan-2-yl)prop-2-en-1-one

Compound A19:



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(thiophen-2-yl)prop-2-en-1-one

3.3 EXPERIMENTAL

3.3.1 Chemicals and Reagents

All chemicals used were of laboratory reagent grade and used without further purification**.** Various aldehydes, 1-(5-hydroxynaphthalen-1-yl)ethan-1-one, 1-chloro-5-fluoro-2-methyl-4-nitrobenzene, NaOH and ethanol were used as received from Merck, Mumbai, India.

3.3.2 Analytical Methods

Bruker Avance-400 MHz instrument was used for Proton NMR study and 100 MHz frequency instrument was used for ^{13}C NMR. Parts per million unit was used to expressed chemical shift value. ABB Bomem Inc. FT-IR 3000 Spectrophotometer was used for Infrared Spectral study. Data obtained was expressed in cm^{-1} unit. Shimadzu LCMS-2010 was used for MASS spectral analysis. Perkin Elmer-2400 Series II CHNS/O Elemental Analyzer was used for Composition measurement.

3.3.3 General Experimental Procedure

3.3.3.1 Synthesis of chalcone A1

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl)ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF

under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and benzaldehyde(0.01 mol) was added drop wise at 0ºC. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A1.

3.3.3.2 Synthesis of chalcone A2

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl)ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 4-hydroxybenzaldehyde (0.01 mol) was added drop wise at 0ºC. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A2.

3.3.3.3 Synthesis of chalcone A3

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl)ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 3-hydroxybenzaldehyde (0.01 mol) was added drop wise at 0ºC. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A3.

3.3.3.4 Synthesis of chalcone A4

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl)ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 2-hydroxybenzaldehyde (0.01 mol) was added drop wise at 0ºC. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A4.

3.3.3.5 Synthesis of chalcone A5

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 2-methoxybenzaldehyde (0.01 mol) was added drop wise at 0^{o}C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A5.

3.3.3.6 Synthesis of chalcone A6

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl)ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol)in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 4-methoxybenzaldehyde (0.01 mol) was added drop wise at 0^{o}C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A6.

2.3.3.7 Synthesis of chalcone A7

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl)ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol)in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 2-chlorobenzaldehyde(0.01 mol) was added drop wise at 0^{o}C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A7.

3.3.3.8 Synthesis of chalcone A8

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl)ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol)in 250 mL RBF under ethanol (40 mL) as the solvent, add 40% sodium hydroxide (40 mL) and 4-chlorobenzaldehyde (0.01 mol) was added drop wise at 0^{o}C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents

were poured into ice water and crystallized from ethanol. The chalcone obtained is called A8.

3.3.3.9 Synthesis of chalcone A9

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl)ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 3-chlorobenzaldehyde (0.01 mol) was added drop wise at 0ºC. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A9.

3.3.3.10 Synthesis of chalcone A10

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 2-nitrobenzaldehyde (0.01 mol) was added drop wise at 0ºC. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A10.

3.3.3.11 Synthesis of Chalcone A11

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 4-nitrobenzaldehyde (0.01 mol) was added drop wise at 0ºC. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A11**.**

3.3.3.12 Synthesis of Chalcone A12

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol)in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 3-nitrobenzaldehyde (0.01 mol) was added drop wise at 0ºC. After the completion of

addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A12.

3.3.3.13 Synthesis of chalcone A13

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl)ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol)in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 3-bromobenzaldehyde (0.01 mol) was added drop wise at 0^{o}C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A13.

3.3.3.14 Synthesis of chalcone A14

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol)in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 2-bromobenzaldehyde (0.01 mol) was added drop wise at 0^{o}C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A14.

3.3.3.15 Synthesis of chalcone A15

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 4-bromobenzaldehyde (0.01 mol) was added drop wise at 0^{o}C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A15.

3.3.3.16 Synthesis of chalcone A16

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol)in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 3,4-

dimethoxybenzaldehyde (0.01 mol) was added drop wise at 0°C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A16.

3.3.3.17 Synthesis of chalcone A17

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol)in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 3,4,6-trimethoxybenzaldehyde (0.01 mol) was added drop wise at 0°C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A17.

3.3.3.18 Synthesis of chalcone A18

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 2-Furaldehyde (0.01 mol) was added drop wise at 0°C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A18.

3.3.3.19 Synthesis of chalcone A19

To a well stirred solution of 1-(5-hydroxynaphthalen-1-yl) ethan-1-one (0.01 mol) and 1-chloro-5-fluoro-2-methyl-4-nitrobenzene (0.01 mol) in 250 mL RBF under ethanol (40 mL) as the solvent, 40% sodium hydroxide (40 mL) and 2-thienaldehyde (0.01 mol) was added drop wise at 0°C. After the completion of addition, the mixture was stirred for further 1-2 hours and left overnight. The contents were poured into ice water and crystallized from ethanol. The chalcone obtained is called A19.

3.4 SYNTHESIS OF CHALCONES A1-A19.

Table 3.1 Synthesis of ChalconesA1-A19

S. No.	Compounds	R	Reaction Time (h)	% Yield[b]
1	**A1**	-H	1.5	73
2	**A2**	4-OH	2	73
3	**A3**	3-OH	2	69
4	**A4**	2-OH	2	76
5	**A5**	2- OCH_3	2.5	69
6	**A6**	4-OCH_3	2.5	68
7	**A7**	2-Cl	1.5	81
8	**A8**	4-Cl	1.5	81
9	**A9**	3-Cl	1.5	76
10	**A10**	2-NO_2	1.5	84
11	**A11**	4-NO_2	1.5	84
12	**A12**	3-NO_2	1.5	83
13	**A13**	3-Br	1.5	79
14	**A14**	2- Br	1.5	76
15	**A15**	4- Br	1.5	79
16	**A16**	3, 4-$(OCH_3)_2$	2.5	73
17	**A17**	3,4,5-$(OCH_3)_3$	2.5	73
18	**A18**	2-furfuryl[c]	1.5	83
19	**A19**	2-Thineyl[c]	1.5	81

[a]Reaction is monitored by TLC, [b]Isolated yield and [c]Names of aldehyde groups

3.5 RESULTS AND DISCUSSION

Various condensation products of reaction between various aromatic aldehyde and 1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)ethan-1-one are given in Table 3.1. It clearly indicates that the compounds bearing electron withdrawing group are synthesized in shorter reaction time as compared to compounds bearing electron donating group. Compounds A7-A15 bearing electron withdrawing were synthesized in 1.5 h as compared to compounds bearing electron donating group compounds A16 and A17having electron donating group were synthesized in 2.5 h.

3.6 PHYSICAL DATA OF SYTHESIZED DERIVATIVES

Table 3.2 Physical data of compounds A1 to A19

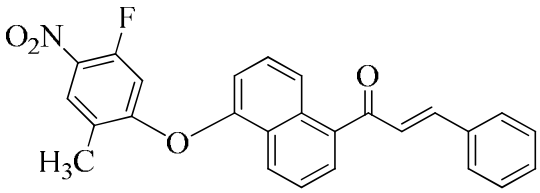
Comp.	R	Molecular Formula	Mol. Wt. (g/m)	% Yield	M.P. °C	% Carbon		% Hydrogen		% Nitrogen	
						Found	Calcd.	Found	Calcd.	Found	Calcd.
A1	-H	$C_{26}H_{18}FNO_4$	427.4	73	237	73.26	73.06	4.20	4.24	3.23	3.28
A2	4-OH	$C_{26}H_{18}FNO_5$	443.4	73	251	70.40	70.42	4.15	4.09	3.10	3.16
A3	3-OH	$C_{26}H_{18}FNO_5$	443.4	69	244	70.38	70.42	4.12	4.09	3.12	3.16
A4	2-OH	$C_{26}H_{18}FNO_5$	443.4	76	255	70.41	70.42	4.10	4.09	3.17	3.16
A5	2- OCH_3	$C_{27}H_{20}FNO_5$	457.4	69	242	70.85	70.89	4.45	4.41	3.10	3.06
A6	4-OCH_3	$C_{27}H_{20}FNO_5$	457.4	68	252	70.83	70.89	4.42	4.41	3.02	3.06
A7	2-Cl	$C_{26}H_{17}FClNO_4$	461.8	81	231	67.65	67.61	3.80	3.71	3.10	3.03
A8	4-Cl	$C_{26}H_{17}FClNO_4$	461.8	81	241	67.68	67.61	3.75	3.71	3.06	3.03
A9	3-Cl	$C_{26}H_{17}FClNO_4$	461.8	76	254	67.66	67.61	3.78	3.71	3.12	3.03
A10	2-NO_2	$C_{26}H_{17}FN_2O_6$	472.4	84	241	66.05	66.10	3.60	3.63	5.85	5.93

A11	4-NO_2	$C_{26}H_{17}FN_2O_6$	472.4	84	255	66.01	66.10	3.66	3.63	5.80	5.93
A12	3-NO_2	$C_{26}H_{17}FN_2O_6$	472.4	83	245	66.15	66.10	3.68	3.63	5.91	5.93
A13	3-Br	$C_{26}H_{17}FBrNO_4$	506.3	79	251	61.60	61.68	3.35	3.38	2.70	2.77
A14	2- Br	$C_{26}H_{17}FBrNO_4$	506.3	76	257	61.61	61.68	3.32	3.38	2.65	2.77
A15	4- Br	$C_{26}H_{17}FBrNO_4$	506.3	79	258	61.62	61.68	3.30	3.38	2.72	2.77
A16	3,4-$(OCH_3)_2$	$C_{28}H_{22}FNO_6$	487.4	73	241	68.90	68.99	4.45	4.55	2.80	2.87
A17	3,4,5-$(OCH_3)_3$	$C_{29}H_{24}FNO_7$	517.5	73	257	67.28	67.31	4.60	4.67	2.65	2.71
A18	2-furfuryl	$C_{24}H_{16}FNO_5$	417.3	83	248	69.10	69.06	3.80	3.86	3.30	3.36
A19	2-Thineyl	$C_{24}H_{16}FSNO_4$	433.4	81	261	66.40	66.50	3.65	3.72	3.20	3.23

3.7 SPECTROSCOPIC CHARACTERIZATION OF COMPOUNDS A1-A19

For characterization, Compound A1 was taken as the model compound from the series and it was characterized by various spectroscopic methods such as ^{1}H NMR, ^{13}C NMR, MASS and IR spectroscopy. Its structure was decided on the basis of ^{1}H NMR, ^{13}C NMR, IR and MASS spectra given in Fig.-3.1 to Fig. 3.4 respectively.

Compound A1



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-phenylprop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Twoα and β CH proton of the vinylic group give doublet at δ 4.5 and 5.5 ppm respectively. All the 13 aromatic protons appeared in aromatic region between δ 6.8 to 8.3 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group is at 32.0. Signals due to carbon of methine groupsare found at 60.2 and 62.4 δ ppm. All aromatic carbons give signals at 127.9, 129.4, 130.3, 131.6, 140.2, 143.6, 151.8, 154.6, 155.1 and 160.8 δ ppm. Carbonyl carbon more down field region at 190.1 δ ppm.

IR Spectroscopy (KBr)

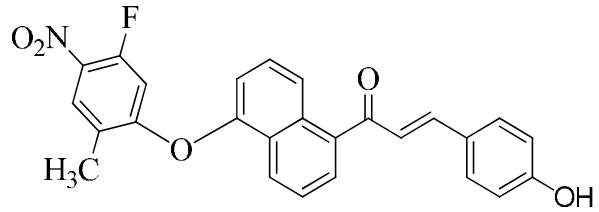
Infrared spectra was recorded in KBr reveals that band at 3120 cm^{-1} indicates the aromatic C-H stretching. Band 2950 cm^{-1} shows aliphatic C-H stretching of the methyl group while band at 1710, 1592 and 1569 cm^{-1} indicate the C=C stretching.

The band at 1480 cm^{-1} indicates the N=O stretching and band at 744 cm^{-1} is for mono- and disubstituted benzene ring C-H bending frequency,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was at M+ 427.4 indicating the molecular weight of the compound.

Compound A2



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(4-hydroxyphenyl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Signal due to -OH proton comes in the more downfield region at 9.2 ppm. Three protons of the CH_3 gives singlet at δ 2.5 ppm in downfield region. Two α and β CH proton of the vinylic group give doublet at δ 4.5 and 5.5 ppm, respectively. All 12 aromatic protons appeared in aromatic region between δ 6.8 to 8.3 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group comes at 31.2. Signals due to carbon of methine groups are found at 60.2 and 63.4 δ ppm. All aromatic carbons give signal at 128.9, 129.4, 130.3, 132.6, 140.2, 143.6, 151.8, 154.6, 154.1 and 160.8 δ ppm. Carbonyl carbon comes in more down field region at 190.3 δ ppm.

IR Spectroscopy (KBr)

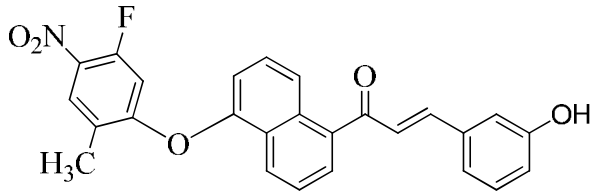
Infrared spectra was recorded using reveals that band at 3356cm^{-1} is due to O-H stretching frequency. A band at 3121 cm^{-1} indicates the aromatic C-H stretching while band at 2952 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at

1710, 1592 and 1569 cm^{-1} indicate the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. The band at 744 cm^{-1} is for mono and disubstituted benzene ring C-H bending frequency,.

Mass Spectroscopy

In the mass spectrum of the given compound molecular ion peak was at M+ 443.4 indicating the molecular weight of the compound.

Compound A3



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(3-hydroxyphenyl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Signal due to -OH proton appeared in the more downfield region at 9.1 ppm. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.5 and 5.5 ppm respectively. All 12aromatic protons appeared in aromatic region between δ 6.8 to 8.3 ppm.

^{13}C NMR Spectroscopy:

100 MHz Apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) wastaken as the solvent. Signal due to carbon of methyl group comes at 31.2. Signal due to carbon of methine groups are found at δ 61.2 and 63.4ppm. All aromatic carbons give signal at δ 124.9, 129.5, 130.3, 132.6, 142.2, 143.6, 151.8, 154.6, 154.2 and 160.4 ppm. Carbonyl carbon comes in more down field region at δ 190.2 ppm.

IR Spectroscopy (KBr)

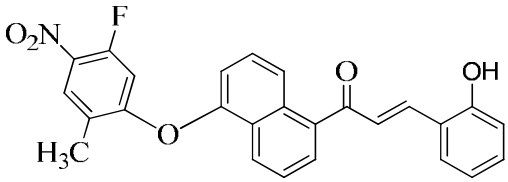
Infrared spectra was recorded in KBr reveals that absorption band at 3356 cm^{-1} is due to O-H stretching frequency. Band at 3122 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2954 cm^{-1} showed aliphatic C-H stretching of the methyl group. Bands at 1710, 1592 and 1568 cm^{-1} are due to the C=C stretching The

absorption at 1480 cm^{-1} indicates the N=O stretching. The band at 744 cm^{-1} may be due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was at M+ 443.4 which indicates the molecular weight of the compound.

Compound A4



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(3-hydroxyphenyl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Signal due to -OH proton appear in the more downfield region at 9.0 ppm. Three protons of the CH_3 gives singlet at δ 2.5 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.5 ppm, respectively. All 12aromatic protons appeared in aromatic region between δ 6.8 to 8.3 ppm.

^{13}C NMR Spectroscopy:

100MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group appeared at δ 31.2. Signal due to carbon of methine groups, were found at 60.2 and 62.4 δ ppm. All aromatic carbons give signal at 125.9, 129.4, 130.3, 131.6, 142.3, 143.6, 151.8, 154.6, 158.2 and 160.4 δ ppm. Carbonyl carbon is more down field at δ 191.0 δ ppm.

IR Spectroscopy (KBr)

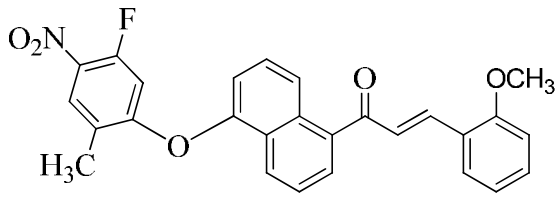
Infrared spectra recorded in KBr reveals that absorption band at 3344cm^{-1} is due to O-H stretching frequency. The band at 3120 cm^{-1} indicates aromatic C-H stretching. Absorption at 2958 cm^{-1} indicates aliphatic C-H stretching of the methyl group. The bands at 1710, 1592 and 1567cm^{-1} indicate the C=C stretching while band at 1480cm^{-1}

indicates the N=O stretching. The band at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound molecular ion peak at M+ 443.4 indicates the molecular weight of the compound.

Compound A5



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(2-methoxyphenyl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in the downfield region. Signal due to -OCH_3 proton appeared in the more downfield region at 3.5 ppm. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.5 ppm, respectively. All 12 aromatic protons appeared in aromatic region between δ 6.8 to 8.3 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 33.2. Signal due to -OCH_3 group was found at 39.8 δ ppm. Signal due to carbon of methine groups were found at 61.2 and 62.4 δ ppm. All aromatic carbons gave signals at 126.9, 128.4, 130.3, 131.6, 142.3, 143.6, 152.7, 154.4, 155.1 and 160.4 δppm. Carbonyl carbon signals was found in more down field region at 191.1 δ ppm.

IR Spectroscopy (KBr)

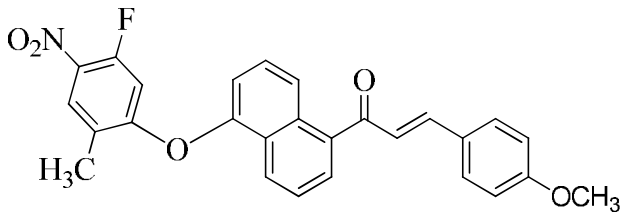
Infrared spectra recorded in KBr reveals that the absorption band at 3122 cm^{-1} indicates the aromatic C-H stretching. The band at 2958 cm^{-1} is due to aliphatic C-H stretching of the methyl group. Absorption at 1708, 1593 and 1568 cm^{-1} indicates the

C=C stretching, while band at 1480cm^{-1} indicates the N=O stretching. The band at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak at M+ 457.4 indicates the molecular weight of the compound.

Compound A6



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(4-methoxyphenyl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.4 ppm in downfield region. Signal due to -OCH_3 proton comes in the more downfield region at 3.5 ppm. Two α and β CH protons of the vinylic group give doublets at δ 4.3 and 5.5 ppm respectively. All 12aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appearing at δ 33.2 ppm. Signal due to -OCH_3 group was found at δ 38.7 ppm. Signal due to carbon of methine groups were found at δ 61.3 and 62.4 ppm. All aromatic carbons give signals at 126.9, 128.4, 130.3, 131.6, 142.3, 143.6, 152.7, 154.4, 155.1and 161.4 δ ppm. Carbonyl carbon showed signal in more down field region at 191.2 δ ppm.

IR Spectroscopy (KBr)

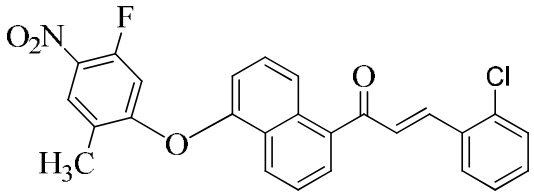
Infrared spectr recorded in KBr reveals that absorption band at 3122 cm^{-1} is due to the aromatic C-H stretching. The band at 2958 cm^{-1}shows aliphatic C-H stretching of the

methyl group. Absorption at 1708, 1593 and 1568 cm^{-1} indicate the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. The band at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak at M+ 457.4 indicates the molecular weight of the compound.

Compound A7



(*E*)-3-(2-chlorophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound appear as singlet at δ 2.4 ppm in downfield region. Two α and β CH protons of the vinylic group gave doublets at 4.4 and 5.5 δ ppm respectively. All 12 aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm.

^{13}C NMR Spectroscopy:

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appered at δ 33.2 ppm. Signal due to carbon of methine groups were found at 61.2 and 62.3 δ ppm. All aromatic carbons gave signals at 124.9, 128.4, 131.3, 132.6, 142.3, 143.6, 152.7, 154.4, 156.1and 161.3 δ ppm. Carbonyl carbon was found in more down field region at 191.1 δ ppm.

IR Spectroscopy (KBr)

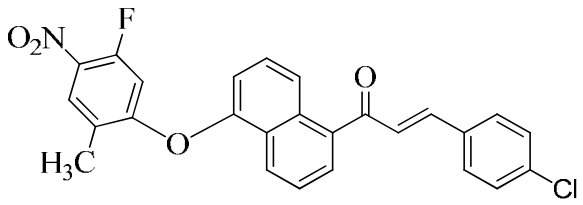
Infrared spectra recorded in KBr reveals that the absorption at 3124 cm^{-1} indicates the aromatic C-H stretching. The band at 2958 cm^{-1}shows aliphatic C-H stretching of the methyl group. The band at 1708, 1594 and 1530 cm^{-1} indicate the C=C stretching and

band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 746 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak at M+ 461.8 indicates the molecular weight of the compound.

Compound A8



(*E*)-3-(4-chlorophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

^{1}H NMR Spectroscopy:

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.5 ppm respectively. All 12 aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm.

^{13}C NMR Spectroscopy:

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring comes at δ 33.2 ppm. Signals due to carbon of methine groups were found at 61.2 and 62.3 δ ppm. All aromatic carbons give signals at δ 124.9, 128.4, 131.3, 132.6, 142.3, 143.6, 152.7, 154.4, 156.1 and 161.2 ppm. Carbonyl carbon gives signal in more down field region at 191.1 δ ppm.

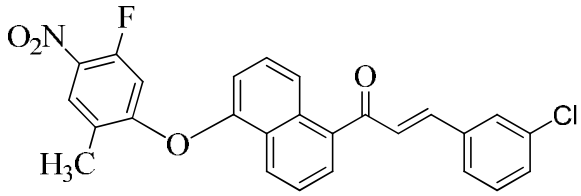
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3124 cm^{-1} can be ascribed to the aromatic C-H stretching. The band at 2958 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1708, 1594 and 1531 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak at M+ 461.8 indicates the molecular weight of the compound.

Compound A9



(*E*)-3-(3-chlorophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

^{1}H NMR Spectroscopy:

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.3 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.4 ppm respectively. All 12 aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm.

^{13}C NMR Spectroscopy:

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.2 ppm. Signals due to carbon of methine groups were found at 61.2 and 62.3 δ ppm. All aromatic carbons give signals at 125.9, 128.4, 130.3, 131.6, 142.3, 143.6, 152.7, 154.4, 156.1 and 161.3 δ ppm. Carbonyl carbon shows signal in more down field region at 191.1 δ ppm.

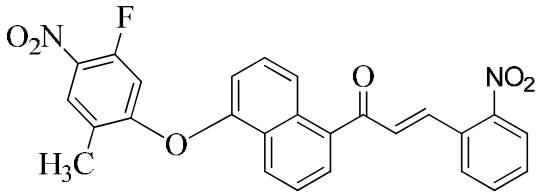
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption band at 3123 cm^{-1} may be due to the aromatic C-H stretching. The band at 2958 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1710, 1594 and 1530 cm^{-1} indicate the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 746 cm^{-1} is due to mono and disubstituted benzene ring C-H bending frequency.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak at M+ 461.8 indicates the molecular weight of the compound.

