SYNTHESIS AND FLUORESCENCE PROPERTIES OF SELECTED PHENOXY DERIVATIVES OF PYRIMIDINES AND PYRAZINES

SHAH BAKHTIAR NASIR

DEPARTMENT OF CHEMISTRY

FACULTY OF SCIENCE

UNIVERSITY OF MALAYA

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ABSTRACT

2-(2-Methoxyphenoxy)pyrimidine **(37),** 2-(4-methoxyphenoxy)pyrimidine **(39),** 2-phenoxypyrimidine **(41),** 2-(3-methoxyphenoxy)pyrimidine **(43),** 2-(*o*-tolyloxy)pyrimidine **(45),** 2-(pyrimidin-2-yloxy)phenol **(47),** 2-(3-nitrophenoxy)pyrimidine **(49)** and 2-(*p*-tolyloxy)pyrimidine **(51)** were prepared by reacting 2-chloropyrimidine **(35)** with *o*-methoxyphenol, *p*-methoxyphenol, phenol, *m*-methoxyphenol, *o*-cresol, 1,2-dihydroxybenzene, *m*-nitrophenol and *p*-cresol respectively. Reactions of 2-chloropyrimidin-4-amine **(52)** with phenol produced 2-phenoxypyrimidin-4-amine **(53)**, while reactions of 2-chloropyrazine **(54)** with *o*-methoxyphenol and *p*-methoxyphenol yielded 2-(2-methoxyphenoxy)pyrazine **(55)** and 2-(4-methoxyphenoxy)pyrazine **(56)** respectively. The structures of these compounds were confirmed using ^{1}H NMR, ^{13}C NMR, IR and GC-MS spectra. The fluorescence properties were recorded using Luminescence Spectrophotometer. All phenoxypyrimidines and phenoxypyrazines showed fluorescence properties in various solvents. Phenoxypyrimidines showed higher fluorescence intensity than phenoxypyrazines.

ABSTRAK

2-(2-Metoksifenoksi)pirimidina **(37)**, 2-(4-metoksifenoksi)pirimidina **(39)**, 2-fenoksipirimidina **(41)**, 2-(3-metoksifenoksi)pirimidina **(43)**, 2-(*o*-metilfenoksi)pirimidina **(45)**, 2-(2-hidroksifenoksi)pirimidina **(47)**, 2-(3-nitrofenoksi)pirimidina **(49)** dan 2-(*p*-metilfenoksi)pirimidina **(51)** disediakan melalui tindak balas 2-kloropirimidina **(35)** masing-masing dengan *o*-metoksifenol, *p*-metoksifenol, fenol, *m*-metoksifenol, *o*-kresol, 1,2-dihidroksibenzena, *m*-nitrofenol dan *p*-kresol. Tindak balas 2-kloropirimidin-4-amina **(52)** dengan fenol menghasilkan 2-fenoksipirimidin-4-amina **(53)**, manakala tindak balas 2-kloropirazina **(54)** dengan *o*-metoksifenol dan *p*-metoksifenol masing-masing menghasilkan 2-(2-metoksifenol)pirazina **(55)** dan 2-(4-metoksifenoksi)pirazina **(56)**. Struktur semua sebatian ditentukan dengan menggunakan spektroskopi RMN ^{1}H dan ^{13}C, IM dan KG-SJ. Ciri pendafluoran telah direkodkan menggunakan Spektrofotometer Pendaran. Semua terbitan-terbitan fenoksipirimidina dan fenoksipirazina menunjukkan sifat-sifat pendafluoran di dalam pelbagai jenis pelarut organik. Terbitan fenoksipirimidina menunjukkan keamatan pendafluoran yang lebih tinggi daripada terbitan fenoksipirazina.

ACKNOWLEDGEMENTS

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TABLE OF CONTENT

LIST OF FIGURES

LIST OF TABLES

LIST OF SCHEMES

LIST OF SYMBOLS AND ABBREVIATIONS

The following symbols and abbreviations have been used throughout this thesis

$CDCl_3$	Deuterated chloroform
CH_3CN	acetonitrile
d	doublet
dd	doublet of doublets
Eq	equivalent
EA	ethyl acetate
EtOH	ethanol
IR	infrared
J	coupling constant
M	mole per litre
m	multiplet
m.p.	melting point
min	minute
MW	molecular weight
NMR	nuclear magnetic resonance
s	singlet
t	triplet
THF	tetrahydrofuran
λ	wavelength
υ	stretching vibration
δ	chemical shift
AR	analytical grade
GC-MS	gas chromatography-mass spectrometry

CHAPTER 1: INTRODUCTION

1.1 Diazines

Heterocyclic compounds are organic compounds containing at least one atom of carbon and at least one element other than carbon such as sulphur, oxygen or nitrogen within a ring structure. The stem '-cyclic' implies a ring structure, whereas 'hetero' refers to an atom other than carbon. Many heterocyclic compounds are carcinogenic. Among the heterocyclic compounds, there are aromatic (e.g. pyridine) and nonaromatic (e.g. tetrahydrofuran).[1]

Heterocyclic compounds can be divided into heteroaromatic and heteroalicyclic types. The chemistry of the heteroalicyclic compounds in general is similar to that of their aliphatic analogous, but that heteroaromatic compounds involve additional principles. Aromatic compounds possess rings in which each of the rings atoms is in the same plane and a *p*-orbital perpendicular to the ring plane.[2]

This research was focused on six-membered ring compounds with two heteroatoms, i.e pyrimidine and pyrazine or also known as diazine. Pyrimidines and pyrazines are stable, colourless compound which are soluble in water. The two parent heterocycles, unlike pyridine are expensive and not readily available and so are seldom used as starting materials for the synthesis of their derivatives.[3]

In diazines, the heteroatoms withdraw electron density from the ring carbons even more than in pyridine, so the unsubsituted diazines are even more resistant to electrophilic substitution than pyridine. This increased electron deficiency at carbon atom makes the diazines more easily attacked by nucleophiles than pyridines. The availability of nitrogen lone pair is also reduced: each of the diazines is appreciably less

basic than pyridine, reflecting the destabilizing influence of the second nitrogen on the *N*-protocation.

Nevertheless, diazines form salts and react with alkyl halides and with peracids to give *N*-alkyl quaternary salts and *N*-oxides, respectively. In general, electrophilic additions take place at one nitrogen only, because the presence of the positive charge renders the second nitrogen extremely unreactive towards a second electrophilic addition. A very characteristic feature of diazine chemistry is associated with their strongly electron-poor nature, therefore they add nucleophilic reagents easily. Without halide to be displaced, such adducts require an oxidation to complete an overall substituton. However, halo-diazines where the halide is α or γ to a nitrogen, undergo very easy nucleophilic displacements, the intermediates being particularly well stabilized.[3] Figure 1.1 shows the typical reactions of diazine illustrated with pyrimidine.