Compound A10



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(2-nitrophenyl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.4 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.4 ppm respectively. All 12 aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.2 ppm. Signal due to carbon of methine groups were found at δ 61.2 and 62.3 ppm. All aromatic carbons give signals at 125.9, 128.4, 130.3, 131.6, 142.3, 143.6, 152.7, 154.4, 157.1 and 161.3 δ ppm. Carbonyl carbon produced signal in more down field region atδ 191.1 δ ppm.

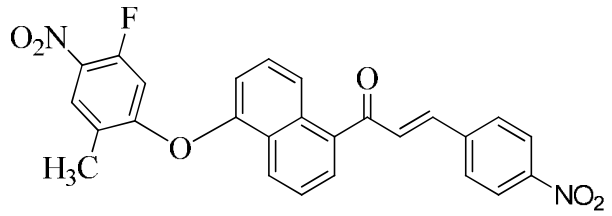
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3123 cm^{-1} indicates the aromatic C-H stretching. The band at 2958 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1711, 1594 and 1530 cm^{-1} indicates the C=C stretching and 1480cm^{-1} indicates the N=O stretching. Absorption at 746 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound molecular ion peak appeared at M+ 472.4 indicating the molecular weight of the compound.

Compound A11



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(4-nitrophenyl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.5 ppm respectively. All 12 aromatic protons appeared in aromatic region between δ 6.6 to 8.4 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.2 δ ppm. Signal due to carbon of methine groups were found at δ 61.2 and 63.3 ppm. All aromatic carbons give signals at 126.8, 128.4, 131.3, 131.6, 142.3, 143.6, 152.7, 154.4, 157.1 and 161.3 δ ppm. Carbonyl carbon gives signal in more down field region atδ 191.2 δ ppm.

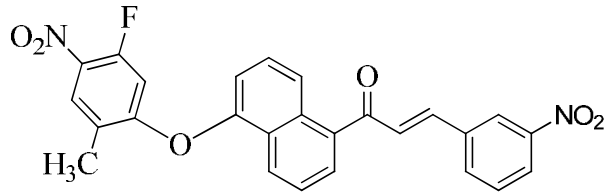
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3123 cm^{-1} indicates aromatic C-H stretching. The band at 2958 cm^{-1}shows aliphatic C-H stretching of the methyl group. Bands at 1711, 1594 and 1530 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 746cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 472.4, which indicates the molecular weight of the compound.

Compound A12



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(3-nitrophenyl)prop-2-en-1-one

^{1}H NMR Spectroscopy:

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.5 ppm respectively. All 12 aromatic protons appeared in aromatic region between δ 6.6 to 8.4 ppm.

^{13}C NMR Spectroscopy:

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.2 ppm. Signals due to carbon of methine groups were found at δ 60.2 and 62.3 ppm. All aromatic carbons give signals at 125.8, 128.4, 131.3, 132.6, 142.3, 143.6, 152.7, 154.4, 157.1 and 162.3 δ ppm. Carbonyl carbon gave signal in more down field region at 192.1 δ ppm.

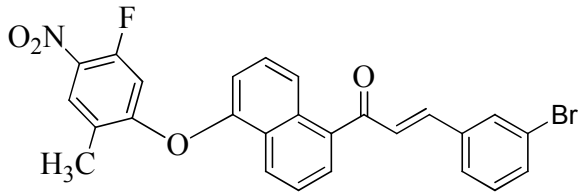
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3123 cm^{-1} indicates the aromatic C-H stretching. The band at 2958 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1711, 1596 and 1530 cm^{-1}indicate the C=C stretching and 1480 cm^{-1} indicates the N=O stretching. Absorption at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound molecular ion peak appeared at M+ 472.4 indicating the molecular weight of the compound.

Compound A13



(*E*)-3-(3-bromophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

^{1}H NMR Spectroscopy:

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.4 ppm in downfield region. Two α and β CH proton of the vinylic group give doublets at δ 4.4 and 5.4 ppm respectively. All 12 aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm.

^{13}C NMR Spectroscopy:

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.2 δ ppm . Signals due to carbon of methine groups were found at δ 62.2 and 62.8 ppm. All aromatic carbons give signals at δ 125.9, 128.4, 130.3, 131.6, 142.3, 143.6, 152.7, 154.4, 156.1and 161.3 ppm. Carbonyl carbon gave signal in more down field region at δ 191.1 ppm.

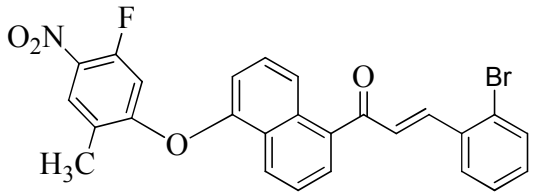
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption band at 3123 cm^{-1} indicates the aromatic C-H stretching. The band at 2958 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1710, 1594 and 1530 cm^{-1} indicate the C=C stretching and 1480 cm^{-1} indicates the N=O stretching. Adsorption at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 506.3 indicating the molecular weight of the compound.

Compound A14



(*E*)-3-(2-bromophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

^{1}H NMR Spectroscopy:

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.4 ppm respectively. All 12 aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm

^{13}C NMR Spectroscopy:

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring was found at 32.2 δ ppm . Signals due to carbon of methine groups were found at δ 62.2 and 62.8 ppm. All aromatic carbons give signals at δ 124.9, 128.4, 130.3, 131.6, 142.3, 143.6, 152.7, 154.4, 156.1 and 161.3 ppm. Carbonyl carbon gave signal in more down field region at δ 191.0 ppm.

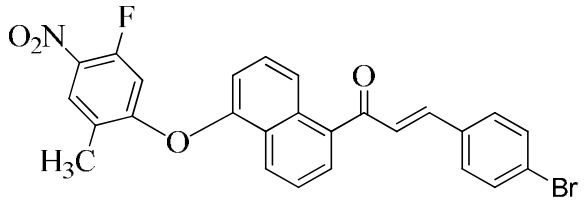
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption band at 3134 cm^{-1} indicates the aromatic C-H stretching. The band at 2958 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1707, 1594 and 1530 cm^{-1} indicate the C=C stretching and 1480 cm^{-1} indicates the N=O stretching. The band at 746 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak appeared at M+ 506.3 indicating the molecular weight of the compound.

Compound A15



(*E*)-3-(4-bromophenyl)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)prop-2-en-1-one

^{1}H NMR Spectroscopy:

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.5 ppm respectively. All 12 aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.2 δ ppm . Signals due to carbon of methine groups were found at 62.2 and 62.8 δ ppm. All aromatic carbons give signals at δ 125.9, 128.4, 131.3, 131.6, 142.3, 143.6, 152.7, 154.4, 157.1 and 161.2 ppm. Carbonyl carbon gave signal in more down field region at δ 191.1 ppm.

IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption band at 3124 cm^{-1} indicates the aromatic C-H stretching. The band at 2957 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1704, 1594 and 1531 cm^{-1} indicate the C=C stretching and the band at 1480 cm^{-1} indicates the N=O stretching. The absorption at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak appeared at M+ 506.3 indicates the molecular weight of the compound.

Compound A16

^{1}H NMR Spectroscopy:

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.4 ppm in downfield region. Signal due to six $–OCH_3$ protons appeared in the more downfield region at δ 3.5 ppm. Two α and β CH protons of the vinylic group give doublets at δ 4.3 and 5.5 ppm, respectively. All 12 aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 33.2 ppm . Signals due to two $–OCH_3$ group was found at 38.7 and 39.2 δ ppm.Signal due to carbon of methine groups were found at 61.1 and 62.3 δ ppm. All aromatic carbons give signals at 126.9, 128.4, 130.3, 131.6, 142.3, 143.6, 152.7, 154.4, 155.2 and 161.3 δ ppm. Carbonyl carbon appeared in more down field region at δ 191.1 ppm.

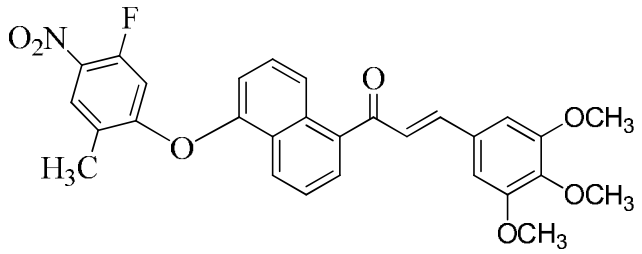
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that the band at 3120 cm^{-1} indicates the aromatic C-H stretching. The band at 2950 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1704, 1594 and 1560 cm^{-1} indicate the C=C stretching and the band at 1480 cm^{-1} indicates the N=O stretching. The absorption at 748 cm^{-1} is indicates C-H bending frequency mono and disubstituted benzene ring,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak appeared at M+ 506.3 which indicates the molecular weight of the compound.

Compound A17



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(3,4,5-trimethoxyphenyl)prop-2-en-1-one

^{1}H NMR Spectroscopy:

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.4 ppm in downfield region. Signal due to six –OCH_3 protons appeared in the more downfield region at δ 3.4 ppm. Two α and β CH protons of the vinylic group give doublets at δ 4.3 and 5.5 ppm, respectively. All 10 aromatic protons appeared in aromatic region between δ 6.7 to 8.4 ppm

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 33.2 ppm . Signals due to three –OCH_3 groups was found at 38.7, 39.2 and 40.2 δ ppm. Signal due to carbon of methine groups were found at 61.1 and 62.3 δ ppm. All aromatic carbons give signals at 126.9, 128.4, 130.3, 131.6, 142.3, 143.6, 152.7, 154.4, 155.2 and 161.3 δ ppm. Carbonyl carbon appeared in more down field region at 191.2 δ ppm.

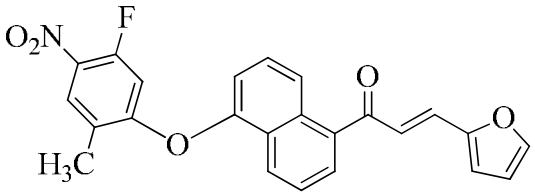
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that the band at 3123 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2950 cm^{-1} shows aliphatic C-H stretching of the methyl group. The bands at 1708, 1595 and 1560 cm^{-1} indicates the C=C stretching and the band at 1480 cm^{-1} indicates the N=O stretching. The absorption at 748 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak appeared at M+ 487.4, which indicates the molecular weight of the compound.

Compound A18



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(furan-2-yl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.3 and 5.5 ppm, respectively. All 11 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 33.1 ppm . Signal due to carbon of methine groups were found at 60.1 and 62.3 δ ppm. All aromatic carbons give signals at 125.8, 128.4, 130.3, 131.6, 142.3, 143.6, 152.7, 154.4, 155.2 and 160.3 δ ppm. Carbonyl carbon produced signal in more down field region at 191.2 δ ppm.

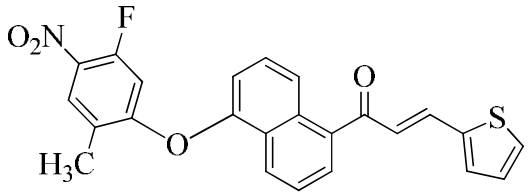
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that the band at 3124 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2952 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1708, 1595 and 1562 cm^{-1} indicates the C=C stretching and the band at 1480 cm^{-1} indicates the N=O stretching. The absorption at 748 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak appeared at M+ 517.5, which indicates the molecular weight of the compound.

Compound A19



(*E*)-1-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-3-(thiophen-2-yl)prop-2-en-1-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.4 ppm in downfield region. Two α and β CH protons of the vinylic group give doublets at δ 4.4 and 5.5 ppm, respectively. All 11 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 33.1 ppm . Signal due to carbon of methine groups were found at 61.1 and 62.3 δ ppm. All aromatic carbons give signals at 125.8, 128.4, 129.3, 131.6, 142.3, 143.6, 152.7, 154.4, 155.2 and 160.3 δ ppm. Carbonyl carbon was found in more down field region at 191.1 δ ppm.

IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3122 cm^{-1} indicates the aromatic C-H stretching. The band at 2952 cm^{-1} shows aliphatic C-H stretching of the methyl group. Bands at 1710, 1595 and 1562 cm^{-1} indicates the C=C stretching and the band at 1480 cm^{-1} indicates the N=O stretching. The band at 750 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak appeared at M+ 417.3, which indicates the molecular weight of the compound.