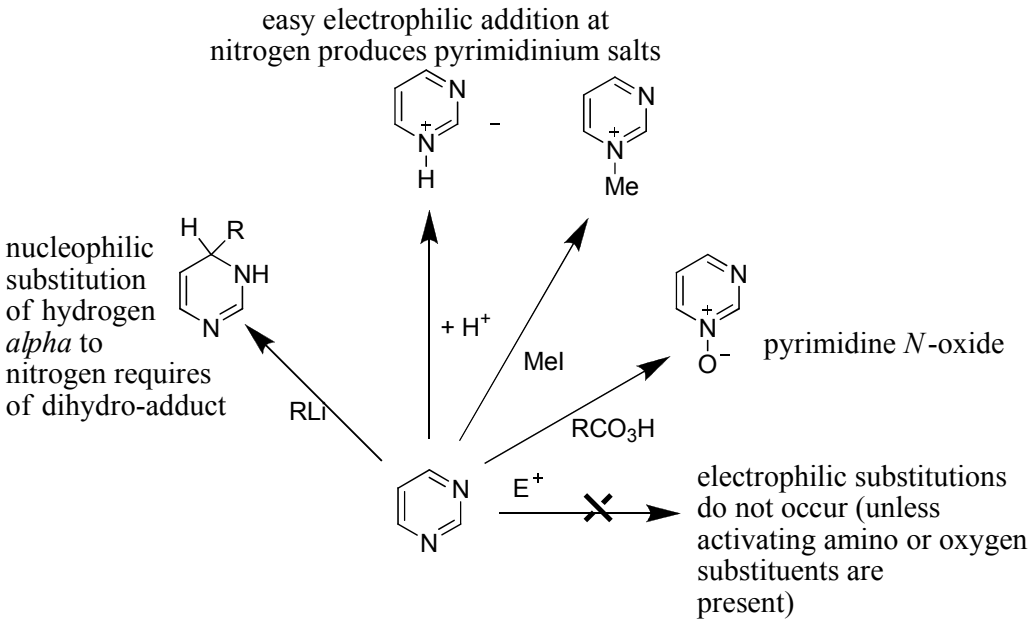


Figure 1.1: Typical reactions of diazine illustrated by pyrimidine

The nucleophilic displacement of halogen and other leaving group by 'soft' nucleophiles i.e amines, thiols, alkoxides and enolates is a very important method for manipulation of diazines. Only 5-halopyrimidines, in analogy to 3-halopyridines, are relatively resistant. Figure 1.2 shows the order of reactivity in nucleophilic displacements of leaving groups[3].

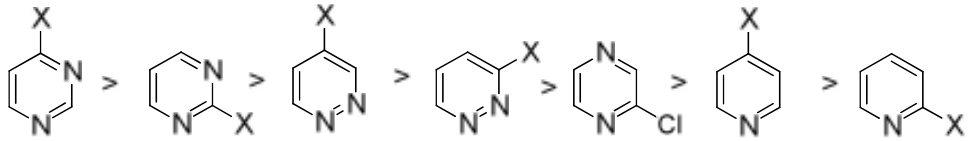
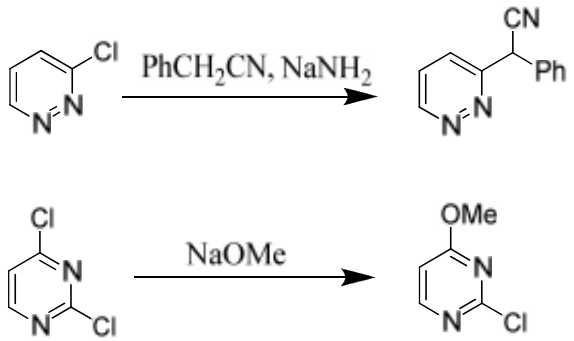
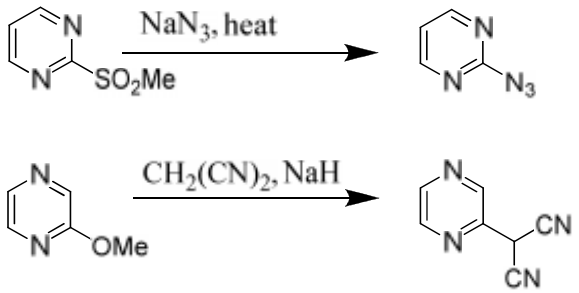


Figure 1.2: The order of reactivity in nucleophilic displacements of leaving groups

Chlorine is the most common leaving group but sulfonates are also useful and even methoxy can be displaced in these highly reactive systems as shown in Scheme 1.1 and Scheme 1.2.