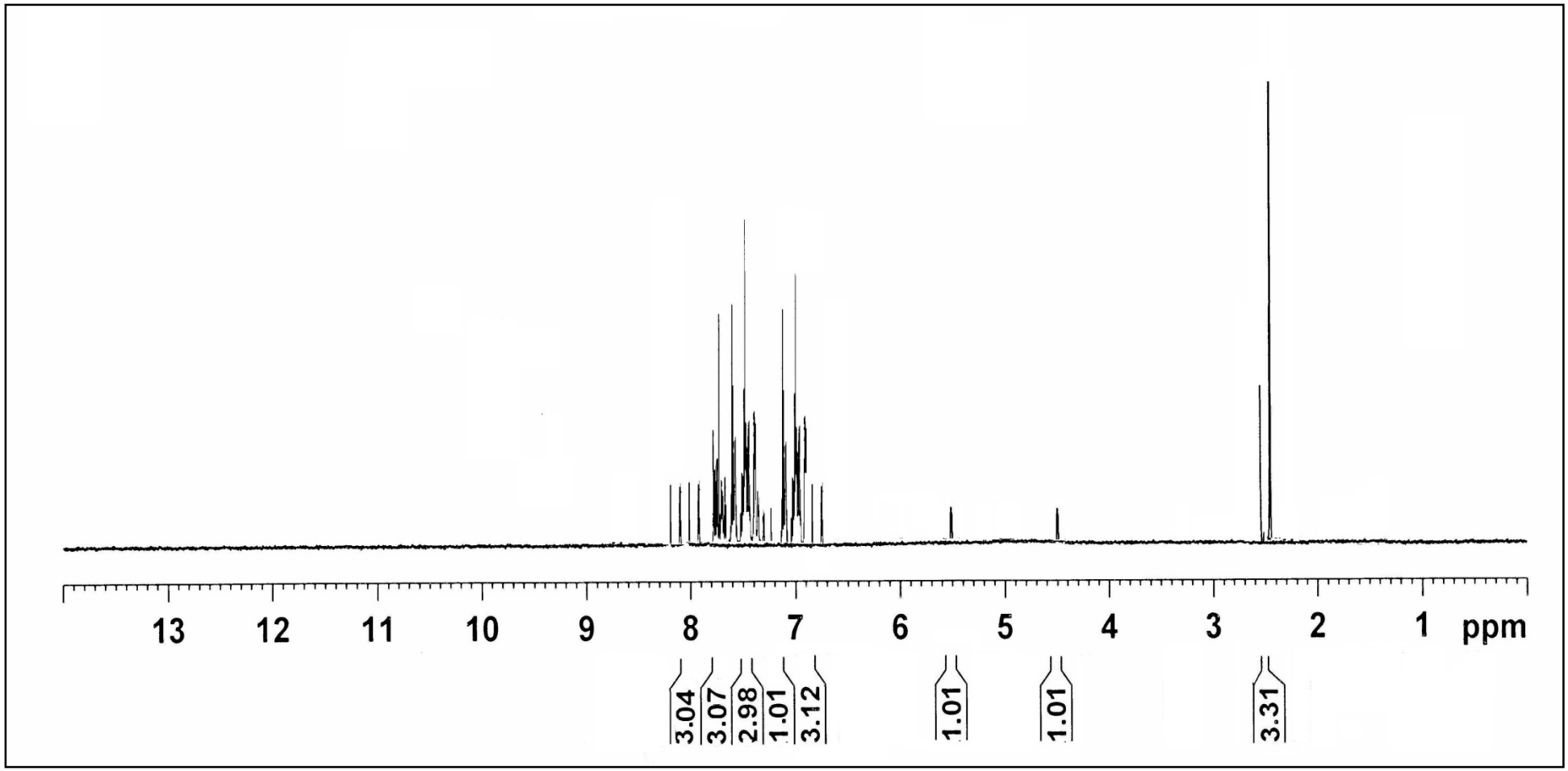


Fig. 3.1: ^{1}H NMR Spectra of Compound A1

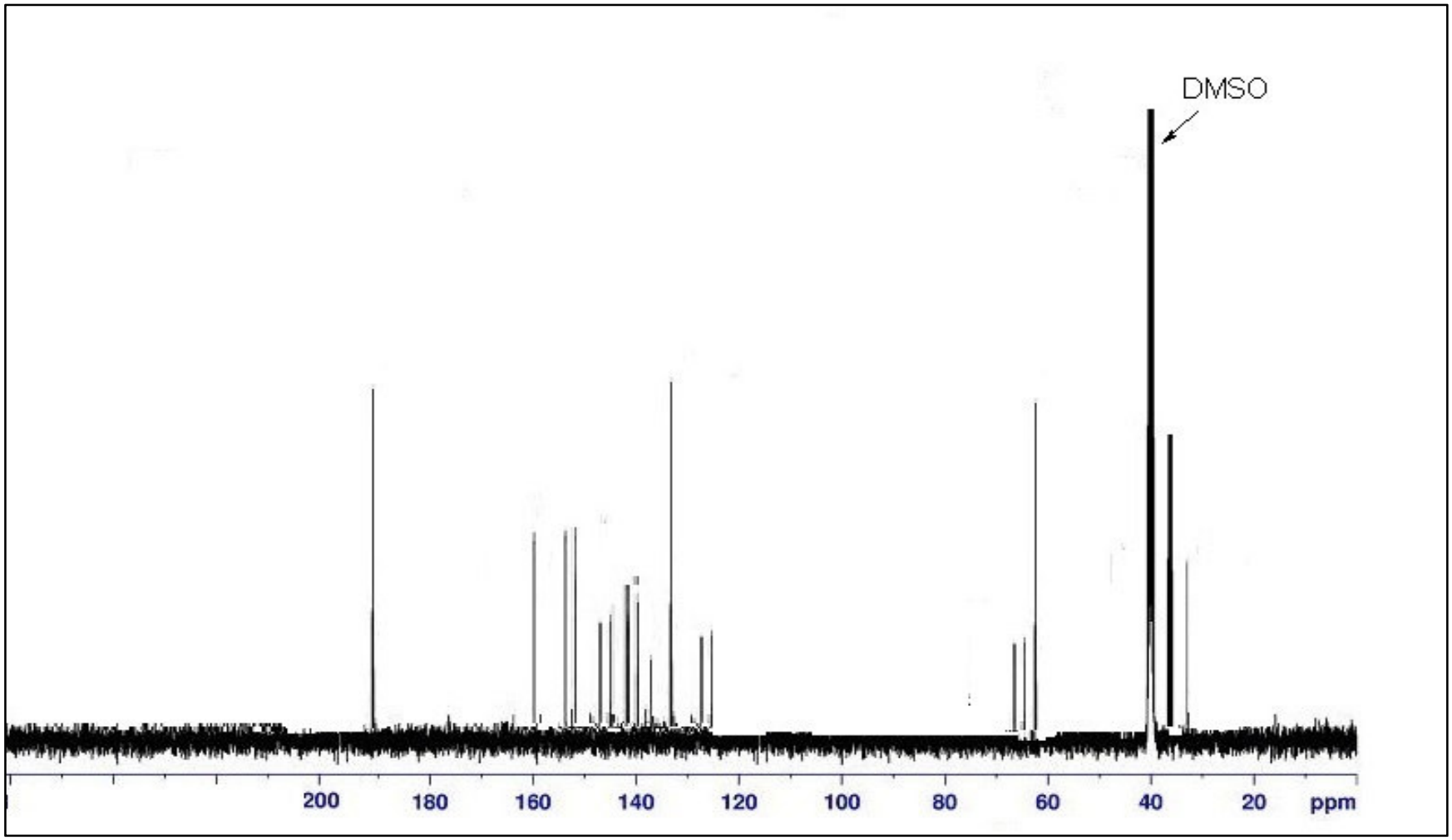


Fig. 3.2: ^{13}C NMR Spectra of Compound A1

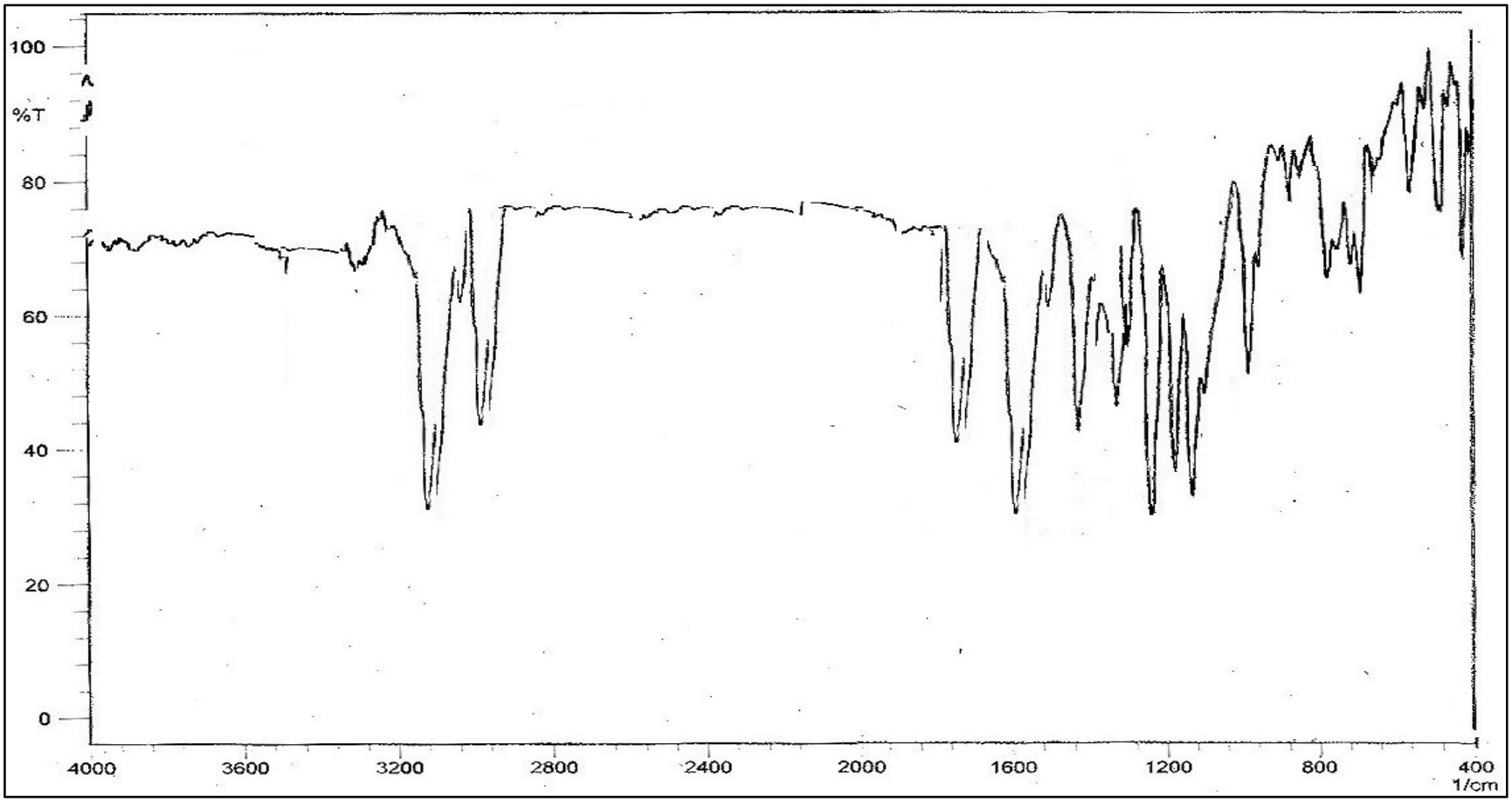


Fig. 3.3: IR Spectra of Compound A1

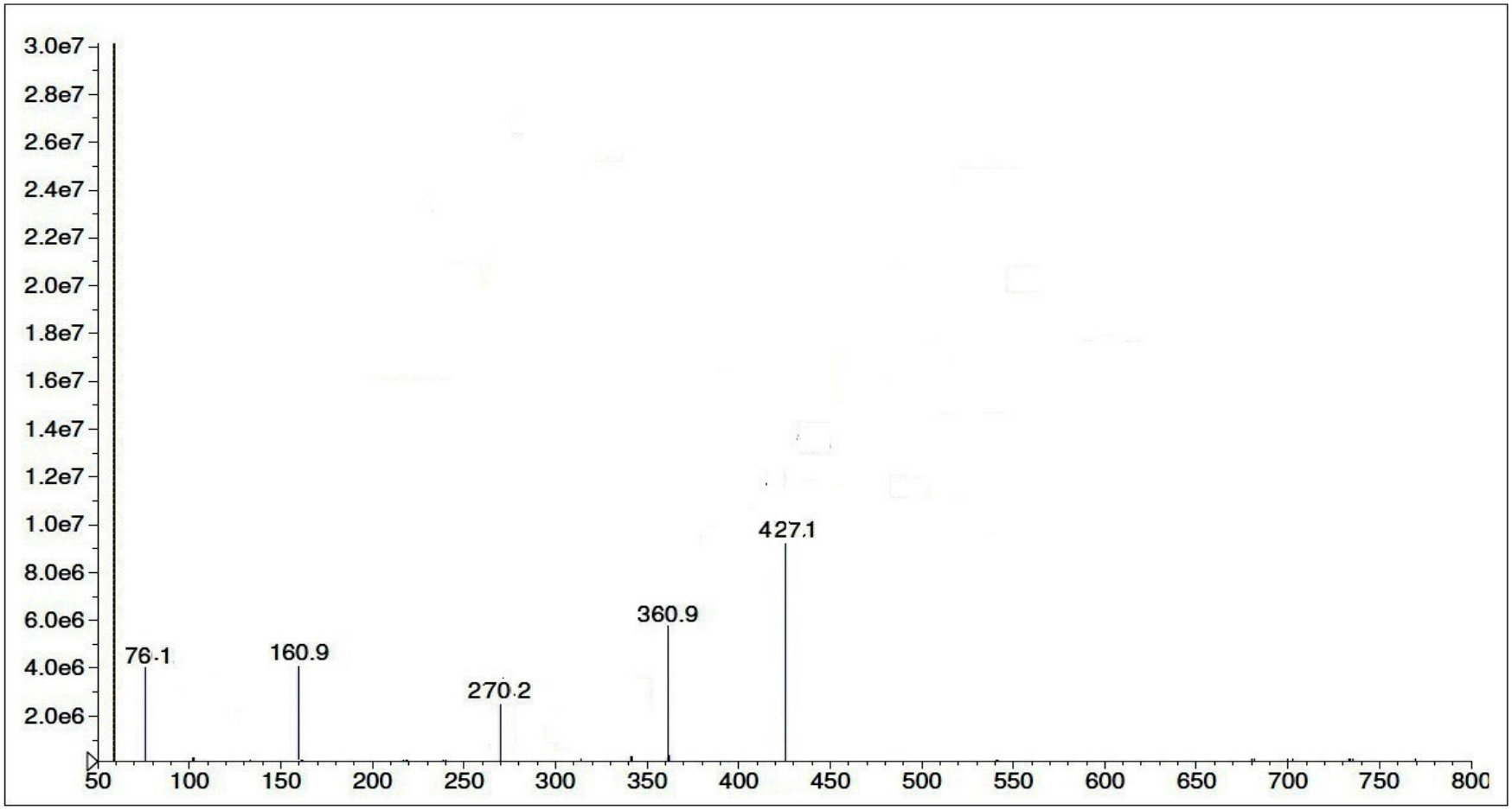


Fig. 3.4: MASS Spectra of Compound A1

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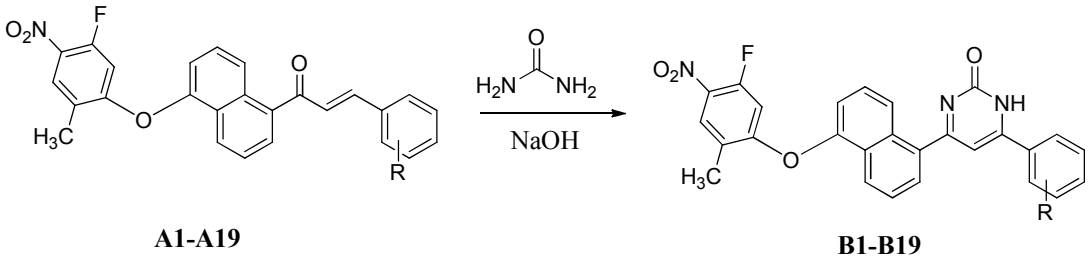
CHAPTER – IV

SYNTHESIS AND CHARACTERIZATION OF PYRIMIDINES

CONTENTS

4.1 REACTION SCHEME

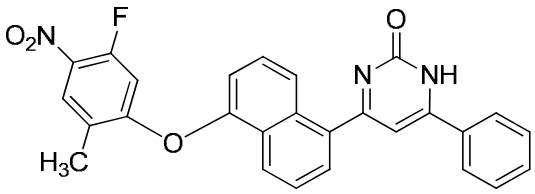
Pyrimidines **B1-B19** planned to prepare by reaction between chalcones **A1-A19** and urea in the presence of ethanol and 40% NaOH (**Scheme 4.1)**.



Scheme 4.1 Synthesis of Pyrimidines B1-B19

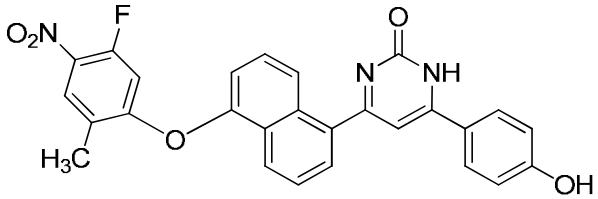
4.2 STRUCTURE OF COMPOUNDS B1 TO B19

Compound B1:



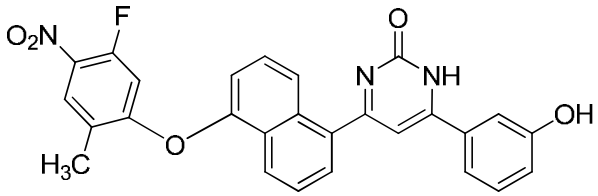
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-phenylpyrimidin-2(1*H*)-one

Compound B2:



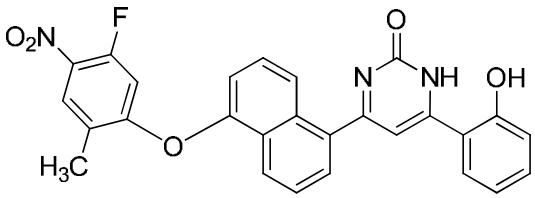
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-hydroxyphenyl)pyrimidin-2(1*H*)-one

Compound B3:



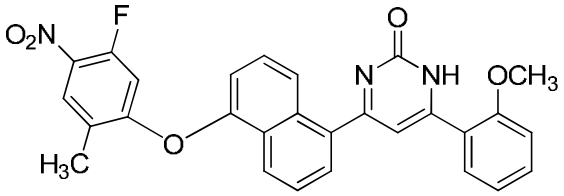
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3-hydroxyphenyl)pyrimidin-2(1*H*)-one

Compound B4:



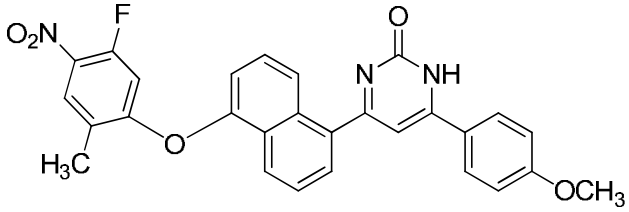
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-hydroxyphenyl)pyrimidin-2(1*H*)-one

Compound B5:



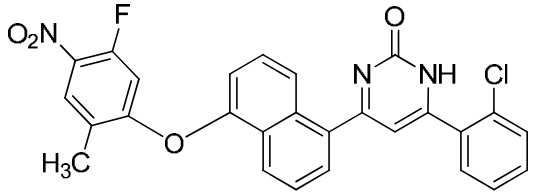
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-methoxyphenyl)pyrimidin-2(1*H*)-one

Compound B6:



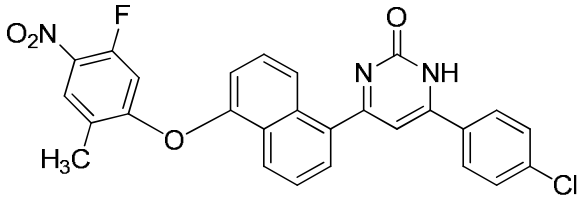
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-methoxyphenyl)pyrimidin-2(1*H*)-one

Compound B7:



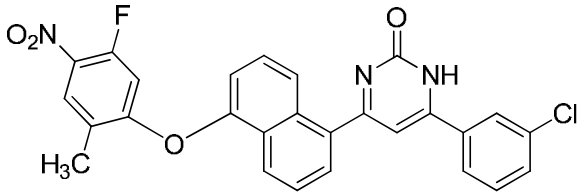
6-(2-chlorophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

Compound B8:



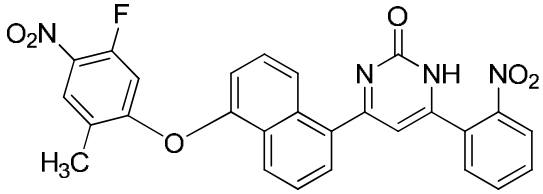
6-(4-chlorophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

Compound B9:



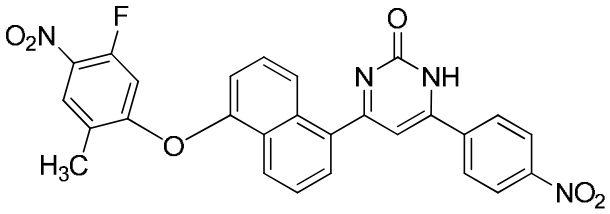
6-(3-chlorophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

Compound B10:



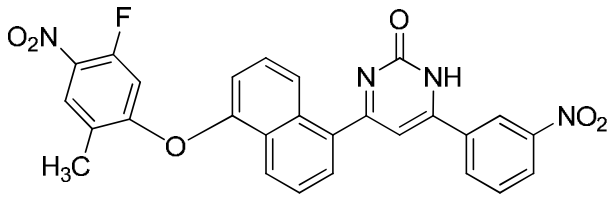
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-nitrophenyl)pyrimidin-2(1*H*)-one

Compound B11:



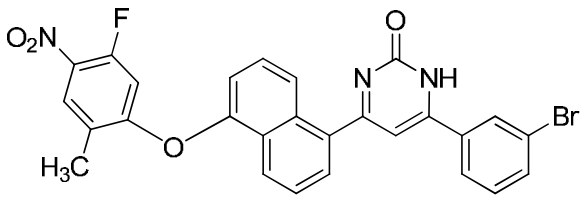
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-nitrophenyl)pyrimidin-2(1*H*)-one

Compound B12:



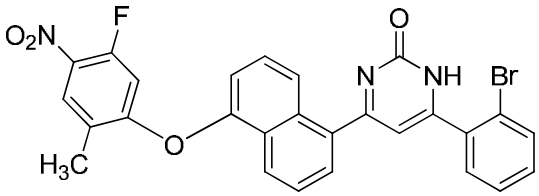
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3-nitrophenyl)pyrimidin-2(1*H*)-one

Compound B13:



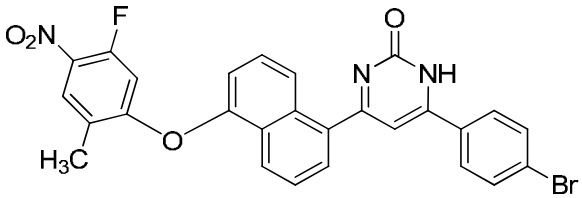
6-(3-bromophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

Compound B14:



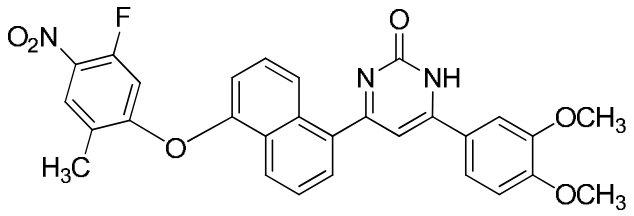
6-(2-bromophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

Compound B15:



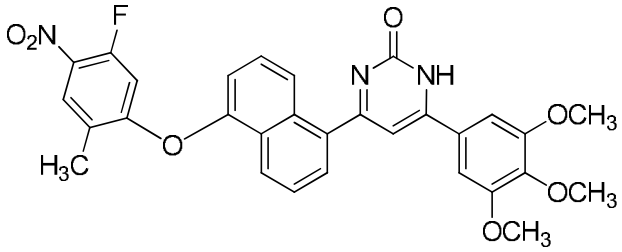
6-(4-bromophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

Compound B16:



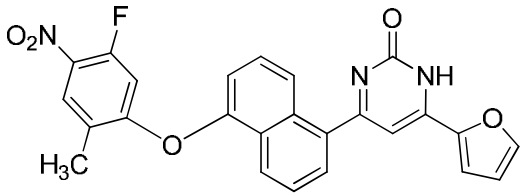
6-(3,4-dimethoxyphenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

Compound B17:



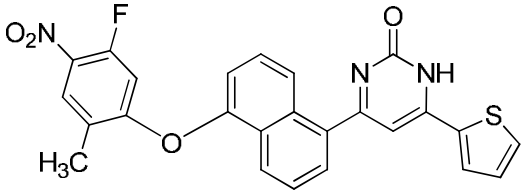
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2(1*H*)-one

Compound B18:



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(furan-2-yl)pyrimidin-2(1*H*)-one

Compound B19:



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(thiophen-2-yl)pyrimidin-2(1*H*)-one

4.3. EXPERIMENTAL

4.3.1 Chemicals and Reagents

All chemicals used were of laboratory reagent grade and used without further purification**.** NaOH, urea and ethanol were used as received from Merck, Mumbai, India.

4.3.2 Analytical Methods

Bruker Avance-400 MHz instrument was used for Proton NMR study and 100 MHz frequency instrument was used for ^{13}C NMR. Parts per million (ppm) unit was used to express chemical shift values. ABB Bomem Inc. FT-IR 3000 Spectrophotometer was used for Infrared Spectral study. Data obtained were expressed in cm^{-1} unit. Shimadzu LCMS-2010 was used for MASS spectral analysis.Perkin Elmer-2400 Series II CHNS/O Elemental Analyzer was used for Composition measurements.

4.3.3 General Experimental procedure

4.3.3.1 Synthesis of Pyrimidine B1

Chalcone **A1** (0.01 ml) was taken in 250 ml RBF, and to this 0.01 mol Urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC. Completion of reaction was checked by TLC. The pyrimidine obtained is called **B1**.

4.3.3.2 Synthesis of Pyrimidine B2

Chalcone **A2** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine so obtained was called **B2**.

4.3.3.3 Synthesis of Pyrimidine B3

Chalcone **A3** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hour to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was checked by TLC. The pyrimidine so obtained was termed as **B3**.

4.3.3.4 Synthesis of Pyrimidine B4

Chalcone **A4** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol Urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is termed as **B4**.

4.3.3.5 Synthesis of Pyrimidine B5

Chalcone **A5** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol Urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of the reaction was checked by TLC. The pyrimidine so obtained was called **B5**.

4.3.3.6 Synthesis of Pyrimidine B6

Chalcone **A6** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol Urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of the reaction was also checked by TLC. The pyrimidine so obtained was called **B6**.

4.3.3.7 Synthesis of Pyrimidine B7

Chalcone **A7** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol Urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of the reaction was also checked by TLC. The pyrimidine so obtained was called **B7**.

4.3.3.8 Synthesis of Pyrimidine B8

Chalcone **A8** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol Urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of the reaction was also checked by TLC. The pyrimidine so obtained was called **B8**.

4.3.3.9 Synthesis of Pyrimidine B9

Chalcone **A9** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion was also checked by TLC. The pyrimidine so obtained was called **B9**.

4.3.3.10 Synthesis of Pyrimidine B10

Chalcone **A10** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine so obtained was called **B10**.

4.3.3.11 Synthesis of Pyrimidine B11

Chalcone **A11** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine so obtained was called **B11**.

4.3.3.12 Synthesis of Pyrimidine B12

Chalcone **A12** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine obtained was called **B12**.

4.3.3.13 Synthesis of Pyrimidine B13

Chalcone **A13** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine obtained was called **B13**.

4.3.3.14 Synthesis of Pyrimidine B14

Chalcone **A14** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine obtained was called **B14**.

4.3.3.15 Synthesis of Pyrimidine B15

Chalcone **A15** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine obtained was called **B15**.

4.3.3.16 Synthesis of Pyrimidine B16

Chalcone **A16** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine obtained was called **B16**.

4.3.3.17 Synthesis of Pyrimidine B17

Chalcone **A17** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine obtained was called **B17**.

4.3.3.18 Synthesis of Pyrimidine B18

Chalcone **A18** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine obtained was called **B18**.

4.3.3.19 Synthesis of Pyrimidine B19

Chalcone **A19** (0.01 mol) was taken in 250 mL RBF, and to it 0.01 mol urea, 40 mL ethanol and 40 mL 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The progress of reaction was monitored by TLC and its completion was also checked by TLC. The pyrimidine obtained was called **B19**.

4.4 CHARACTERSTICS DATA SHOWING SYNTHESIS OF PYRIMIDINE B1-B19.

Table 4.1 Synthesis of Pyrimidine B1-B19

Sr. No.	Compounds	R	Reaction Time (h)	% Yield[b]
1	**B1**	-H	3	72
2	**B2**	4-OH	3	72
3	**B3**	3-OH	3	68
4	**B4**	2-OH	3	75
5	**B5**	2- OCH_3	3.5	68
6	**B6**	4-OCH_3	3.5	67
7	**B7**	2-Cl	2.5	80
8	**B8**	4-Cl	2.5	80
9	**B9**	3-Cl	2.5	75
10	**B10**	2-NO_2	2.5	83
11	**B11**	4-NO_2	2.5	83
12	**B12**	3-NO_2	2.5	82
13	**B13**	3-Br	3	78
14	**B14**	2- Br	3	75
15	**B15**	4- Br	3	78
16	**B16**	3, 4-$(OCH_3)_2$	3.5	72
17	**B17**	3,4,5-$(OCH_3)_3$	3.5	72
18	**B18**	2-furfuryl[c]	2.5	82
19	**B19**	2-Thineyl[c]	2.5	80

[a]Reaction is monitored by TLC, [b]Isolated yield and [c]Names of aldehyde groups

4.5 RESULTS AND DISCUSSION

Table 4.1 shows the data for various condensation products of reaction between various chalcones andurea. It clearly indicates that the compounds bearing electron withdrawing groups are synthesized in shorter reaction time as compared to compounds bearing electron donating group. Compounds **B7-B15** bearing electron withdrawing groups were synthesized in **2.5 to 3 h** as compared to compounds bearing electron donating group. Compounds **B5, B6, B16** and **B17** which have electron donating groups were synthesized in **3.5 h**.

4.6 PHYSICAL DATA OF SYNTHESIZED DERIVATIVES

Table 4.2 Physical data of compounds B1 to B19.

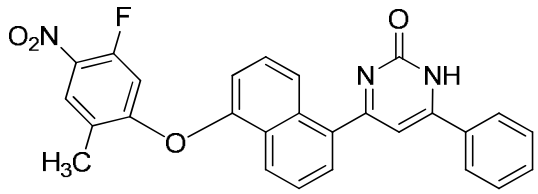
Comp.	R	Molecular Formula	Mol. Wt. (g/m)	% Yield	M.P. °C	% Carbon		% Hydrogen		% Nitrogen	
						Found	Calcd.	Found	Calcd.	Found	Calcd.
B1	-H	$C_{27}H_{18}FN_3O_4$	467.4	72	234	69.30	69.37	3.80	3.88	8.85	8.99
B2	4-OH	$C_{27}H_{18}FN_3O_5$	483.4	72	210	67.10	67.08	3.70	3.75	8.60	8.69
B3	3-OH	$C_{27}H_{18}FN_3O_5$	483.4	68	215	67.12	67.08	3.78	3.75	8.62	8.69
B4	2-OH	$C_{27}H_{18}FN_3O_5$	483.4	75	250	67.08	67.08	3.80	3.75	8.64	8.69
B5	2- OCH_3	$C_{28}H_{20}FN_3O_5$	494.7	68	240	67.70	67.60	4.10	4.05	8.40	8.45
B6	4-OCH_3	$C_{28}H_{20}FN_3O_5$	494.7	67	230	67.72	67.60	4.12	4.05	8.38	8.45
B7	2-Cl	$C_{27}H_{17}FClN_3O_4$	501.8	80	225	64.65	64.61	3.45	3.41	8.42	8.37
B8	4-Cl	$C_{27}H_{17}FClN_3O_4$	501.8	80	230	64.69	64.61	3.47	3.41	8.30	8.37
B9	3-Cl	$C_{27}H_{17}FClN_3O_4$	501.8	75	242	64.66	64.61	3.48	3.41	8.43	8.37

B10	2-NO_2	$C_{27}H_{17}FN_4O_6$	512.4	83	223	63.22	63.28	3.28	3.34	10.85	10.93
B11	4-NO_2	$C_{27}H_{17}FN_4O_6$	512.4	83	225	63.24	63.28	3.29	3.34	10.86	10.93
B12	3-NO_2	$C_{27}H_{17}FN_4O_6$	512.4	82	224	63.20	63.28	3.30	3.34	10.87	10.93
B13	3-Br	$C_{27}H_{17}FBrN_3O_4$	546.3	78	235	59.28	59.36	3.10	3.14	7.62	7.69
B14	2- Br	$C_{27}H_{17}FBrN_3O_4$	546.3	75	240	59.22	59.36	3.12	3.14	7.65	7.69
B15	4- Br	$C_{27}H_{17}FBrN_3O_4$	546.3	78	245	59.29	59.3	3.09	3.14	7.63	7.69
B16	3, 4-$(OCH_3)_2$	$C_{29}H_{22}FN_3O_6$	527.5	72	245	66.10	66.03	4.10	4.20	7.90	7.97
B17	3,4,5-$(OCH_3)_3$	$C_{30}H_{24}FN_3O_7$	557.5	72	260	64.68	64.63	4.39	4.34	7.45	7.54
B18	2-furfuryl	$C_{25}H_{16}FN_3O_5$	457.4	82	255	65.60	65.65	3.58	3.53	9.10	9.19
B19	2-Thineyl	$C_{25}H_{16}FSN_3O_4$	473.4	80	225	63.48	63.42	3.45	3.41	8.83	8.87

4.7 SPECTROSCOPIC CHARACTERIZATION OF COMPOUNDS B1-B19.

For characterization,**compound B1** was taken as the model compound from the series and it was characterized by various spectroscopic methods such as ^{1}H NMR, ^{13}C NMR, MASS and IR spectroscopy. Its structure was decided by these spectroscopic technique. (as shown in Fig. 4.1 to Fig. 4.4)

Compound B1



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-phenylpyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. All 14 aromatic protons appeared in aromatic region between δ 6.8 to 8.3 ppm. Singlet due to NH proton appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.0 ppm. All aromatic carbons give signals at δ 128.9, 129.4, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 ppm and carbonyl carbon of amide group comes at δ 165.2 ppm.

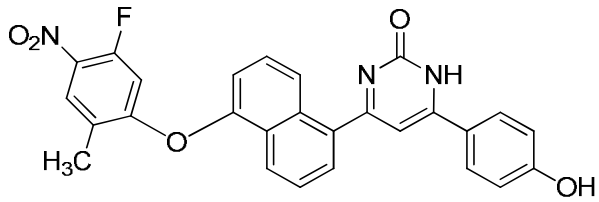
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3311 cm^{-1} indicates the N-H stretching. The bands at 3120 cm^{-1} indicates thearomatic C-H stretching, and at 2950 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1611, 1592 and 1569 cm^{-1} and due to the C=C and N=O stretching. The band at 744 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 467.4, which indicates the molecular weight of the compound.

Compound B2



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-hydroxyphenyl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.4 ppm in downfield region. Singlet due to one –OH proton appeared at δ 2.7 ppm. All 13 aromatic protons appeared in aromatic region between δ 6.8 to 8.3 ppm. Singlet due to NH proton is shown at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.0 ppm. All aromatic carbons give signals at δ 128.9, 130.3, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 ppm and carbonyl carbon of amide group at δ 164.2 ppm.

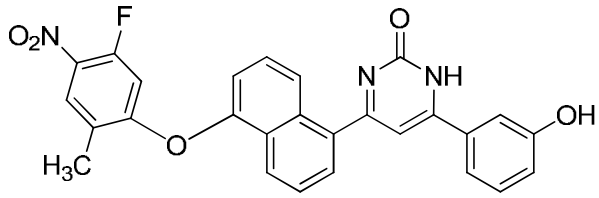
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3415 and 3310 cm^{-1} indicates the O-H and N-H stretching, respectively. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. The band at 2950 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1610, 1592 and 1569 cm^{-1} and due to the C=C and N=O stretching. The band at 744 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 483.4, which indicates the molecular weight of the compound.

Compound B3



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3-hydroxyphenyl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.4 ppm in downfield region. Singlet due to one –OH proton appeared at δ 2.7 ppm. All 13 aromatic protons appeared in aromatic region between δ 6.6 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.0 ppm. All aromatic carbons give signals at δ 129.4, 130.4, 131.6, 140.2, 146.6, 151.7, 153.7, 155.1 ppm and signal due to carbonyl carbon of amide group appeared at 164.2 δ ppm.

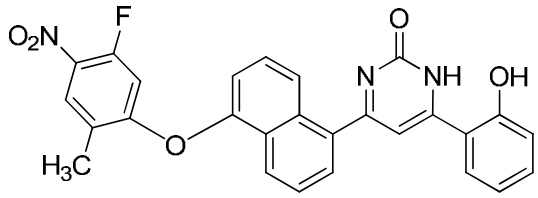
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3419 and 3310 cm^{-1} indicates the O-H and N-H stretching, respectively. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2951 cm^{-1} shows aliphatic C-H stretching of the methyl group. The band at 1611, 1592 and 1569 cm^{-1} and due to the C=C and N=O stretching. The band at 746 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 483.4, which indicates the molecular weight of the compound.

Compound B4



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-hydroxyphenyl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. Singlet due to one –OH proton appeared at δ 2.6 ppm. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH proton is appeared at δ 9.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.0 ppm. All aromatic carbons give signals at δ 128.9, 130.4, 131.6, 140.2, 146.6, 151.7, 154.7, 156.1 ppm and signal due to carbonyl carbon of amide group appeared at 165.2 δ ppm.

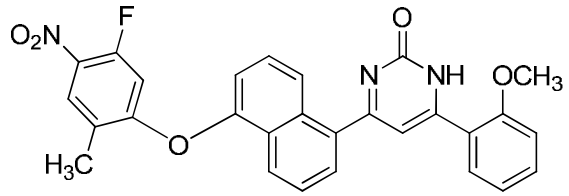
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3420 and 3312 cm^{-1} indicates the O-H and N-H stretching, respectively. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2952 cm^{-1} shows aliphatic C-H stretching of the methyl group. The band at 1611, 1590 and 1565 cm^{-1} and due to the C=C and N=O stretching. The band at 750 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 483.4, which indicates the molecular weight of the compound.

Compound B5



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-methoxyphenyl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. Singlet due to $–OCH_3$ proton appeared at δ 3.4 ppm. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH proton is appeared at δ 9.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.0 ppm. Signal due to $–OCH_3$ group is comes at 39.0 δ ppm. All aromatic carbons give signals at δ 127.9, 129.4, 131.6, 140.2, 146.6, 151.7, 154.7, 156.1 ppm and signal due to carbonyl carbon of amide group appeared at 164.2 δ ppm.

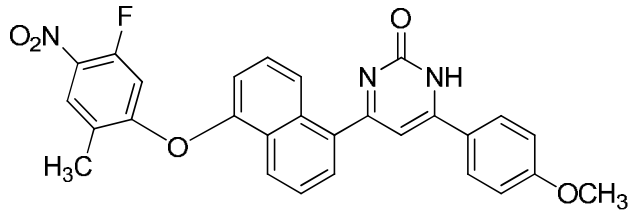
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3312 cm^{-1} indicates the N-H stretching. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2951 cm^{-1} shows aliphatic C-H stretching of the methyl group. The band at 1612, 1590 and 1568 cm^{-1} and due to the C=C and N=O stretching. The band at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 494.7, which indicates the molecular weight of the compound.

Compound B6



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-methoxyphenyl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. Singlet due to $–OCH_3$ proton appeared at δ 3.4 ppm. All 13 aromatic protons appeared in aromatic region between δ 6.4 to 8.4 ppm. Singlet due to NH proton is appeared at δ 9.6 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.1 ppm. Signal due to $–OCH_3$ group is comes at 39.0 δ ppm. All aromatic carbons give signals at δ 127.9, 129.4, 131.4, 131.6, 140.2, 146.6, 152.7, 154.7, 156.1 ppm and signal due to carbonyl carbon of amide group appeared at 164.2 δ ppm.

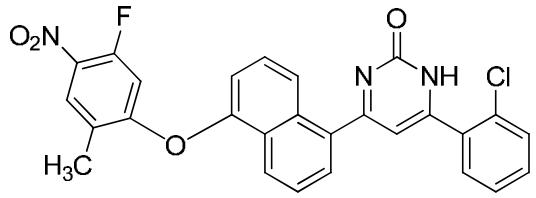
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3316 cm^{-1} indicates the N-H stretching. The band at 3132 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2971 cm^{-1} shows aliphatic C-H stretching of the methyl group. The band at 1612, 1590 and 1568 cm^{-1} and due to the C=C and N=O stretching. The band at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 494.7, which indicates the molecular weight of the compound.

Compound B7



6-(2-chlorophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 33.0 ppm. All aromatic carbons give signals at δ 129.4, 130.3, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 ppm and signal due to carbonyl carbon of amide group appeared at 164.2 δ ppm.

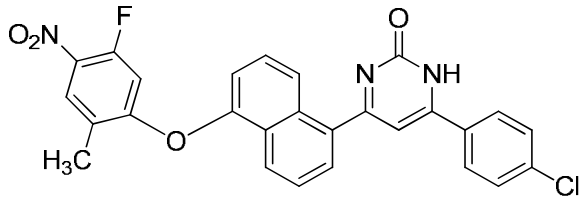
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3311 cm^{-1} indicates the N-H stretching. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2960 cm^{-1} shows aliphatic C-H stretching of the methyl group. The band at 1610, 1592 and 1567 cm^{-1} and due to the C=C and N=O stretching. The band at 744 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 501.8, which indicates the molecular weight of the compound.

Compound B8



6-(4-chlorophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 31.5 ppm. All aromatic carbons give signals at δ 128.5, 130.2, 131.6, 140.2, 146.6, 151.9, 153.6, 155.1 ppm and signal due to carbonyl carbon of amide group appeared at 165.2 δ ppm.

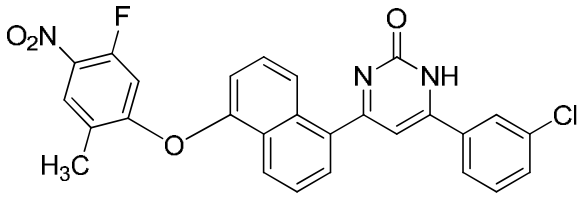
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3370 cm^{-1} indicates the N-H stretching. The band at 3121 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2980 cm^{-1} shows aliphatic C-H stretching of the methyl group. The band at 1610, 1595 and 1567 cm^{-1} and due to the C=C and N=O stretching. The band at 746 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 501.8, which indicates the molecular weight of the compound.

Compound B9



6-(3-chlorophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.6 ppm in downfield region. All 13 aromatic protons appeared in aromatic region between δ 6.4 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.1 ppm. All aromatic carbons give signals at δ 129.4, 130.3, 133.6, 140.2, 146.6, 151.9, 152.6, 155.1 ppm and signal due to carbonyl carbon of amide group appeared at 164.2 δ ppm.

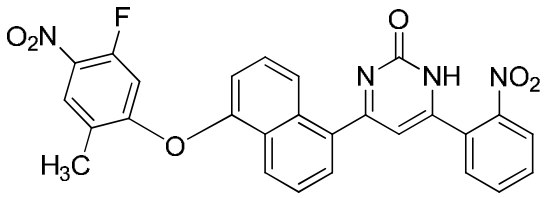
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that the absorption band at 3320 cm^{-1} indicates the N-H stretching. The band at 3121 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2985 cm^{-1} shows aliphatic C-H stretching of the methyl group. The band at 1609, 1595 and 1567 cm^{-1} indicates the C=C and N=O stretching. Band at 746 cm^{-1} attributed to C-H bending vibrations disubstituted benzene ring.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 501.8, which indicates the molecular weight of the compound.

Compound B10



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-nitrophenyl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.2 δ ppm. All aromatic carbons give signals at δ 128.4, 130.4, 131.6, 140.2, 146.6, 155.8, 155.6, 155.2 ppm and carbonyl carbon of amide group appeared at 164.1 δ ppm.

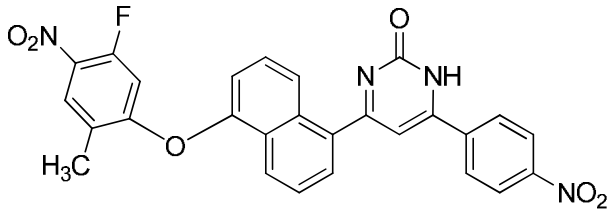
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that the absorption band at 3311 cm^{-1} indicates the N-H stretching. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Absorption at 2960 cm^{-1} shows aliphatic C-H stretching of the methyl group. The band at 1610, 1592 and 1567 cm^{-1} indicates the C=C and N=O stretching. Band at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 512.4, which indicates the molecular weight of the compound.

Compound B11



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-nitrophenyl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.6 ppm in downfield region. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.2 ppm. All aromatic carbons give signals at δ 129.4, 130.3, 131.6, 140.2, 146.6, 151.9, 153.6, 155.1 ppm and carbonyl carbon of amide group appeared at δ 165.2 ppm.

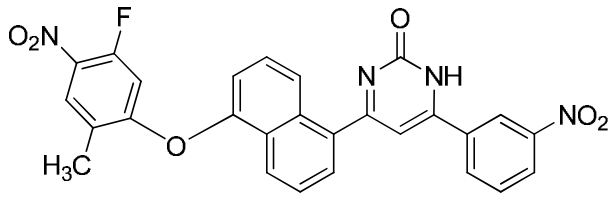
IR Spectroscopy (KBr)

Infrared spectra was recorded using KBr reveals that the absorption band at 3310 cm^{-1} indicates the N-H stretching. Absorption at 3120 cm^{-1} indicates the aromatic C-H stretching. Band at 2982 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1610, 1590 and 1567 cm^{-1} indicates the C=C and N=O stretching. Band at 746 cm^{-1} is due to C-H bending vibrations mono and disubstituted benzene ring.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 512.4, which indicates the molecular weight of the compound.

Compound B12



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3-nitrophenyl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.2 ppm. All aromatic carbons give signals at δ 126.4, 130.3, 131.6, 141.2, 146.6, 151.8, 153.6, 154.1 ppm and carbonyl carbon of amide group appeared at δ 164.2 ppm.

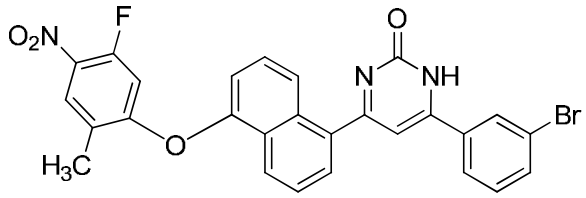
IR Spectroscopy (KBr)

Infrared spectra was recorded using KBr reveals that the absorption band at 3411 cm^{-1} indicates the N-H stretching. Absorption at 3020 cm^{-1} indicates the aromatic C-H stretching. Band at 2960 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1610, 1590 and 1567 cm^{-1} indicates the C=C and N=O stretching. Band at 744 cm^{-1} is due to C-H bending vibrations mono and disubstituted benzene ring.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 512.4, which indicates the molecular weight of the compound.

Compound B13



6-(3-bromophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.4 ppm in downfield region. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 31.1 ppm. All aromatic carbons give signals at δ 129.4, 130.3, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 ppm and carbonyl carbon of amide group appeared at δ 164.2 ppm.

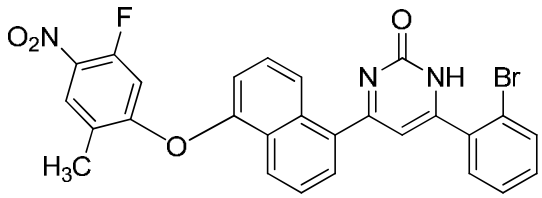
IR Spectroscopy (KBr)

Infrared spectra was recorded using KBr reveals that the absorption band at 3316 cm^{-1} indicates the N-H stretching. Absorption at 3121 cm^{-1} indicates the aromatic C-H stretching. Band at 2930 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1610, 1591 and 1565 cm^{-1} indicates the C=C and N=O stretching. Band at 740 cm^{-1} is due to C-H bending vibrations mono and disubstituted benzene ring.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 546.3, which indicates the molecular weight of the compound.

Compound B14



6-(2-bromophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.0 ppm. All aromatic carbons give signals at δ 129.4, 130.4, 131.6, 140.2, 146.6, 151.9, 153.6, 155.1 ppm and carbonyl carbon of amide group appeared at δ 165.2 ppm.

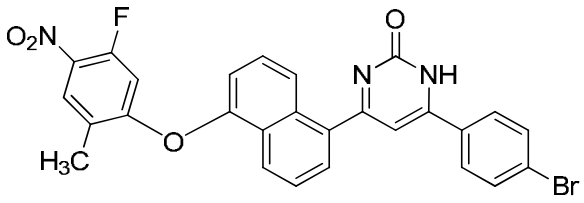
IR Spectroscopy (KBr)

Infrared spectra was recorded using KBr reveals that the absorption band at 3360 cm^{-1} indicates the N-H stretching. Absorption at 3121 cm^{-1} indicates the aromatic C-H stretching. Band at 2980 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1610, 1593 and 1560 cm^{-1} indicates the C=C and N=O stretching. Band at 750 cm^{-1} is due to C-H bending vibrations mono and disubstituted benzene ring.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 546.3, which indicates the molecular weight of the compound.

Compound B15



6-(4-bromophenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.4 ppm in downfield region. All 13 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.1 ppm. All aromatic carbons give signals at δ 128.9, 130.3, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 ppm and carbonyl carbon of amide group appeared at δ 164.2 ppm.

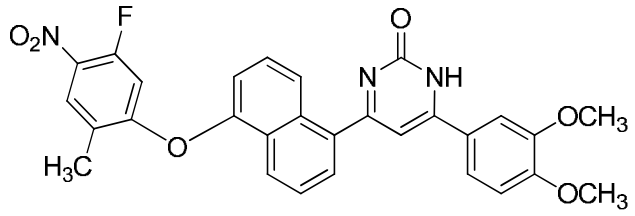
IR Spectroscopy (KBr)

Infrared spectra was recorded using KBr reveals that the absorption band at 3310 cm^{-1} indicates the N-H stretching. Absorption at 3105 cm^{-1} indicates the aromatic C-H stretching. Band at 2960 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1610, 1590 and 1550 cm^{-1} indicates the C=C and N=O stretching. Band at 750 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 546.3, which indicates the molecular weight of the compound.

Compound B16



6-(3,4-dimethoxyphenyl)-4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. Singlet due to two –OCH_3 proton appeared at δ 3.5 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 31.2 ppm. Signal due to two –OCH_3 group is appeared at 39.0 and 40.1 δ ppm. All aromatic carbons give signals at δ 127.9, 131.4, 131.6, 140.2, 146.6, 152.7, 154.7, 157.1 ppm and carbonyl carbon of amide group appeared at δ 164.2 ppm.

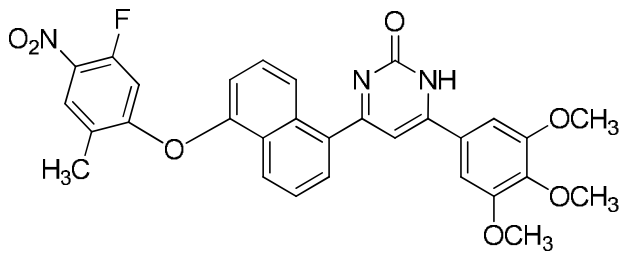
IR Spectroscopy (KBr)

Infrared spectra was recorded using KBr reveals that the absorption band at 3320 cm^{-1} indicates the N-H stretching. Absorption at 3130 cm^{-1} indicates the aromatic C-H stretching. Band at 2970 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1612, 1592 and 1568 cm^{-1} indicates the C=C and N=O stretching. Band at 741 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 527.5, which indicates the molecular weight of the compound.

Compound B17



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. Singlet due to two –OCH_3 proton appeared at δ 3.4 ppm. All 11 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH proton is appeared at δ 9.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.0 ppm. Signal due to three –OCH_3 group is appeared at 38.6, 39.0 and 40.1 δ ppm. All aromatic carbons give signals at δ 127.9, 131.4, 131.6, 140.2, 146.6, 152.7, 154.7, 157.1 ppm and carbonyl carbon of amide group appeared at δ 164.2 ppm.

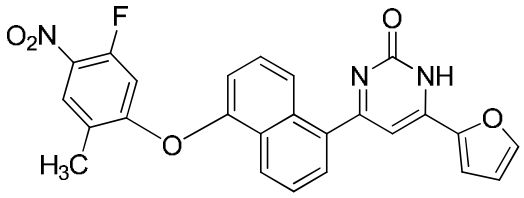
IR Spectroscopy (KBr)

Infrared spectra was recorded using KBr reveals that the absorption band at 3312 cm^{-1} indicates the N-H stretching. Absorption at 3130 cm^{-1} indicates the aromatic C-H stretching. Band at 2972 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1612, 1590 and 1565 cm^{-1} indicates the C=C and N=O stretching. Band at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 557.5, which indicates the molecular weight of the compound.

Compound B18



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(furan-2-yl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH proton is appeared at δ 9.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.0 ppm. All aromatic carbons give signals at δ 128.9, 130.4, 131.6, 131.6.2, 142.6, 146.6, 153.7, 154.7, 157.1 ppm and carbonyl carbon of amide group appeared at δ 164.3 ppm.

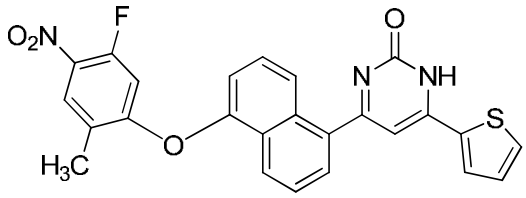
IR Spectroscopy (KBr)

Infrared spectra was recorded using KBr reveals that the absorption band at 3315 cm^{-1} indicates the N-H stretching. Absorption at 3130 cm^{-1} indicates the aromatic C-H stretching. Band at 2929 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1613, 1590 and 1560 cm^{-1} indicates the C=C and N=O stretching. Band at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 557.4, which indicates the molecular weight of the compound.

Compound B19



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(thiophen-2-yl)pyrimidin-2(1*H*)-one

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound give singlet at δ 2.5 ppm in downfield region. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH proton is appeared at δ 9.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at δ 32.0 ppm. All aromatic carbons give signals at δ 129.4, 131.4, 131.6, 142.2, 146.6, 152.7, 154.7, 157.1 ppm and carbonyl carbon of amide group appeared at δ 164.2 ppm.

IR Spectroscopy (KBr)

Infrared spectra was recorded using KBr reveals that the absorption band at 3315 cm^{-1} indicates the N-H stretching. Absorption at 3130 cm^{-1} indicates the aromatic C-H stretching. Band at 2973 cm^{-1} shows aliphatic C-H stretching of the methyl group. Absorption at 1612, 1590 and 1565 cm^{-1} indicates the C=C and N=O stretching. Band at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the Mass spectrum of the given compound, molecular ion peak appeared at M+ 473.4, which indicates the molecular weight of the compound.