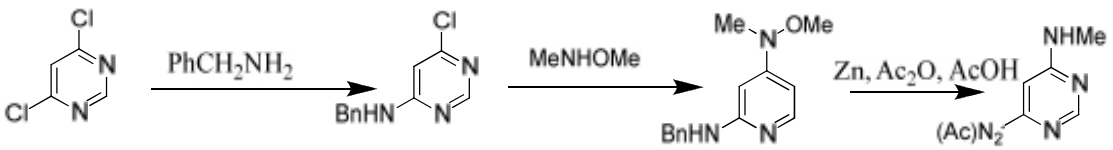


Scheme 1.1: Typical nucleophilic displacement of chlorine



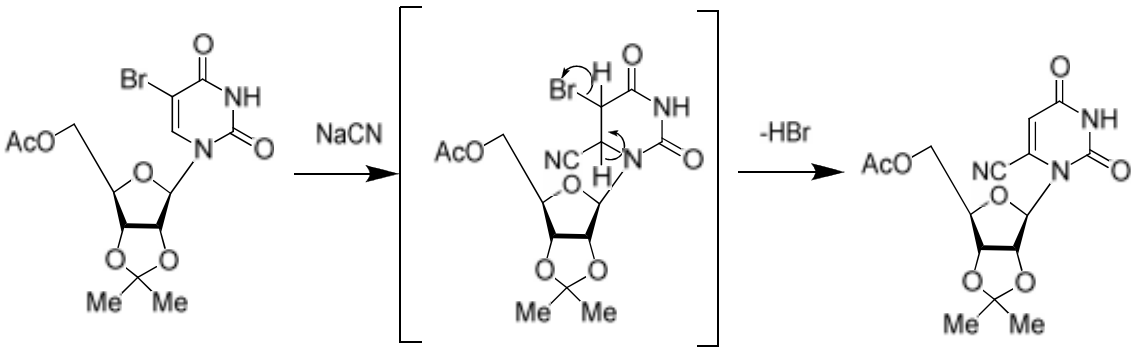
Scheme 1.2: Sulfone and methoxy act as good leaving groups

An important point to remember is that the presence on the ring of an electron-donating group, particularly an amino group, will greatly increase or decrease the reactivity of a halide. Although this means that clean mono-substitution in dihalo compounds is easy, special methods may be necessary to achieve displacement of the second halide, such as the use of 'supernucleophiles'. Hydroxylamines are very reactive nucleophiles and, since the N-O bond in the products can be hydrogenolysed, nucleophilic substitution with a hydroxylamine provides a means for the introduction of a second amine. Scheme 1.3 shows the use of a hydroxylamine as a 'supernucleophile' to displace a relatively unreactive chlorine.[5]



Scheme 1.3: The use of a hydroxylamine as a 'supernucleophile' to displace a relatively unreactive chlorine

The oxydiazine can also undergo nucleophilic addition or displacement of halide. Uracil[5] and its riboside (uridine)[5] are particularly prone to Michael-type addition to the double bond leading to *cine*-substitution rather than the usual *ipso*-substitution, for example from 5-bromouridine to the 6-cyanouridine shown in Scheme 1.4.



Scheme 1.4: *Cine*-substitution of a 5-bromouridine derivative

1.2. Pyrimidine

(1)

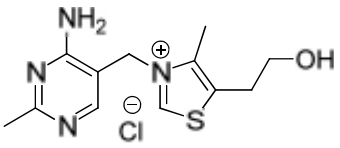
Pyrimidine is the most important member of all diazines as this ring system occurs widely in living organisms. Pyrimidine **(1)**, also known as *m*-diazine. Purines, uric acid and barbituric acid also contain pyrimidine ring. The chemistry has been widely studied. [8-11] Pyrimidine was first isolated by Gabriel and Colman in 1899. Since pyrimidine is symmetrical about the line passing C-2 and C-5, the position C-4 and C-6 are equivalent and so are N-1 and N-3.[12]

In early history of organic chemistry, compounds belonging to this group were known as breakdown products of uric acid, but the systematic study of the ring system really began with the work of Pinner[13], who first applied the name pyrimidine to the unsubstituted parent body.

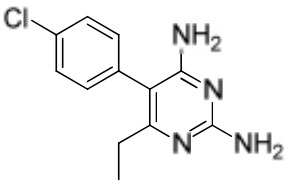
Pyrimidine is a colorless compound, melts at 22.5 °C and boils at 124 °C. It is weakly basic (pKa 1.3) as compared to pyridine (pKa 5.2) or imidazole (pKa 7.2). The decrease in its basicity is due to the electron-withdrawing effect of the second nitrogen atom present in the ring. Moreover, the addition of the proton does not increase the probability for mesomerism and hence the resonance energy. The presence of alkyl groups, however, enhances the basicity, thus 4-methylpyrimidine has pKa 2.0 while 4, 6-dimethylpyrimidine has a value of 2.8. The 2- and 4-aminopyrimidines are more basic with pKa 3.54 and 5.71 repectively. In these two compounds, more resonance structure are possible in the cation than in the neutral molecule. The close relationship of

pyrimidine with benzene suggests the former is also highly aromatic and the ring is virtually planar.