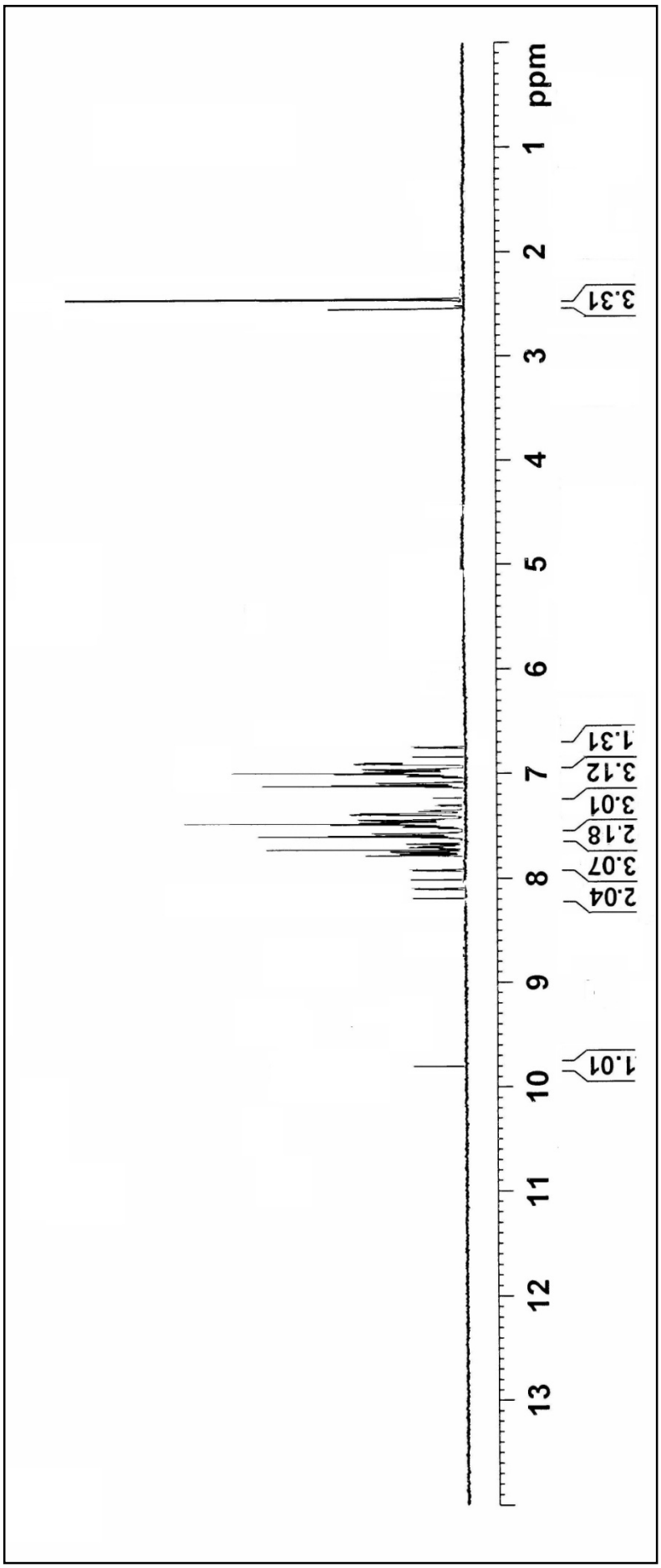


Fig. 4.1: ^{1}H NMR spectrum of B1

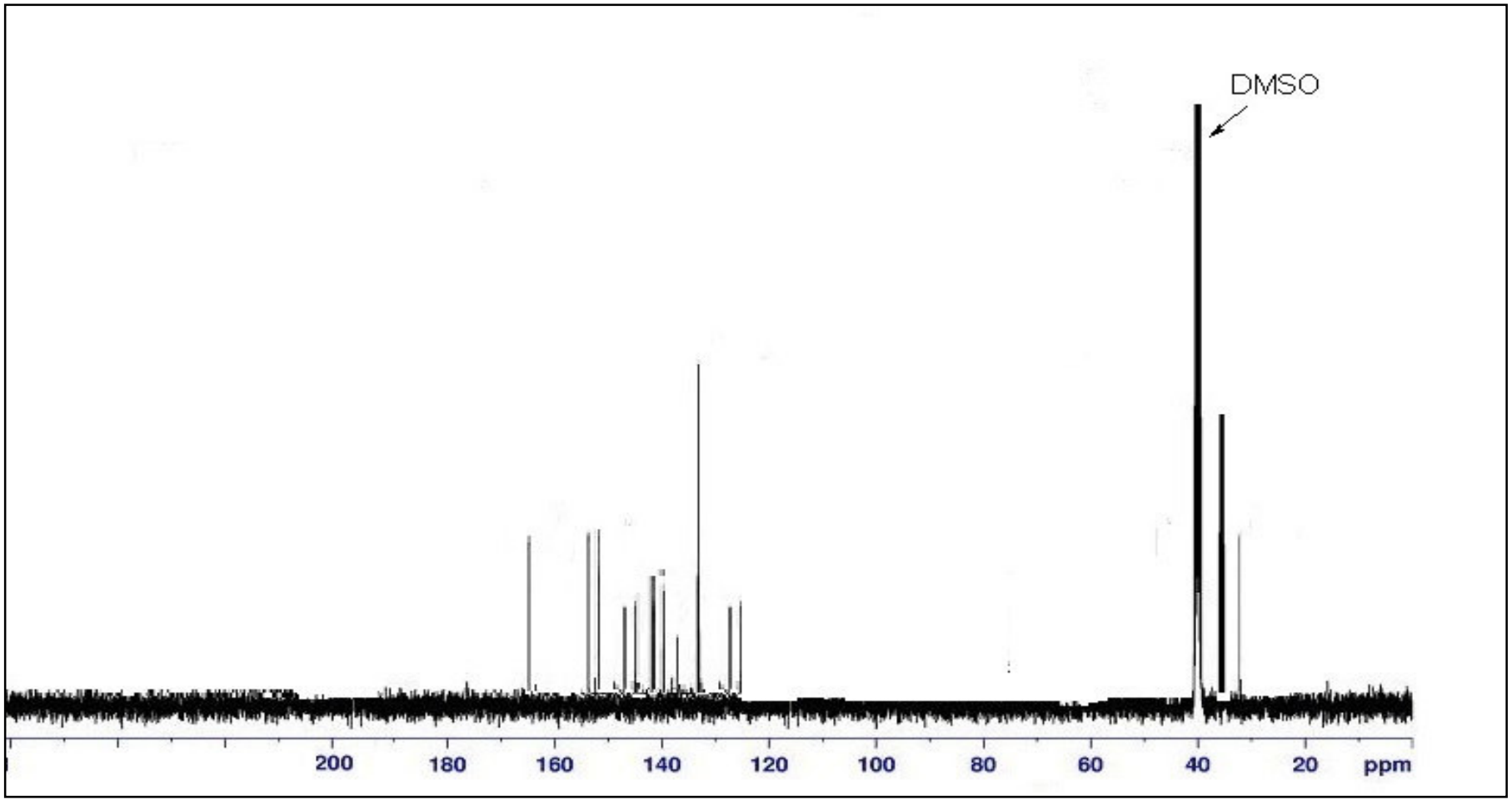


Fig. 4.2: ^{13}C NMR spectrum of B1

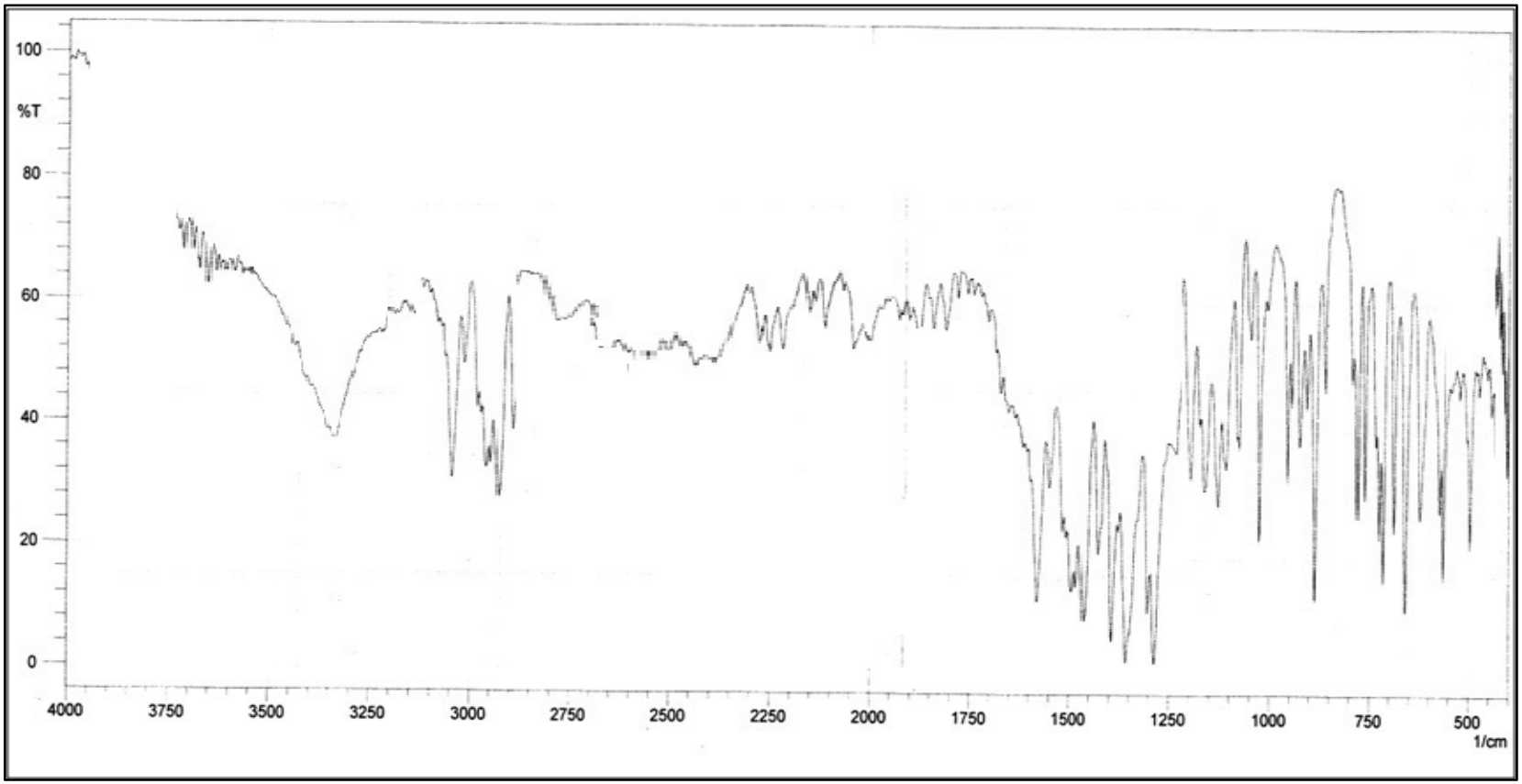


Fig. 4.3: IR spectrum of B1

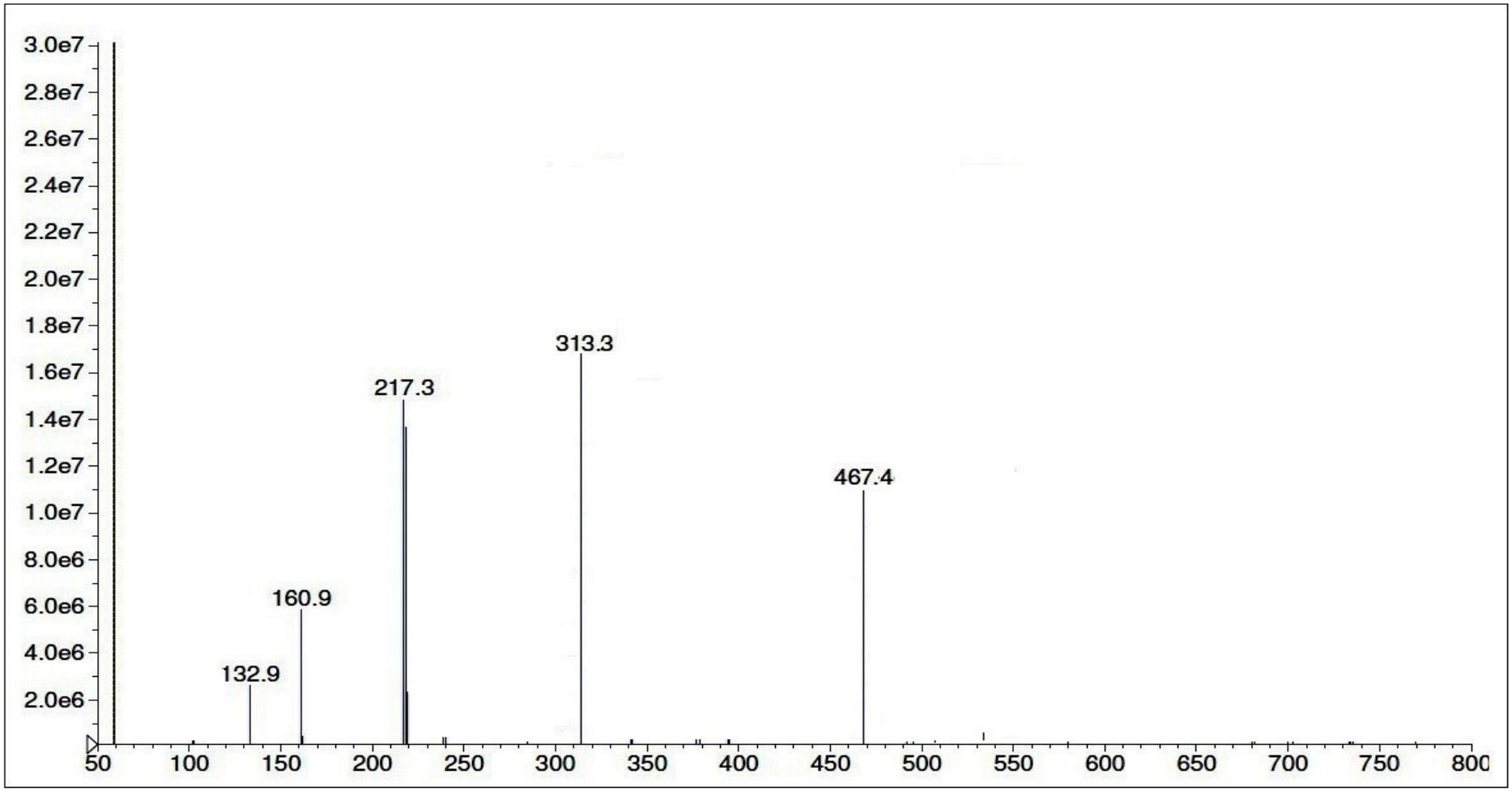


Fig. 4.4: Mass spectrum of B1

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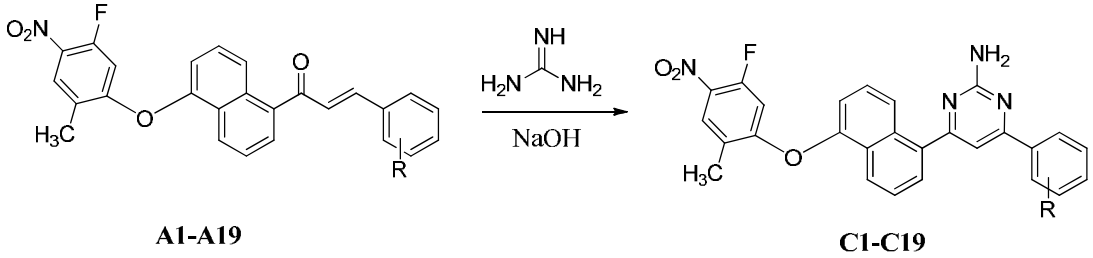
CHAPTER – V

SYNTHESIS AND CHARACTERIZATION OF PYRIMIDINES

CONTENTS

5.1 REACTION SCHEME

Pyrimidines **C1-C19** were planned to prepare by reaction between chalcones **A1-A19** and Guanidine in the presence of ethanol and 40% NaOH (**Scheme 5.1)**.

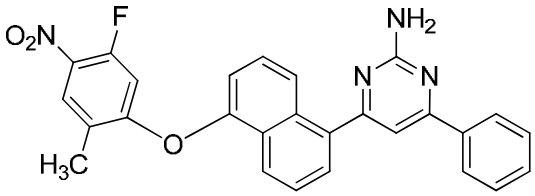


A1-A19 **C1-C19**

Scheme 5.1 Synthesis of Pyrimidines C1-C19

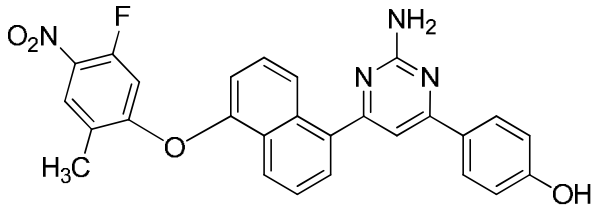
5.2 STRUCTURE OF COMPOUNDS C1 TO C19

Compound C1:



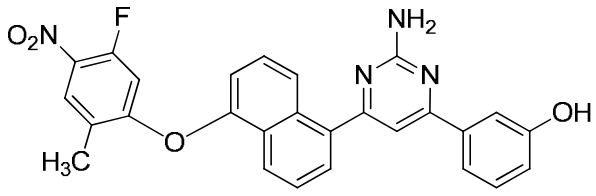
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-phenylpyrimidin-2-amine

Compound C2:



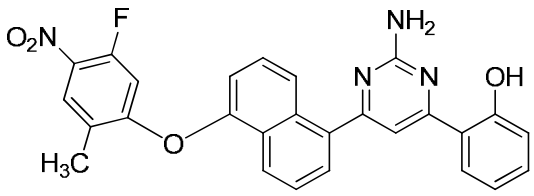
4-(2-amino-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-4-yl)phenol

Compound C3:



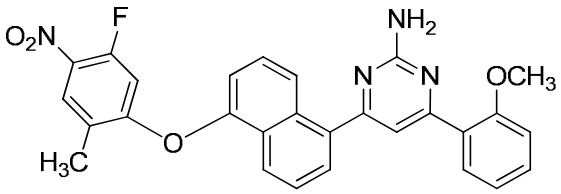
3-(2-amino-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-4-yl)phenol

Compound C4:



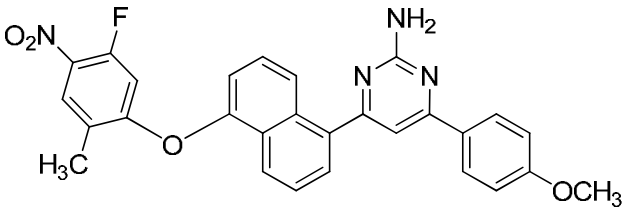
2-(2-amino-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-4-yl)phenol

Compound C5:



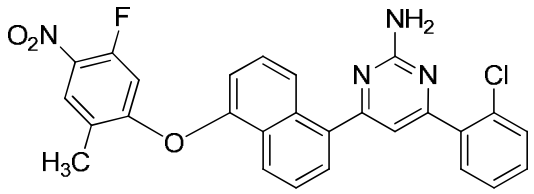
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-methoxyphenyl)pyrimidin-2-amine

Compound C6:



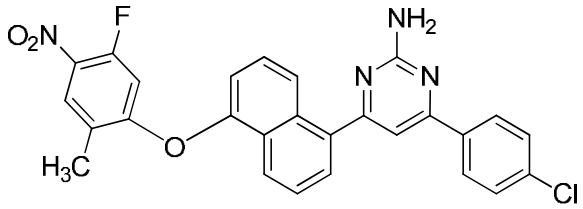
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-methoxyphenyl)pyrimidin-2-amine

Compound C7:



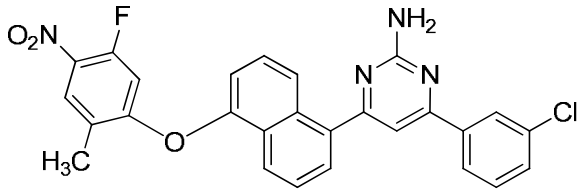
4-(2-chlorophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

Compound C8:



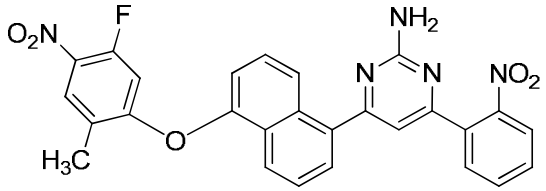
4-(4-chlorophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

Compound C9:



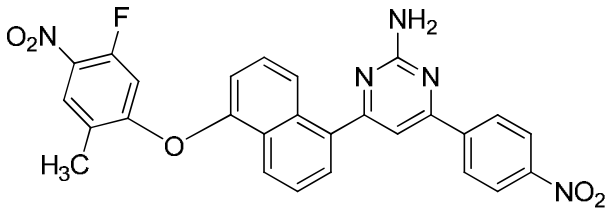
4-(3-chlorophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

Compound C10:



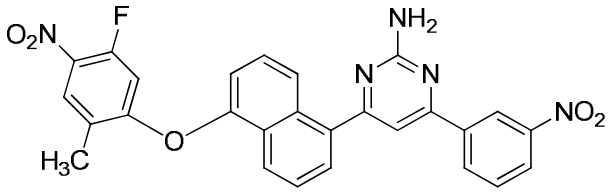
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-nitrophenyl)pyrimidin-2-amine

Compound C11:



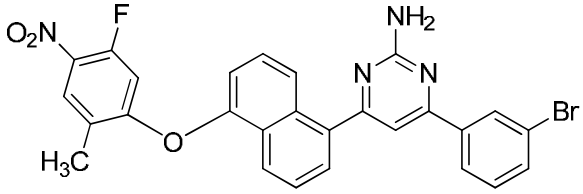
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-nitrophenyl)pyrimidin-2-amine

Compound C12:



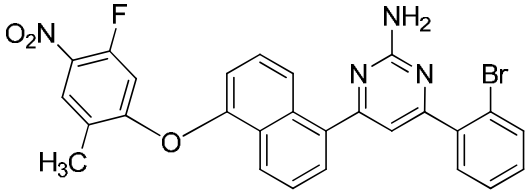
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3-nitrophenyl)pyrimidin-2-amine

Compound C13:



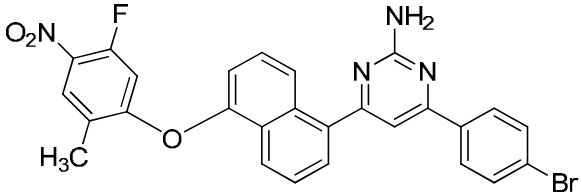
4-(3-bromophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

Compound C14:



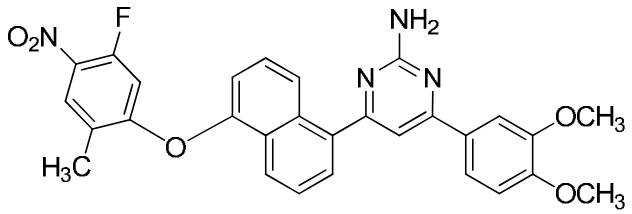
4-(2-bromophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

Compound C15:



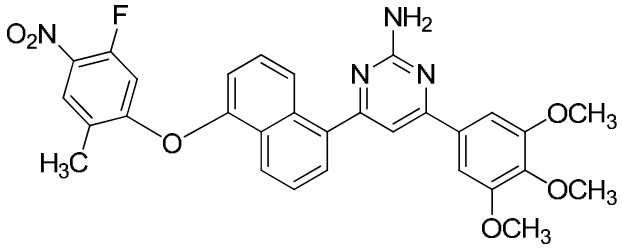
4-(4-bromophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

Compound C16:



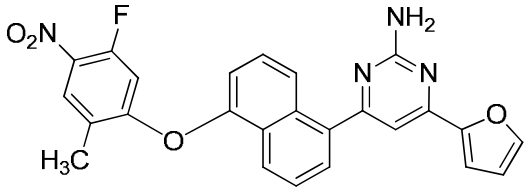
4-(3,4-dimethoxyphenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

Compound C17:



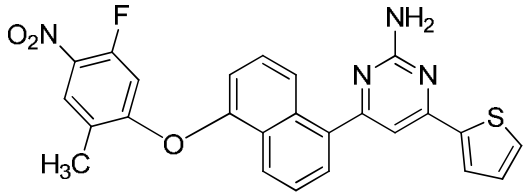
4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-amine

Compound C18:



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(furan-2-yl)pyrimidin-2-amine

Compound C19:



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(thiophen-2-yl)pyrimidin-2-amine

5.3 EXPERIMENTAL

5.3.1 Chemicals and Reagents

All chemicals used were of laboratory reagent grade and used without further purification**.** NaOH, Guanidine and ethanol were used as received from Merck, Mumbai, India.

5.3.2 General Experimental procedure

5.3.2.1 Synthesis of Pyrimidine biosynthesis C1

Chalcone **A1** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine,40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C1**.

5.3.2.2 Synthesis of Pyrimidine C2

Chalcone **A2** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine,40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C2**.

5.3.2.3 Synthesis of Pyrimidine C3

Chalcone **A3** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine,40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C3**.

5.3.2.4 Synthesis of Pyrimidine C4

Chalcone **A4** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C4**.

5.3.2.5 Synthesis of Pyrimidine C5

Chalcone **A5** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C5**.

5.3.2.6 Synthesis of Pyrimidine C6

Chalcone **A6** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C6**.

5.3.2.7 Synthesis of Pyrimidine C7

Chalcone **A7** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C7**.

5.3.2.8 Synthesis of Pyrimidine C8

Chalcone **A8** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C8**.

5.3.2.9 Synthesis of Pyrimidine C9

Chalcone **A9** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C9**.

5.3.2.10 Synthesis of Pyrimidine C10

Chalcone **A10** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for

1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C10**.

5.3.2.11 Synthesis of Pyrimidine C11

Chalcone **A11** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C11**.

5.3.2.12 Synthesis of Pyrimidine C12

Chalcone **A12** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C12**.

5.3.2.13 Synthesis of Pyrimidine C13

Chalcone **A13** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C13**.

5.3.2.14 Synthesis of Pyrimidine C14

Chalcone **A14** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C14**.

5.3.2.15 Synthesis of Pyrimidine C15

Chalcone **A15** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C15**.

5.3.2.16 Synthesis of Pyrimidine C16

Chalcone **A16** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C16**.

5.3.2.17 Synthesis of Pyrimidine C17

Chalcone **A17** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C17**.

5.3.2.18 Synthesis of Pyrimidine C18

Chalcone **A18** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C18**.

5.3.2.19 Synthesis of Pyrimidine C19

Chalcone **A19** (0.01 mol) was taken in 250 ml RBF, and to this 0.01 mol Guanidine, 40 ml ethanol and 40 ml 40% NaOH were added. The entire mixture was refluxed for 1-2 hours to produce Primidone**.** The reaction was monitored by TLC and completion of reaction was also checked by TLC. The pyrimidine obtained is called **C19**.

5.4 CHARACTERSTICS DATA SHOWING SYNTHESIS OF PYRIMIDINE C1-C19.

Table 5.1 Synthesis of Pyrimidine C1-C19

Sr. No.	Compounds	R	Reaction Time (hr)	% Yield[b]
1	**C1**	-H	4	80
2	**C2**	4-OH	4	75
3	**C3**	3-OH	4	83
4	**C4**	2-OH	4	83
5	**C5**	2- OCH_3	4.5	82
6	**C6**	4-OCH_3	4.5	78
7	**C7**	2-Cl	3.5	72
8	**C8**	4-Cl	3.5	72
9	**C9**	3-Cl	3.5	68
10	**C10**	2-NO_2	3.5	75
11	**C11**	4-NO_2	3.5	68
12	**C12**	3-NO_2	3.5	67
13	**C13**	3-Br	4	80
14	**C14**	2- Br	4	72
15	**C15**	4- Br	4	82
16	**C16**	3, 4-$(OCH_3)_2$	4.5	80
17	**C17**	3,4,5-$(OCH_3)_3$	4.5	75
18	**C18**	2-furfuryl[c]	3.5	78
19	**C19**	2-Thineyl[c]	3.5	72

[a]Reaction is monitored by TLC, [b]Isolated yield and [c]Names of aldehyde groups

5.5 RESULTS AND DISCUSSION

Table 5.1 shows the data for various condensation products of reaction between various chalcones andguanidine. It clearly indicates that the compounds bearing electron withdrawing groups are synthesized in shorter reaction time as compared to compounds bearing electron donating group. Compounds **C7-C15** bearing electron withdrawing groups were synthesized in **3.5 to 4h** as compared to compounds bearing electron donating group. Compounds **C5, C6, C16** and **C17 which have** electron donating groups were synthesized in **4.5 h**.

5.6 PHYSICAL DATA OF SYNTHESIZED DERIVATIVES

Table 5.2 Physical data of compounds C1 to C19

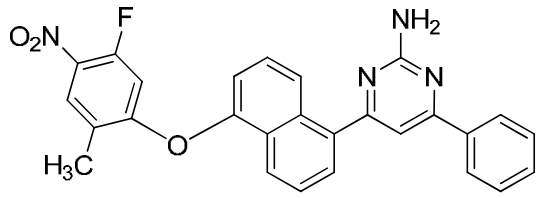
Comp.	R	Molecular Formula	Mol. Wt. (g/m)	% Yield	M.P. °C	% Carbon		% Hydrogen		% Nitrogen	
						Found	Calcd.	Found	Calcd.	Found	Calcd.
C1	-H	$C_{27}H_{19}FN_4O_3$	466.1	80	236	69.60	69.52	4.15	4.11	12.07	12.01
C2	4-OH	$C_{27}H_{19}FN_4O_4$	482.4	75	252	67.25	67.22	3.92	3.97	11.65	11.61
C3	3-OH	$C_{27}H_{19}FN_4O_4$	482.4	83	246	67.28	67.22	3.90	3.97	11.64	11.61
C4	2-OH	$C_{27}H_{19}FN_4O_4$	482.4	83	258	67.24	67.22	3.91	3.97	11.67	11.61
C5	2- OCH_3	$C_{28}H_{21}FN_4O_4$	496.4	82	244	67.70	67.74	4.20	4.26	11.20	11.28
C6	4-OCH_3	$C_{28}H_{21}FN_4O_4$	496.4	78	232	67.72	67.74	4.21	4.26	11.21	11.28
C7	2-Cl	$C_{27}H_{18}FClN_4O_3$	500.9	72	235	64.70	64.74	3.58	3.62	11.14	11.19
C8	4-Cl	$C_{27}H_{18}FClN_4O_3$	500.9	72	245	64.71	64.74	3.56	3.62	11.13	11.19
C9	3-Cl	$C_{27}H_{18}FClN_4O_3$	500.9	68	258	64.69	64.74	3.57	3.62	11.12	11.19
C10	2-NO_2	$C_{27}H_{18}FN_5O_5$	511.4	75	242	63.35	63.40	3.50	3.55	13.60	13.69

C11	4-NO_2	$C_{27}H_{18}FN_5O_5$	511.4	68	255	63.36	63.40	3.51	3.55	13.62	13.69
C12	3-NO_2	$C_{27}H_{18}FN_5O_5$	511.4	67	248	63.33	63.40	3.52	3.55	13.61	13.69
C13	3-Br	$C_{27}H_{18}FBrN_4O_3$	445.3	80	252	59.40	59.46	3.30	3.33	10.25	10.27
C14	2- Br	$C_{27}H_{18}FBrN_4O_3$	445.3	72	252	59.41	59.46	3.31	3.33	10.21	10.27
C15	4- Br	$C_{27}H_{18}FBrN_4O_3$	445.3	82	256	59.42	59.46	3.36	3.33	10.29	10.27
C16	3, 4-$(OCH_3)_2$	$C_{29}H_{23}FN_4O_5$	526.5	80	245	66.10	66.15	4.30	4.40	10.60	10.64
C17	3,4,5-$(OCH_3)_3$	$C_{30}H_{25}FN_4O_6$	556.5	75	257	64.70	64.74	4.45	4.53	10.11	10.07
C18	2-furfuryl	$C_{25}H_{17}FN_4O_4$	456.4	78	248	65.85	65.79	3.80	3.75	12.20	12.28
C19	2-Thineyl	$C_{25}H_{17}FSN_4O_3$	472.4	72	262	63.45	63.55	3.58	3.63	11.80	11.86

5.7 SPECTROSCOPIC CHARACTERIZATION OF COMPOUNDS C1-C19

For characterization,**compound C1** was taken as the model compound from the series and it was characterized by various spectroscopic methods such as ^{1}H NMR, ^{13}C NMR, MASS and IR spectroscopy. Its structures was decided by these spectroscopic techniques. (As shown in Fig. 5.1 to Fig. 5.4).

Compound C1



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-phenylpyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.6 ppm. All 13 aromatic protons appeared in aromatic region between δ 6.8 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.5 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.0 δ ppm. Signal due to carbon of methine groups were found at δ 62.2 ppm. All aromatic carbons give signals at 129.4, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 and 160.2 δ ppm.

IR Spectroscopy (KBr)

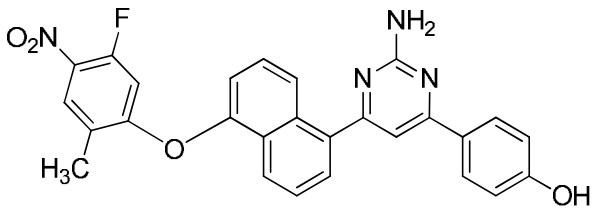
Infrared spectra recorded in KBr reveals that absorption at 3311 and 3415 cm^{-1} indicates the N-H stretching. The band at 3120 cm^{-1} shows aromatic C-H stretching. Bands at 2950 cm^{-1} indicates aliphatic C-H stretching of the methyl group. Bands at 1612, 1592 and 1569 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1}

indicates the N=O stretching. Absorption at 744 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 466.1, which indicates the molecular weight of the compound.

Compound C2



4-(2-amino-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-4-yl)phenol

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.4 ppm in downfield region. Singlet due to one –OH proton appeared at δ 2.7 ppm. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.8 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.3 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.0 δ ppm. Signal due to carbon of methine groups were found at δ 62.2 ppm. All aromatic carbons give signals at 128.9, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 and 160.2 δ ppm.

IR Spectroscopy (KBr)

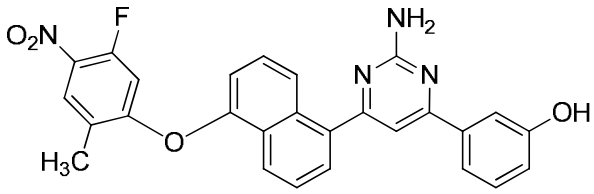
Infrared spectra recorded in KBr reveals that absorption 3415 cm^{-1} indicates the O-H stretching and the band at 3360 and 3310 cm^{-1} shows the N-H stretching. Bands at 3120 cm^{-1} indicates the aromatic C-H stretching. Bands at 2950 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1610, 1592 and 1569 cm^{-1} indicates the

C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 482.4, which indicates the molecular weight of the compound.

Compound C3



3-(2-amino-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-4-yl)phenol

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.4 ppm in downfield region. Singlet due to one –OH proton appeared at δ 2.7 ppm. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.6 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.0 δ ppm. Signal due to carbon of methine groups were found at δ 62.1 ppm. All aromatic carbons give signals at 129.4, 130.4, 140.2, 146.6, 151.7, 153.6, 155.1 and 160.2 δ ppm.

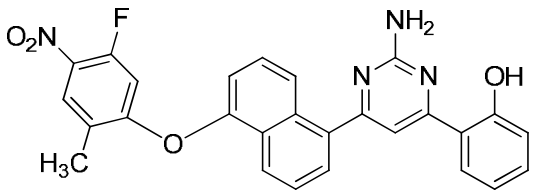
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption 3415 cm^{-1} indicates the O-H stretching and the band at 3360 indicates the N-H stretching. Bands at 3120 cm^{-1} indicates the aromatic C-H stretching. Bands at 2951 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1611, 1592 and 1569 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 746 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 482.4, which indicates the molecular weight of the compound.

Compound C4



2-(2-amino-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-4-yl)phenol

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Singlet due to one –OH proton appeared at δ 2.6 ppm. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH_2 proton comes at δ 4.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.0 δ ppm. Signal due to carbon of methine groups were found at δ 61.1 ppm. All aromatic carbons give signals at 129.9, 130.4, 131.6, 146.6, 151.7, 154.7, 156.1 and 161.2 δ ppm.

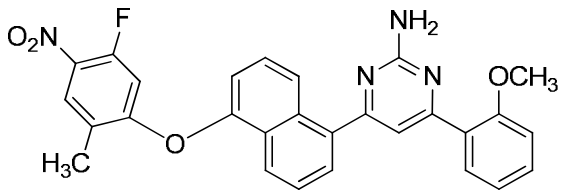
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption 3420 cm^{-1} indicates the O-H stretching and the bands at 3360 and 3310 cm^{-1} indicates the N-H stretching. Bands at 3120 cm^{-1} indicates the aromatic C-H stretching. Bands at 2952 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1611, 1590 and 1565 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 750 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 482.4, which indicates the molecular weight of the compound.

Compound C5



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-methoxyphenyl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Singlet due to –OCH_3 proton appeared at δ 3.4 ppm. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH_2 proton comes at δ 4.5 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.0 δ ppm. Signal due to –OCH_3 group is appeared at 39.0 δ ppm. Signal due to carbon of methine groups were found at δ 61.1 ppm. All aromatic carbons give signals at 127.9, 129.4, 131.6, 140.2, 151.7, 154.7, 156.1 and 161.2 δ ppm.

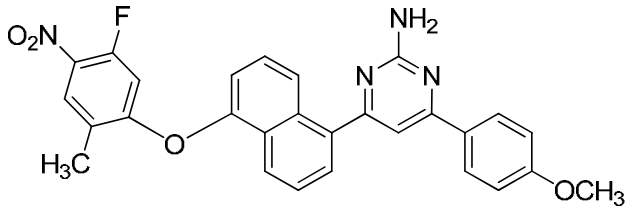
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3312 and 3310 cm^{-1} indicates the N-H stretching, respectively. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Value at 2951 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1612, 1590 and 1568 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations,.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 496.4, which indicates the molecular weight of the compound.

Compound C6



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-methoxyphenyl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Singlet due to –OCH_3 proton appeared at δ 3.4 ppm. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.4 to 8.4 ppm. Singlet due to NH_2 proton comes at δ 4.6 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.1 δ ppm. Signal due to –OCH_3 group is appeared at 39.0 δ ppm. Signal due to carbon of methine groups were found at δ 61.1 ppm. All aromatic carbons give signals at 127.9, 129.4, 131.6, 140.2, 146.6, 152.7, 157.1 and 160.2 δ ppm.

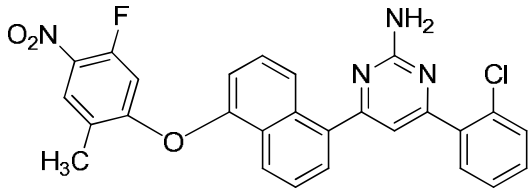
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3410 and 3316 cm^{-1} indicates the N-H stretching, respectively. The band at 3132 cm^{-1} indicates the aromatic C-H stretching. Value at 2971 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1612, 1590 and 1568 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 496.4, which indicates the molecular weight of the compound.

Compound C7



4-(2-chlorophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 33.0 δ ppm. Signal due to carbon of methine groups were found at δ 62.2 ppm. All aromatic carbons give signals at 129.4, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 and 160.2 δ ppm.

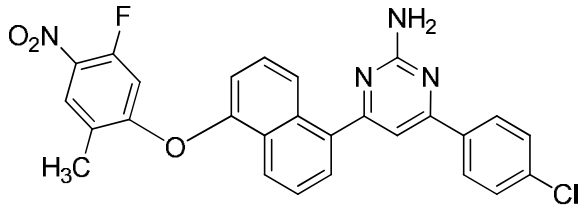
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3350 and 3311 cm^{-1} indicates the N-H stretching, respectively. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Value at 2960 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1610, 1592 and 1567 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 744 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 500.9, which indicates the molecular weight of the compound.

Compound C8



4-(4-chlorophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.5 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 31.5 δ ppm. Signal due to carbon of methine groups were found at δ 61.2 ppm. All aromatic carbons give signals at 128.5, 130.2, 140.2, 146.6, 151.9, 153.6, 155.1 and 160.2 δ ppm.

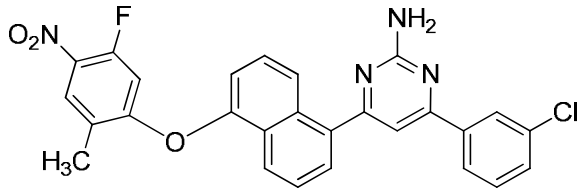
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3410 and 3370 cm^{-1} indicates the N-H stretching, respectively. The band at 3121 cm^{-1} indicates the aromatic C-H stretching. Value at 2980 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1610, 1595 and 1567 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 746 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 500.9, which indicates the molecular weight of the compound.

Compound C9



4-(3-chlorophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.6 ppm in downfield region. One vinylic group give singlet at δ 5.5 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.4 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.1 δ ppm. Signal due to carbon of methine groups were found at δ 62.2 ppm. All aromatic carbons give signals at 129.4, 132.6, 140.2, 146.6, 151.9, 152.6, 155.1 and 160.2 δ ppm.

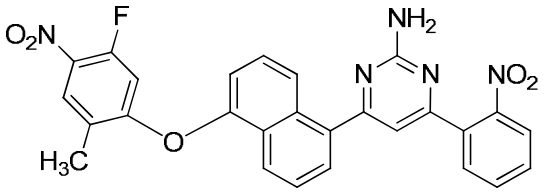
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3370 and 3320 cm^{-1} indicates the N-H stretching, respectively. The band at 3121 cm^{-1} indicates the aromatic C-H stretching. Value at 2985 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1609, 1595 and 1567 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 746 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 500.9, which indicates the molecular weight of the compound.

Compound C10



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(2-nitrophenyl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 31.2 δ ppm. Signal due to carbon of methine groups were found at δ 62.2 ppm. All aromatic carbons give signals at 128.4, 131.6, 140.2, 146.6, 155.8, 153.6, 155.2 and 160.1 δ ppm.

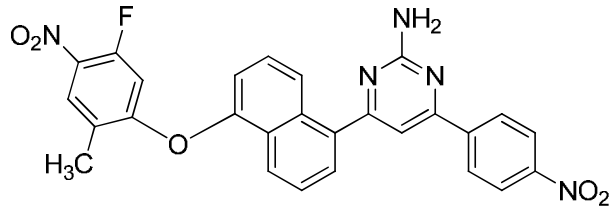
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3340 and 3315 cm^{-1} indicates the N-H stretching, respectively. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Value at 2960 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1610, 1592 and 1567 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 511.4, which indicates the molecular weight of the compound.

Compound C11



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(4-nitrophenyl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.5 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 31.2 δ ppm. Signal due to carbon of methine groups were found at δ 61.2 ppm. All aromatic carbons give signals at 129.4, 131.6, 140.2, 146.6, 151.9, 153.6, 155.1 and 160.2 δ ppm.

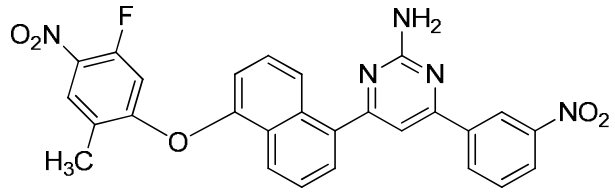
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3350 and 3310 cm^{-1} indicates the N-H stretching. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Value at 2982 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1610, 1591 and 1567 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 742 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 511.4, which indicates the molecular weight of the compound.

Compound C12



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3-nitrophenyl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.4 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.6 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 31.4 δ ppm. Signal due to carbon of methine groups were found at δ 61.2 ppm. All aromatic carbons give signals at 126.4, 131.6, 141.2, 146.6, 151.8, 153.6, 154.1 and 160.2 δ ppm.

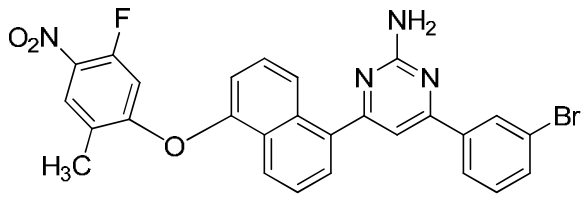
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3411 and 3350 cm^{-1} indicates the N-H stretching. The band at 3120 cm^{-1} indicates the aromatic C-H stretching. Value at 2960 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1610, 1592 and 1567 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 744 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 511.4, which indicates the molecular weight of the compound.

Compound C13



4-(3-bromophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.6 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 31.1 δ ppm. Signal due to carbon of methine groups were found at δ 62.2 ppm. All aromatic carbons give signals at 129.4, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 and 160.2 δ ppm.

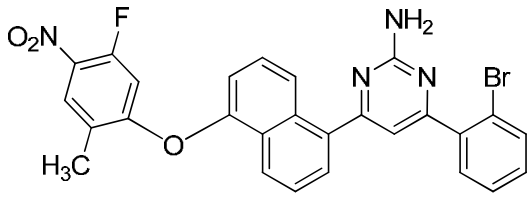
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3350 and 3316 cm^{-1} indicates the N-H stretching. The band at 3121 cm^{-1} indicates the aromatic C-H stretching. Value at 2930 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1610, 1591 and 1565 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 445.3, which indicates the molecular weight of the compound.

Compound C14



4-(2-bromophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.5 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.0 δ ppm. Signal due to carbon of methine groups were found at δ 61.2 ppm. All aromatic carbons give signals at 129.4, 131.6, 140.2, 146.6, 151.9, 153.6, 155.1 and 160.2 δ ppm.

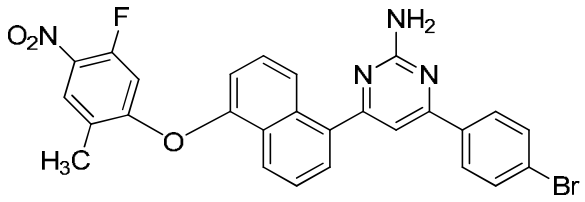
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3360 and 3310 cm^{-1} indicates the N-H stretching. The band at 3123 cm^{-1} indicates the aromatic C-H stretching. Value at 2930 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1610, 1593 and 1560 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 750 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 445.3, which indicates the molecular weight of the compound.

Compound C15



4-(4-bromophenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.4 ppm in downfield region. One vinylic group give singlet at δ 5.6 ppm. All 12 aromatic protons appeared in aromatic region between δ 6.5 to 8.3 ppm. Singlet due to NH_2 proton comes at δ 4.4 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.1 δ ppm. Signal due to carbon of methine groups were found at δ 62.2 ppm. All aromatic carbons give signals at 128.9, 130.3, 131.6, 140.2, 146.6, 151.8, 153.6, 155.1 and 161.2 δ ppm.

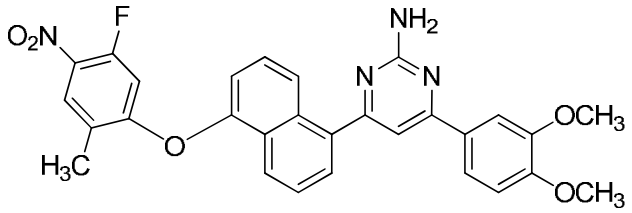
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3340 and 3310 cm^{-1} indicates the N-H stretching. The band at 3105 cm^{-1} indicates the aromatic C-H stretching. Value at 2960 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1610, 1590 and 1550 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 750 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 445.3, which indicates the molecular weight of the compound.

Compound C16



4-(3,4-dimethoxyphenyl)-6-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Singlet due to two –OCH_3 protons appeared at δ 3.5 ppm. One vinylic group give singlet at δ 5.6 ppm. All 11 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH_2 proton comes at δ 4.8 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 31.2 δ ppm. Singlet due to two –OCH_3 protons appeared at 39.0 and 40.1 δ ppm. Signal due to carbon of methine groups were found at δ 61.1 ppm. All aromatic carbons give signals at 127.9, 131.6, 140.2, 146.6, 152.7, 154.7, 157.1 and 160.2 δ ppm.