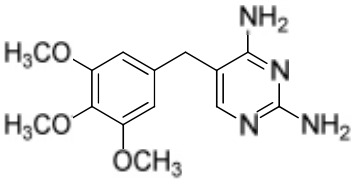
Pyrimidine-containing molecules are paramount importance in nucleic acid chemistry. Their derivatives including uracil, thymine, cytosine, adenine and guanine are fundamental building blocks for deoxyribonucleic acid (DNA) and ribonucleic acid (RNA). Vitamin B1 (thiamine) **(2)** is another well-known example of naturally occuring pyrimidines encountered in our daily lives. Synthetic pyrimidine-containing compounds occupy a prominent place in the pharmaceutical arena. Pyrimethamine **(3)** and Trimethoprim **(4)** are two representative pyrimidine-containing chemotherapeutics. Compound **(3)** is a dihydrofolate reductase inhibitor which is effective for toxoplasmosis in combination with a sulphonamide whereas compound **(4)** is an anti-malarial drug, widely used as a general systemic anti-bacterial agent in combination with sulfamethoxazole.[14-15]



(2)



(3)



(4)

Due to the electronegativity of the two nitrogen atoms, pyrimidine is a deactivated, π-electron-deficient heterocycle. Its chemical behaviour is comparable to that of 1,3-dinitrobenzene or 3-nitropyridine. One or more electron-donating substituents on the pyrimidine ring are required for electrophilic substitution to occur. In contrast, nucleophilic displacement takes place on pyrimidine more readily than pyridine. The trend also translates to palladium chemistry; whereby 4-chloropyrimidine

oxidatively adds to Pd (0) more readily than does 2-chloropyridine. Remarkable differences in reactivity for each position on pyrimidinyl halides and triflates have been observed. The C-4 and C-6 positions of a halopyrimidine are more prone to S_NAr process than the C-2 position. The order of S_NAr displacement for halopyrimidines is as shown is Figure 1.3.[14]

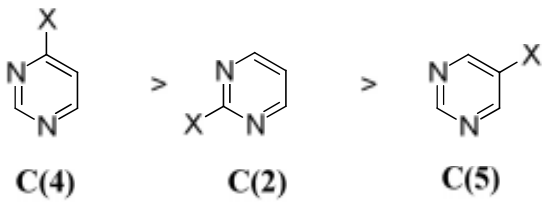


Figure 1.3: The order of S_NAr displacement for halopyrimidines

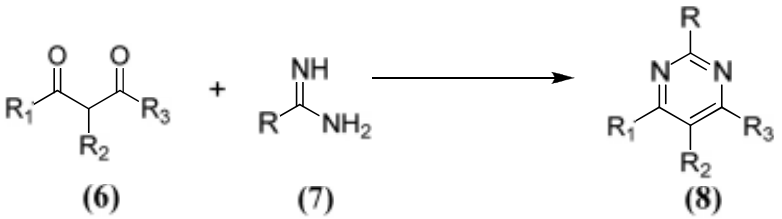
This trend is also observed in palladium chemistry where the general order for oxidative addition often correlates with that of nucleophilic substitution. Not only are 2-, 4- and 6- chloropyrimidines viable substrates for Pd-catalyzed reactions, but 4- and 6-chloropyrimidines react more readily than 2-chloropyrimidines.[14]

Undheim and Benneche reviewed the Pd-catalyzed reactions of pyrimidines, among other π-deficient azaheterocycles including pyridines, quinolines and pyrazines. A review by Kalinin also contains some early examples in which C-C formation on the pyrimidine ring is accomplished using Pd-catalyzed reaction.[14]

1.2.1 Ring synthesis of pyrimidines

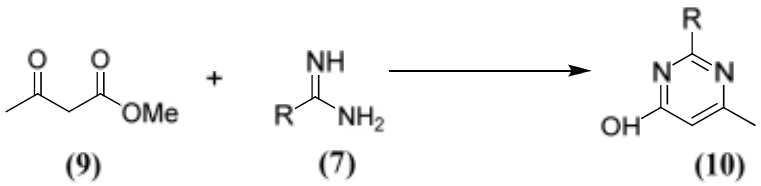
1.2.1.1 Pinner Pyrimidine Synthesis

The condensation of 1,3-dicarbonyl compounds **(6)** with amidines **(7)** catalyzed by acids or bases to give pyrimidine derivatives **(8)** is generated as the Pinner[13] pyrimidines synthesis as shown in Scheme 1.5