IR Spectroscopy (KBr)

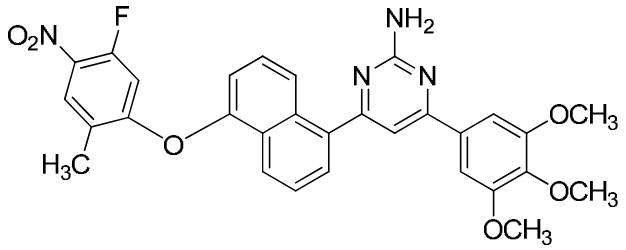
Infrared spectra recorded in KBr reveals that absorption at 3320 and 3315 cm^{-1} indicates the N-H stretching. The band at 3130 cm^{-1} indicates the aromatic C-H stretching. Value at 2970 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1612, 1592 and 1592 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1}

indicates the N=O stretching. Absorption at 741 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 526.5, which indicates the molecular weight of the compound.

Compound C17



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(3,4,5-trimethoxyphenyl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. Singlet due to three –OCH_3 protons appeared at δ 3.4 ppm. One vinylic group give singlet at δ 5.6 ppm. All 10 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH_2 proton comes at δ 4.5 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.0 δ ppm. Singlet due to two –OCH_3 protons appeared at 39.0 and 40.1 δ ppm. Signal due to carbon of methine groups were found at δ 61.1 ppm. All aromatic carbons give signals at 127.9, 131.6, 140.2, 146.6, 152.7, 154.7, 157.1 and 160.2 δ ppm.

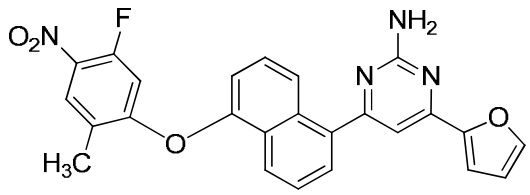
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3410 and 3312 cm^{-1} indicates the N-H stretching. The band at 3130 cm^{-1} indicates the aromatic C-H stretching. Value at 2972 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1612, 1590 and 1565 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 740 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 526.5, which indicates the molecular weight of the compound.

Compound C18



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(furan-2-yl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.8 ppm. All 11 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH_2 proton comes at δ 4.7 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 31.2 δ ppm. Signal due to carbon of methine groups were found at δ 62.1 ppm. All aromatic carbons give signals at 128.9, 131.4, 131.6, 142.2, 146.6, 153.7, 154.7, 157.1 and 161.3 δ ppm.

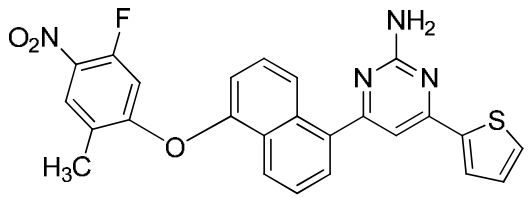
IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3350 and 3315 cm^{-1} indicates the N-H stretching. The band at 3130 cm^{-1} indicates the aromatic C-H stretching. Value at 2929 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1613, 1590 and 1560 cm^{-1} indicates the C=C stretching and band at 1480 cm^{-1} indicates the N=O stretching. Absorption at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 456.4, which indicates the molecular weight of the compound.

Compound C19



4-(5-(5-fluoro-2-methyl-4-nitrophenoxy)naphthalen-1-yl)-6-(thiophen-2-yl)pyrimidin-2-amine

^{1}H NMR Spectroscopy

400 MHz apparatus was used to record ^{1}H NMR spectra. Deuterated chloroform was used as the solvent. Three protons of the CH_3 of the compound gives singlet at δ 2.5 ppm in downfield region. One vinylic group give singlet at δ 5.6 ppm. All 11 aromatic protons appeared in aromatic region between δ 6.5 to 8.4 ppm. Singlet due to NH_2 proton comes at δ 4.3 ppm.

^{13}C NMR Spectroscopy

100 MHz apparatus was used to record ^{13}C NMR spectra. Deuterated chloroform ($CDCl_3$) was used as the solvent. Signal due to carbon of methyl group attached to aryl ring appeared at 32.0 δ ppm. Singlet due to two $–OCH_3$ protons appeared at 39.0 and 40.1 δ ppm. Signal due to carbon of methine groups were found at δ 61.1 ppm. All aromatic carbons give signals at 129.4, 131.4, 131.6, 142.2, 146.6, 152.7, 154.7, 157.1 and 161.2 δ ppm.

IR Spectroscopy (KBr)

Infrared spectra recorded in KBr reveals that absorption at 3350 and 3315 cm^{-1} indicates the N-H stretching. The band at 3130 cm^{-1} indicates the aromatic C-H stretching. Value at 2973 cm^{-1} shows aliphatic C-H stretching of the methyl group. Value at 1612, 1590 and 1565 cm^{-1} indicates the C=C stretching and band at 1480cm^{-1} indicates the N=O stretching. Absorption at 745 cm^{-1} is due to mono and disubstituted benzene ring C-H bending vibrations.

Mass Spectroscopy

In the mass spectrum of the given compound, molecular ion peak was found at M+ 472.4, which indicates the molecular weight of the compound.

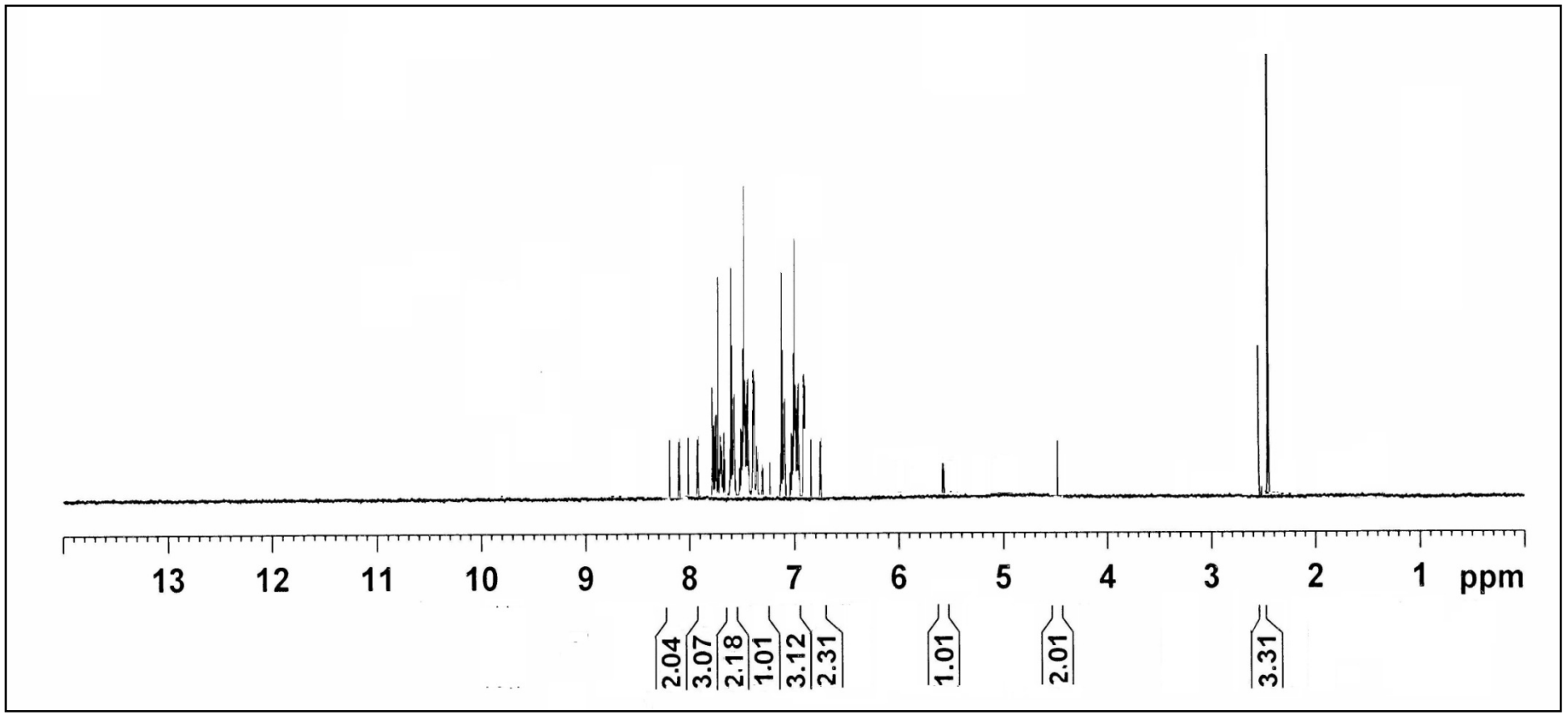


Fig. 5.1: ^{1}H NMR spectrum of C1

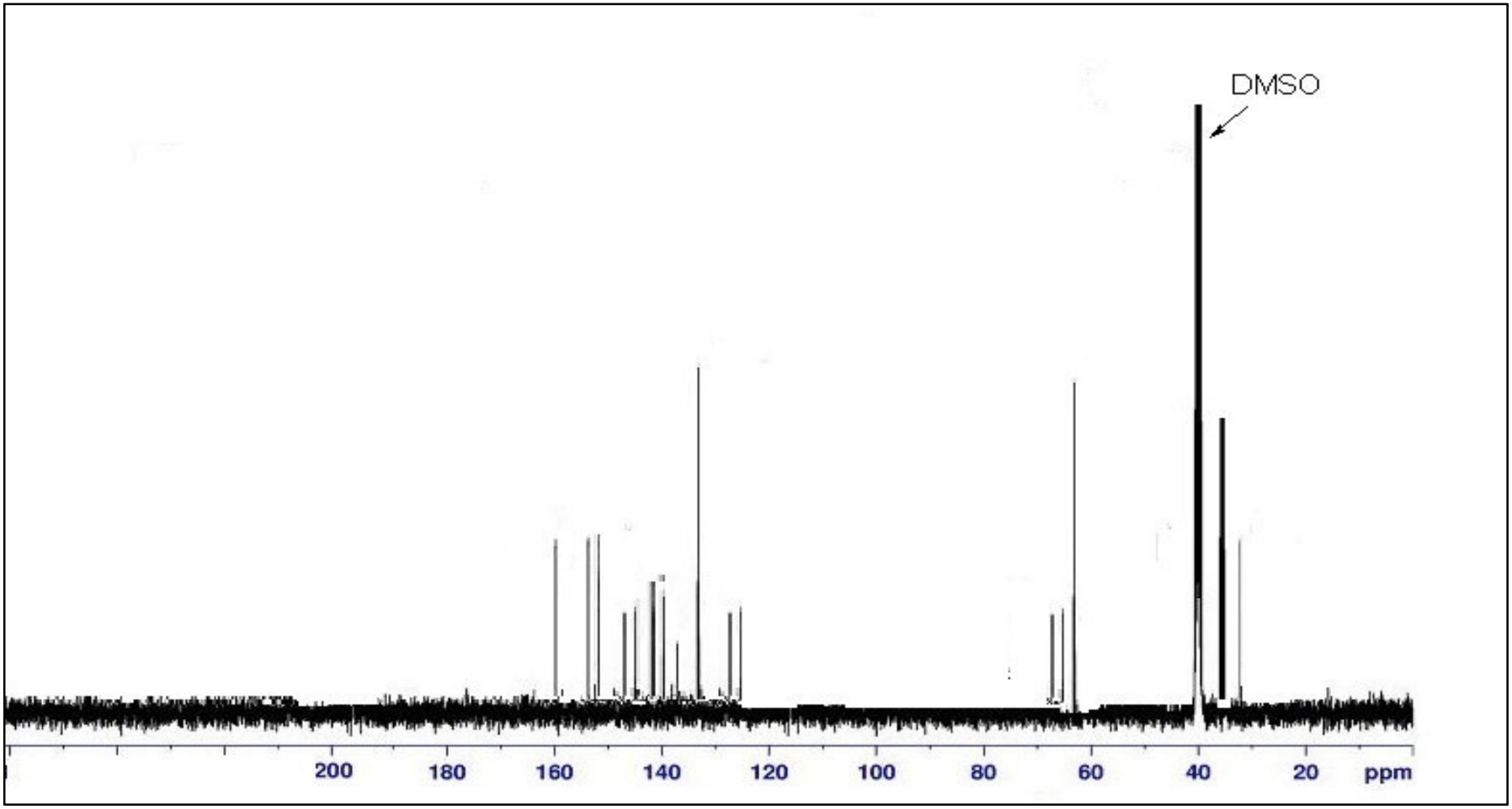


Fig. 5.2: ^{13}C NMR spectrum of C1

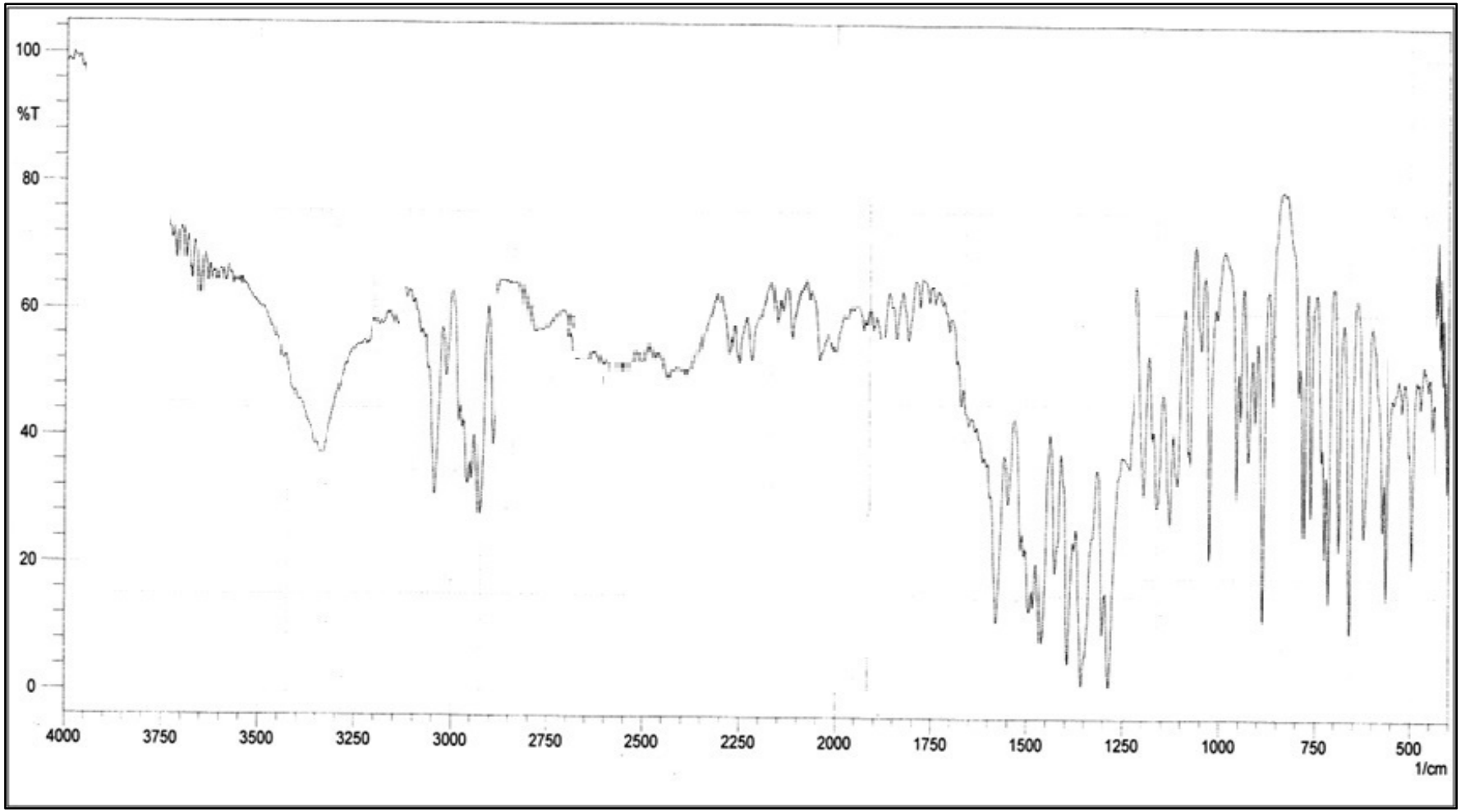


Fig. 5.3: IR spectrum of C1

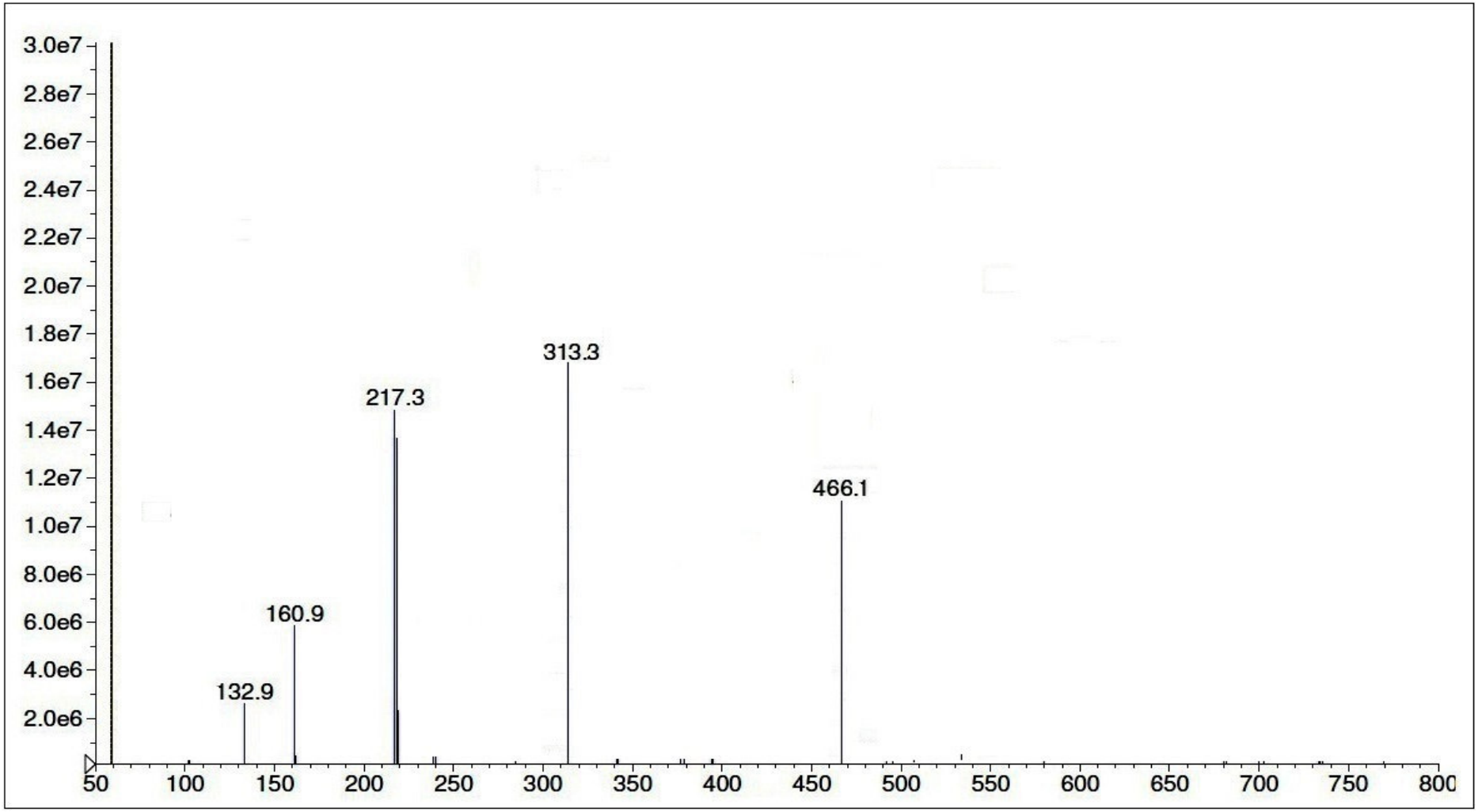


Fig. 5.4: Mass spectrum of C1

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CHAPTER – VI

ANTIMICROBIAL ACTIVITY

CONTENTS

6.1 ANTIMICROBIAL ACTIVITY

Disease in human is majority caused by infection. Skilled running of antimicrobial medicine is of the first significance. The word chemotherapy is utilized for the drug action of freeloading infections in that the parasites (bacteria, viruses, protozoa, worms and fungi) are smashed or eliminate without injuring the host.

Large number of substances that we are known to have therapeutic usefulness were first utilized in the distant past. The Ancient Greeks utilized male fern, and the Aztecs chenopodium, used as intestinal anthelmintics. The Ancient Hindus treated leprosy and chaulmoogra. For 100 years ago moulds have been given to cured wounds, but in spite of the beginning of mercury as a action for syphilis (16th century), and the application of cinchona bark against malaria (17th century), the history of recent rational chemotherapy did not begin until Paul Ehrlich produced the thought from his surveillance that aniline dyes selectively stained bacteria in tissue microscopic synthesis and could selectively kill them. He introduced the word 'chemotherapy' and in 1906 he wrote:

"In order to use chemotherapy successfully, we must search for substances which have an affinity for the cells of the parasites and a power of killing them greater than the damage such substances cause to the organism itsel. This means… we must learn to aim, learn to aim with chemical substances."

The pamaquin, mepacrine and antimalerials were produced from dyes and in 1935 dye (Prontosil) linked sulphonamides was first given as a outcome of systematic analysis by Domagk. The data derived from sulphonamides in meningitis, pneumonia and puerperal sepsis were dramatic and caused a revolution in medical and scientific thought.

In 1928, Fleming fortuitously rediscovered the long-known capability of Penicillium fungi to stifle the escalation of bacterial cultures but put the judgment sideways as a curiosity.

In 1939, mainly as an academic work out, Florey and Chain undertook discovery of antibiotics, i.e. medicine formed by microorganisms which are antagonistic to the escalation or life of other microorganisms. They synthesized penicillin and established its significant lack of poisionicity.

When the synthesis was administered to a policeman by joining streptococcal septicemia and staphylococcal there was spectacular development; unluckily the produce of penicillin (in the local Pathology Laboratory) could not maintain pace with the necessities (it was obtained from the urine of patient and re-injected); it run out and the patient afterward succumbed to infection. Subsequent growth amply confirmed the significant therapeutic capability of penicillin.

6.2 CLASSIFICATION OF ANTIMICROBIAL DRUGS

On the basis of type of organism antimicrobial agents can be divided as follow:

- Anthelmintic drugs.
- Antibacterial drugs
- Antiviral drugs
- Antiprotozoal drugs
- Antifungal drugs

A minute antimicrobials have useful activity across various of these groups. Some examples are metronidazole inhibits necessitate anaerobic bacteria (like Clostridium perfringens) and few protozoa that rely on anarobolic pathways (like Trichomonas vaginalis).

Antimicrobial medicine mainly of two type as follow:

- Bacteriostatic: Drug which can inhibit the bacteria. For example chloramphenicol and sulphonamides, tetracyclines.
- Bactericidal, Drug which can kill the bacteria. For example rifampicin, cephalosporins, penicillins, isoniazide and aminoglycosides.

6.3 CLASSIFICATION OF ORGANISMS

- Staphylococcus aureus is species of schizomycetes class; having Eubacterials order, micrococeaceac family and staphylococcus genus.
- Escherichia coli is species of schizomycetes class; having Eubacterial order, Enterobacteriaceae family and Escherichia genus.

- Bacillus subtillis is species of schizomycetes class; having Eubacterials order, Bacteriodaceac family and fusobacterium streptobacillus and sphaerophorus genus.
- Pseudomonas aeruginosa is species of schizomycetes class; having pseudominodales order, pseudominadaceac family and pseudomonas genus.

6.4 EXPERIMENTAL

The microbial potency of drugs was found by disc plate process. The test discs possessing 50mg per disc of sample compound. The potency was exhibit vst gram +ve bacteria are *Bacillus megaterium* [MTCC (121)] and*Staphylococcus aureus* [MTCC(96)] and gram –ve bacteria and*Proteus vulgaris* [MTCC(1771)], *Escherichia coli* [MTCC(443)].

Preparation of Media:

Bacterial potency nutrient agar is applicable. Nutrient agar is made as below.

1) 5 g Peptone
2) 3 g Meat Extract
3) 5 g Sodium chloride :
4) 15 g Agar Agar

These four compounds are mixed well and made solution 1 liter by distilled water. 15 pound pressure was used in autoclave for stabilization at 125 ^{o} C temperature for 25 min. Then entire medium frozen at 45^{o}C and 20 ml poured sterilized Petri-dish was added. P^{H} of medium keeps 7.0 to 7.5

The civilization of bacteria was made in nutrient and dd water used for dilution. The composition of nutrient broth below:

1) 10 g Beef extract
2) 5 g Sodium chloride
3) 10 g Peptone

This media was utilized for the culture function. The civilization was cooled at 37^{o}C using incubator. Culture was spread on agar plates using swab under particular condition

5 mm diameter paper discs were made and above sterilized using autoclave. These discs were dried out to eliminate the solvent. Sterile test drug coated by discs were reserved in Petri dish possessing culture media.

6.4.1 ANTIMICROBIAL ACTIVITY OF COMPOUNDS B1-B19

Table 6.1 Experimental data of Compounds B1-B19

Samples	*S.aureus* (+Ve)	*B.megaterium* (+Ve)	*E.coli* (-Ve)	*P.vulgaris* (-Ve)
B1	4	9	7	4
B2	5	9	8	8
B3	7	11	6	4
B4	9	10	6	9
B5	7	8	9	12
B6	8	8	4	8
B7	8	9	9	6
B8	10	12	12	9
B9	12	10	11	12
B10	12	10	7	12
B11	5	8	8	12
B12	7	6	10	10
B13	6	8	4	6
B14	3	3	7	7
B15	11	10	6	4
B16	6	9	10	5
B17	6	8	4	10
B18	9	9	6	12
B19	11	11	6	7
Ampicillin	**15**	**14**	**17**	**19**
Gentamycin	**16**	**15**	**14**	**16**

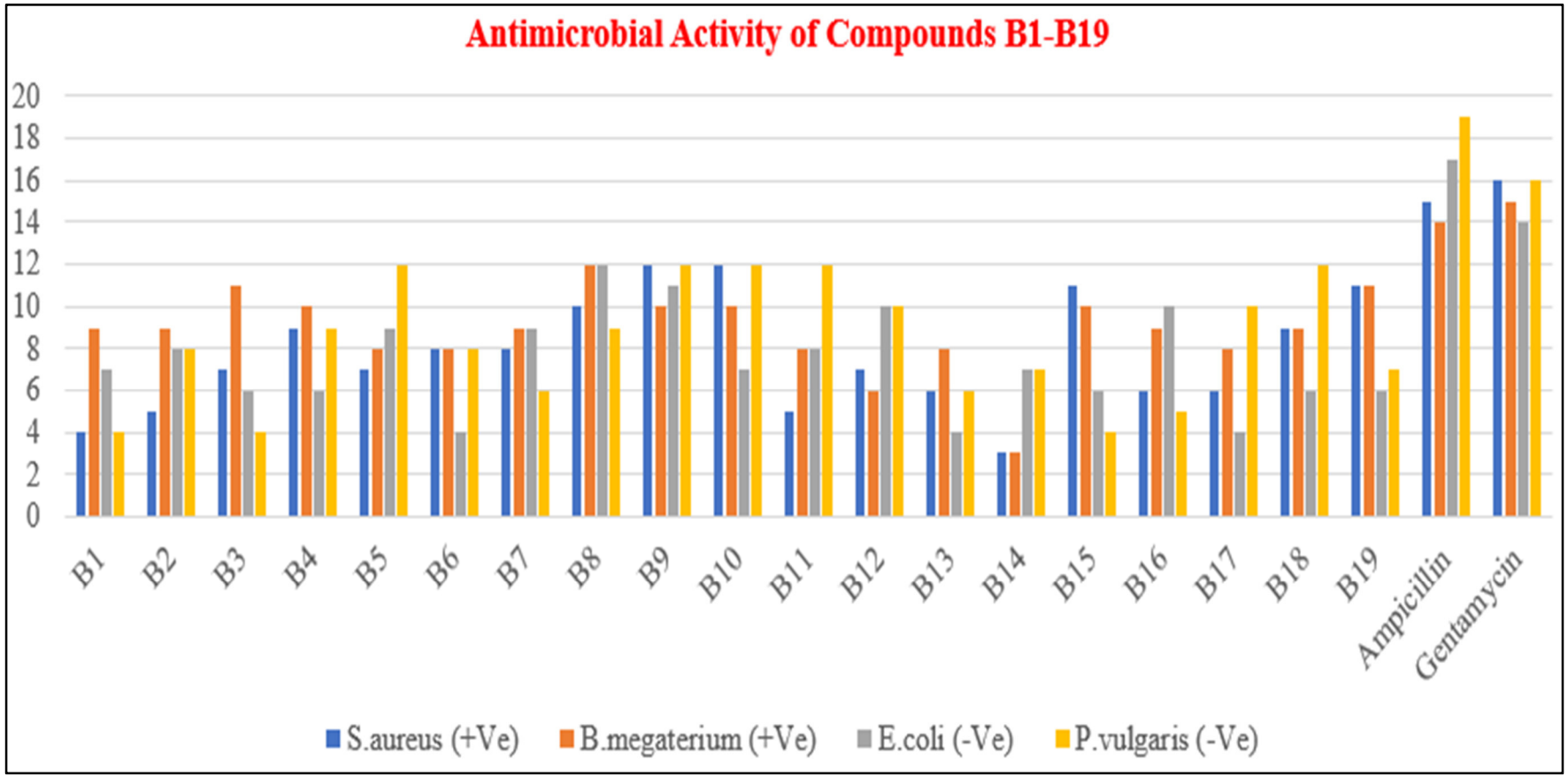


Fig. 6.1: Antimicrobial activity of Compounds B1-B19

A short review of results of antibacterial screening of the compounds is mentioned here:

(I) **Against *Staphylococcus aureus*:**

Maximum activity was found in compounds (B9 and B10) zone of inhibition-12.0 m.m. and minimum activity were found in compounds (B14) zone of inhibition -3.0 m.m

(II) **Against *Bacillus megaterium*:**

Maximum activity were found in compounds (B3, and B19) zone of inhibition -11.0 m.m whereas minimum activity were found in compound (B14) zone of inhibition -3.0 m.m.

(III) **Against *Escherichia coli*:**

Maximum activity were found in compounds (B8) zone of inhibition -12.0 m.m and minimum activity were found in compounds (B6, B13 and B17) zone of inhibition -4.0 m.m

(IV) **Against *Proteus vulgaris*:**

Maximum activity was found in compound (B5, B9-B11 and B18) zone of inhibition -12.0 m.m (near to standard drug) and minimum activity were found in compounds (B1, B3 and B15) zone of inhibition -4.0 m.m

6.4.2 ANTIMICROBIAL ACTIVITY OF CCOMPOUNDS C1-C19

Table 6.2 Experimental data of Compounds C1-C19

Samples	*S.aureus* (+Ve)	*B.megaterium* (+Ve)	*E.coli* (-Ve)	*P.vulgaris* (-Ve)
C1	9	4	5	4
C2	9	9	12	8
C3	7	12	10	10
C4	9	8	8	6
C5	7	6	8	7
C6	8	9	9	6
C7	8	12	12	5
C8	10	12	10	10
C9	12	12	10	12
C10	12	6	4	7
C11	7	7	7	6
C12	6	8	6	8
C13	8	6	3	10
C14	3	6	11	4
C15	10	9	6	7
C16	9	4	6	6
C17	8	9	9	10
C18	9	12	11	4
C19	11	11	4	6
Ampicillin	**15**	**14**	**17**	**19**
Gentamycin	**16**	**15**	**14**	**16**

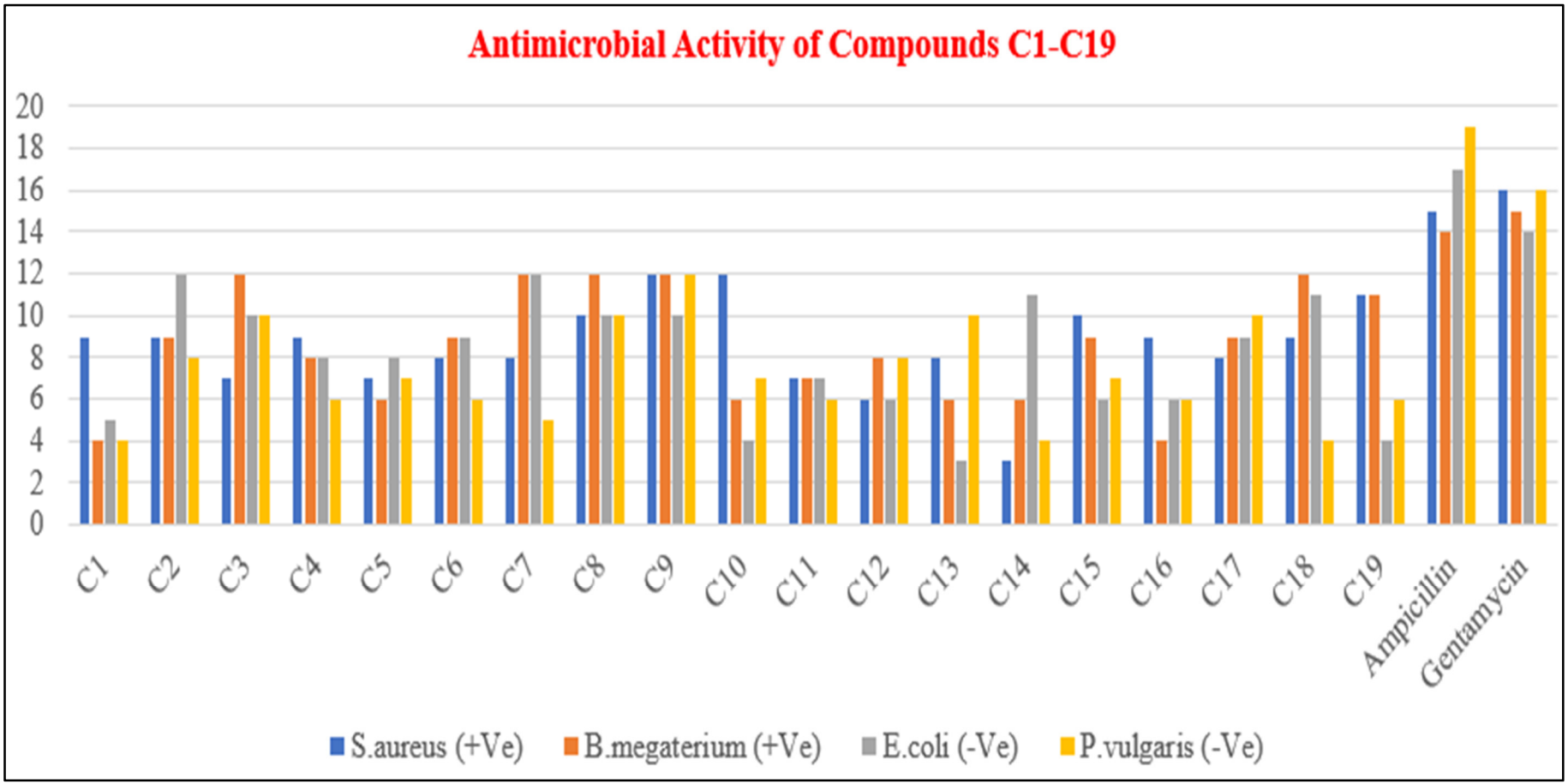


Fig. 6.2: Antimicrobial activity of Compounds C1-C19

A short review of results of antibacterial screening of the compounds is mentioned here:

(I) Against *Staphylococcus aureus*:

Maximum activity were found in compounds (C9 and C10) zone of inhibition -12.0 m.m whereas minimum activity was found in compound (C14) zone of inhibition -3.0 m.m.

(II) **Against *Bacillus megaterium*:**

Maximum activity was found in compound (C3, C7-C10 and C18) zone of inhibition -12.0 m.m (near to standard drug) and minimum activity were found in compounds (C1 and C16) zone of inhibition -4.0 m.m.

(III) **Against *Escherichia coli*:**

Maximum activity was found in compounds (C2 and C7) zone of inhibition-12.0 m.m. and minimum activity was found in compound (C13) zone of inhibition -3.0 m.m.

(IV) **Against *Proteus vulgaris*:**

Maximum activity was found in compound (C9) zone of inhibition -12.0 m.m and minimum activity were found in compounds (C1, C14 and C17) zone of inhibition -4.0 m.m.

❐❐❐

SUMMARY

The work presented in the present thesis deals with the synthesis and characterization of novel chalcones from readily available starting materials and modified prepared products using urea and Guanidine to produce a library of compounds which gives good antimicrobial activities.This thesis incorporate seven chapters dealing with the synthesis of two different pyrimidine moieties. The biological activity of all the synthesized compounds is discussed in chapter VI.

CHAPTER-I: INTRODUCTION

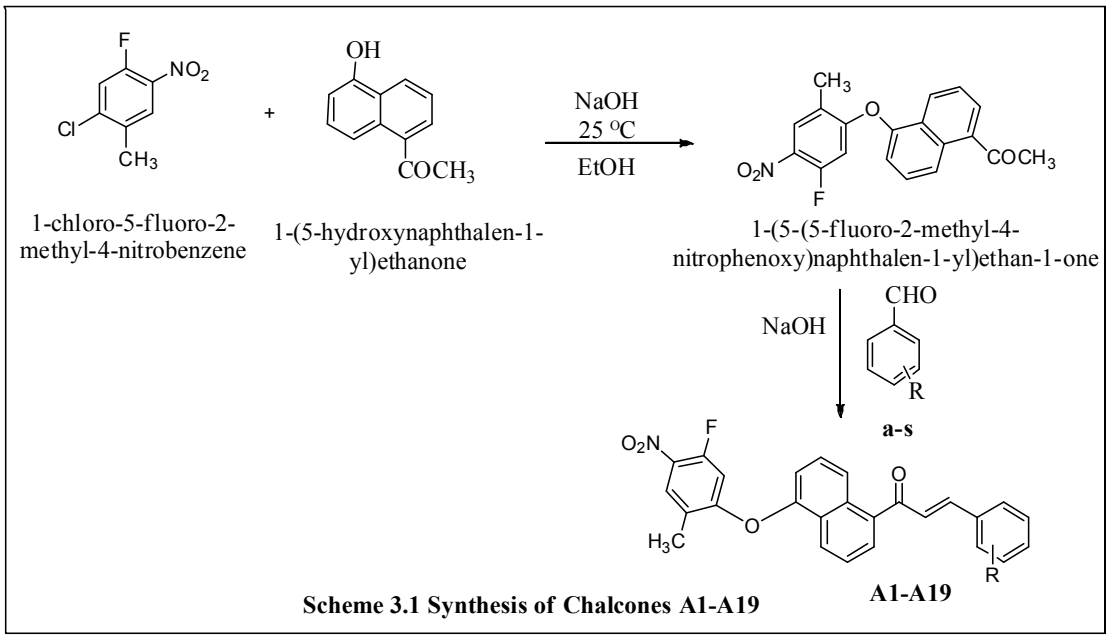
This chapter deals with the general introduction to heterocyclic compounds and its synthesis using different catalyst and energy sources. This chapter also describes aim and objectives of the present work.

CHAPTER-II: LITERATURE REVIEW

This chapter deals with the general introduction and detail literature study of pyrimidine moiety.

CHAPTER-III: SYNTHESIS AND CHARACTERIZATION OF CHALCONES A1-A19.

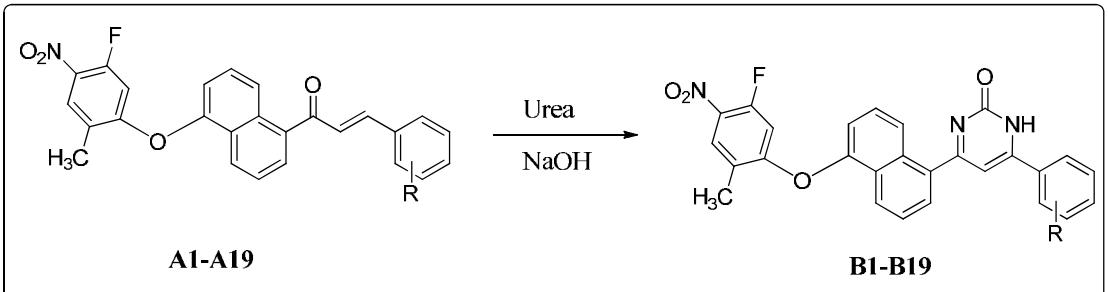
This chapter describe the synthesis of chalcone compounds **A1-A19**. First synthesized 1-(5-(5-fluoro-2methyl-4-nitrophenoxy) naphthalen-1-yl) ethan-1-one by refluxing 1-(5-hydroxynaphthalen-1-yl)ethan-1-one with 1-chloro-5-fluoro-2-methyl-4-nitrobenzene in the presence of sodium hydroxide under ethanol as the solvent. (**Scheme 3.1**). All the synthesized compounds have been characterized by using ^{1}H NMR, ^{13}C NMR, IR and Mass spectroscopy.



Scheme 3.1 Synthesis of Chalcones A1-A19

CHAPTER-IV: SYNTHESIS AND CHARACTERIZATION OF PYRIMIDINES B1-B19.

This chapter describe the synthesis of Pyrimidines **B1-B19**. Chalcones synthesized in chapter-3 were allowed to react with urea in the presence of sodium hydroxide as the base under ethanol as the solvent which gives pyrimidines **B1-B19** (**Scheme 4.1)**. All the synthesized compounds have been characterized by using ^{1}H NMR, ^{13}C NMR, IR and Mass spectroscopy.

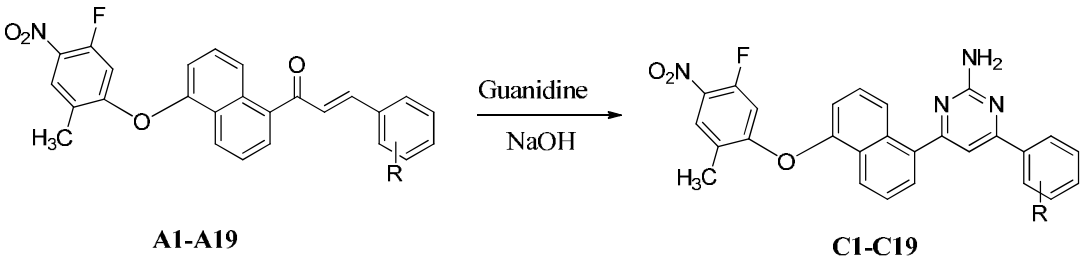


Scheme 4.1 Synthesis of Pyrimidines B1-B19

CHAPTER-V: SYNTHESIS AND CHARACTERIZATION OF PYRIMIDINES C1-C19

This chapter describe the synthesis of novel Pyrimidines **C1-C19**. Chalcones synthesized in chapter-3 were subjected to react with Guanidine in the presence of sodium hydroxide as the base under ethanol as the solvent gives pyrimidines **C1-C19**

(**Scheme 5.1)**. All the synthesized compounds have been characterized by using ^{1}H NMR, ^{13}C NMR, IR and Mass spectroscopy.



Scheme 5.1 Synthesis of Pyrimidines C1-C19

CHAPTER-VI: ANTIMICROBIAL ACTIVITY

This chapter includes antimicrobial activity of pyrimidines synthesized in chapter-IV and chapter-V. The invitro antimicrobial activity of all the synthesized compound were screened against two Gram(+ve) strains, *Staphylococcus aureus* and *Bacillus megaterium* and two Gram (−ve) strains, *Escherichia coli* and *Proteus vulgaris*.

Pyrimidine is a remarkable bioactive moiety due to its diverse biological and pharmacolpgical activities. The present synthesis of thirty eight pyrimidine based compounds have also shown antimicrobial activity. The global health challenge the humanity is facing is cancer. The treatment of cancer is also suffering from serious side effects with multidrug resistance. Pyrimidine is considered as privileged scaffold and therefore present investigation opened new avenues for synthesis of novel pyrimidine based compounds having more potent biological and pharmacological activity to pave the way for better treatment of cancer.

PUBLICATIONS

SYNTHESIS AND BIOLOGICAL ACTIVITY OF AMINOPYRIMIDINE DERIVATIVES

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ABSTRACT

Heterocyclic compounds are useful in medicinal field. Heterocyclic compound with pyrimidine, pyrazole, quinine etc. nucleus is very importance for the biological activity. In presence study, we have synthesized various pyrimidines by reaction between chalcones and Guanidine in the presence of sodium hydroxide as the base. Antimicrobial activity of all the synthesized compounds were perform against gram +ve and gram -ve bacteria. All synthesized compounds were done by 1H NMR, 13C NMR, IR, MASS techniques.

Key Words: Guanidine, Pyrimidine, Aldehydes, Antimicrobial Activity and Spectroscopy.

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SYNTHESIS AND CHARACTERIZATION OF FLUORINE CONTAINING NOVEL CHALCONES

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ABSTRACT

For synthesis of various heterocyclic compounds Chalcones are very important intermediate. It is useful for the synthesis of flavones, flavanols, pyrimidines, pyrazolines, anthocyanins, benzal coumarones as well as certain compounds like deoxybenzoins and hydantoins which are of some medicinal application. In presence study we have synthesized various fluorine based chalcones by reaction between 1-(5-hydroxynaphthalen-1-yl) ethan-1-oneand 1-chloro-5-fluoro-2-methyl-4-nitrobenzene followed by condensation with various aromatic aldehyde. All synthesized compounds were done by ^{1}H NMR, ^{13}C NMR, IR, MASS techniques.

Keywords: ***1-chloro-5-fluoro-2-methyl-4-nitrobenzene, Aldehydes, Chalcone and Spectroscopy***

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SYNTHESIS AND BIOLOGICAAL ACTIVITY OF FLUORINE BASED NOVEL PYRIMIDINES

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ABSTRACT

Synthesis of various heteroatom bearing compounds are very useful as the drugs intermediates. Heterocyclic compound with pyrimidine, pyrazole, quinine etc. nucleus are very essential for the biological activity. In presence paper we have prepared various fluorine based chalcones by reaction between 1-(5-hydroxynaphthalen-1-yl) ethan-1-oneand1-chloro-5-fluoro-2-methyl-4-nitrobenzene followed by condensation with various aromatic aldehyde. This prepared chalcones are used for synthesis of pyrimidines by reaction with urea in the presence of sodium hydroxide as the base. All synthesized compounds were done by ^{1}H NMR, ^{13}C NMR, IR, MASS techniques.

Keywords: ***Fluorine, Pyrimidine, Aldehydes, Antimicrobial Activity and Spectroscopy.***

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