Scheme 1.5: Pinner pyrimidine synthesis

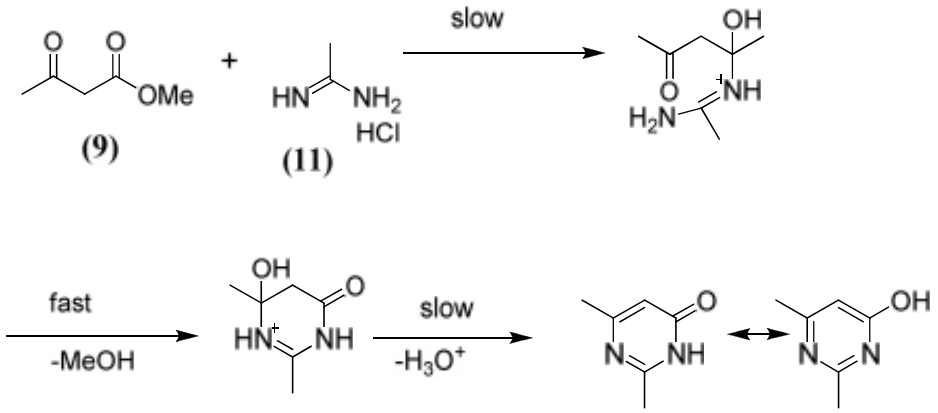
In the 1880's, Pinner found that the amidine derivatives **(7)** reacted with acetoacetic ester **(9)** to furnish 2-substituted-6-hydroxy-4-methylpyrimidine **(10)**[16]. The condensation of amidine derivative **(7)** with other β-keto ester, malonic ester, and β-diketones proceed similarly. Scheme 1.6 shows the synthesis of 2-substituted-6-hydroxy-4-methylpyrimidine.



Scheme 1.6: Synthesis of 2-substituted-6-hydroxy-4-methylpyrimidine

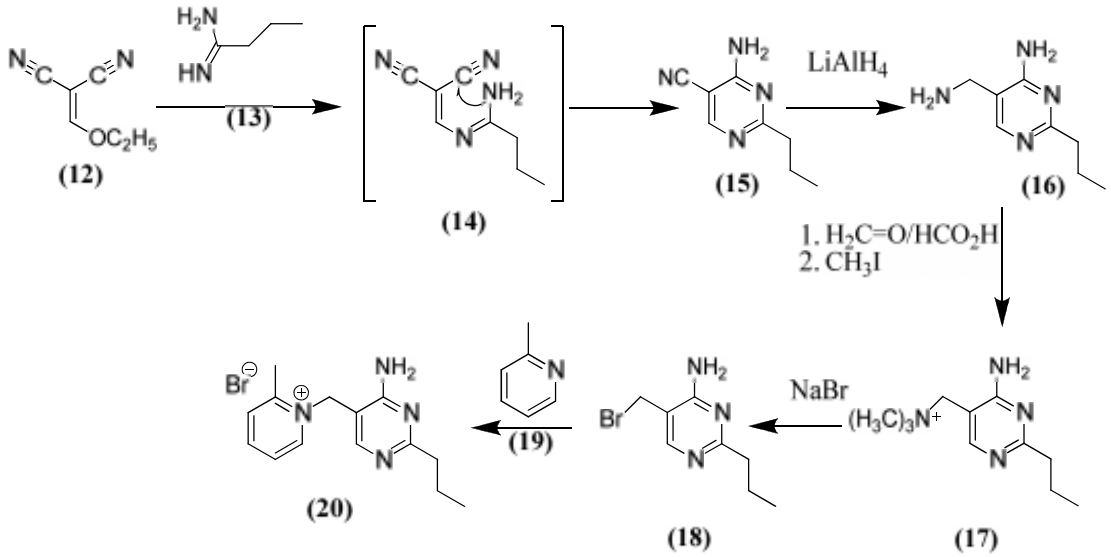
Although the Pinner pyrimidine synthesis was disovered a century ago, a few reports on the reaction mechanism have appeared. The condensation of acetylacetone,

methyl acetoacetate, or dimethyl malonate with acetamide **(11)** has been studied by Kartrizky *et-al.* The reaction mechanism for these processes has been proposed by these authors. Scheme 1.7 shows the proposed mechanism of the condensation of methyl acetate **(9)** with acetamide **(11**[16]**)**.



Scheme 1.7: Proposed mechanism of the condensation of methyl acetate (9) with acetamide (11).

Other than that, a compound that includes an aminopyrimidine ring as well as the quaternary salt present in thiamine shows preferential inhibition of absorption of that co-factor by coccidia parasites over uptake by vertebrates. The compound is thus used in poultry where coccidiosis is an economically important disease. Condensation of ehtoxymethylenemalonitrile **(12)** with the amidine **(13)** aminopyrimidine **(14)**. The reaction was probably occurred via addition-elimination intermediate **(15)**. The nitrile group is then reduced to the methylamino derivative **(16)** by means of lithium aluminium hydride. Exhaustive methylation, for example by reaction with formaldehyde and formic acid, followed by methyl iodide leads to the quaternary methiodide **(17)**. The quaternary salt is then displaced by bromine to form benzylic-like cyclic halide, **(18)** which was then displaced by 2-picoline **(19)**. Finally, amprolium **(20)**[17] was obtained. Scheme 1.8 shows the mechanism of formation of **(20).**



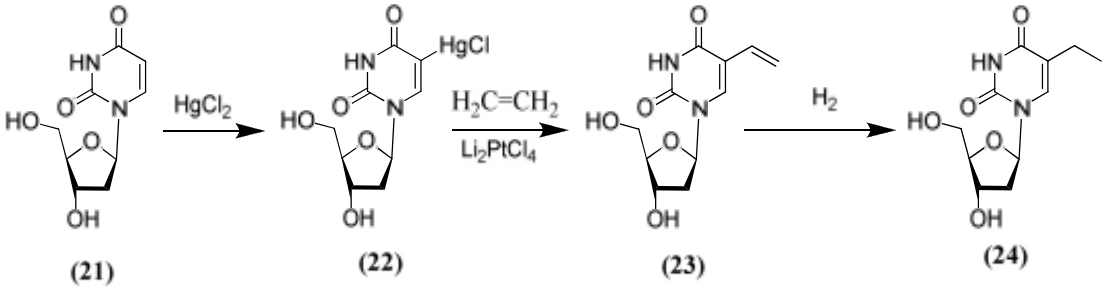
Scheme 1.8: Formation of amprolium (20)

1.2.1.2 Antiviral pyrimidines

Viruses differ from bacteria and fungi in most fundamental way in that they are not able to reproduce independently. A virion in essence consists of a chain of DNA or RNA in the case of a retrovirus, packaged with a small group of specialized proteins. The virus actually replicates by taking over the infected cells' reproductive apparatus, in effect causing the cell to synthesize new virions. Chemotherapy of viral disease must thus rely on very subtle biochemical differences between normal and infected cells instead of the large divergences in biochemistry between microbial and host cells that provide the basis of antibiotics. The somewhat lesser discriminatory power of the enzymes in viral cells for the nucleotides involved in replication has made it possible to identify a number of closely related false substrates.

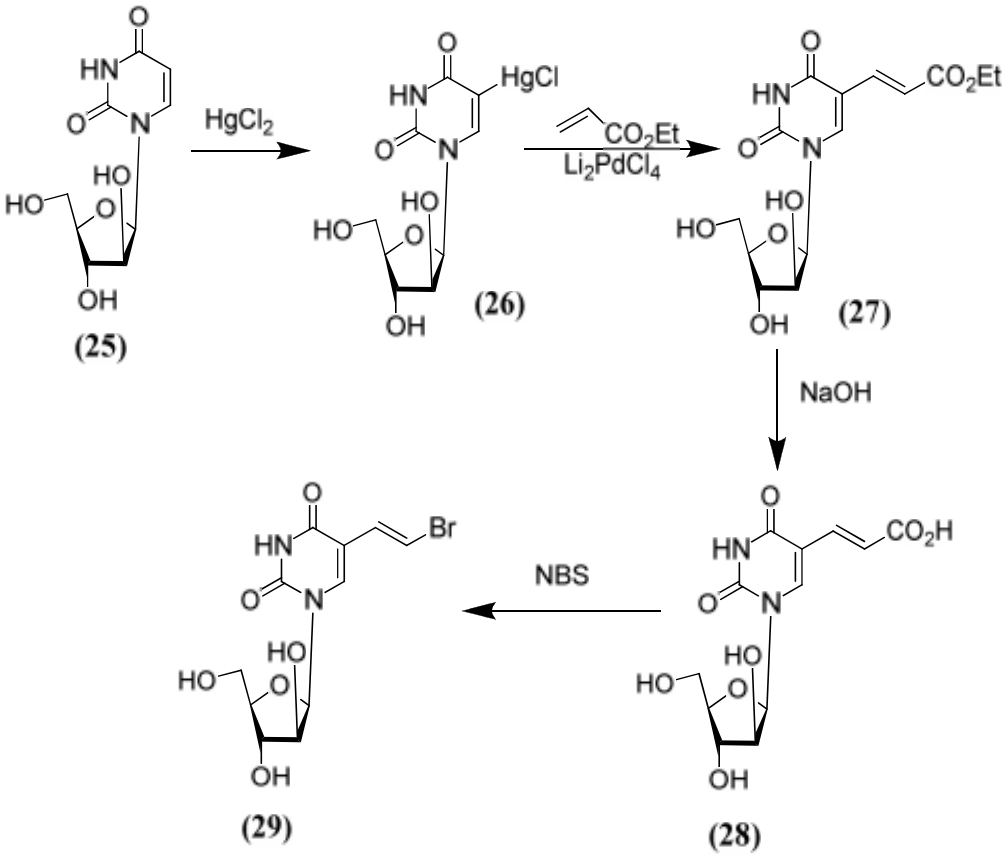
The nucleotide, uridine **(21)** provides the starting material for one of these agents. Treatment of **(21)** with mercuric chloride leads to the mercuration of the

pyrimidine ring to afford **(22)**. Reaction of this organometallic derivative wih ethylene in the presence of a platinum salt leads to the formation alkylated product **(23)**. Catalytic hydrogenation of the double bond then affords the antiviral compound edoxudine **(24)**[17]. Scheme 1.9 shows the mechanism of formation of edoxudine **(24)**



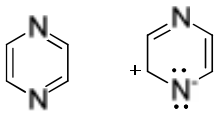
Scheme 1.9: Formation of edoxudine (24)

Similar chemistry is used to prepare the antiviral agent sorivudine **(29)**; this compound is also endowed with an unnatural sugar in the arabinose configuration. The side chain is attached as above by chloromercuration of uracyl arabinoside **(25)**. Reaction of the organometallic **(26)** with ethyl acrylate leads to the coupling product **(27)**. The ester group is then saponified to the corresponding acid **(28)**. Treating the acid with *N*-bromosuccinimide leads to a Borodin-like replacement of the carboxyl group by bromine. The resulting reactive allylic halogen in the product, sorivudine **(29)**[18], may play a role in the compound's activity against herpes virus. Scheme 1.10 shows the formation of soruvidine **(29).**



Scheme 1.10: Formation of soruvidine (29)

1.3 Pyrazine



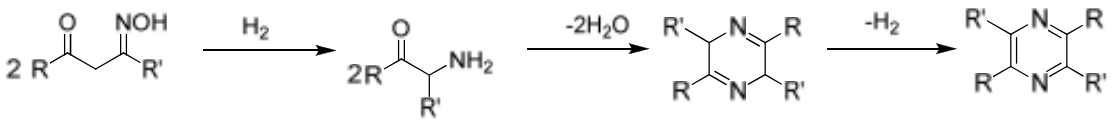
(30) **(31)**

The pyrazines **(30)** are aromatic compounds as well as tertiary amines, and their properties are closely resemble to those of pyridines. The pyrazines nucleus may be considered as a resonance hybrid of which two of the contributing forms are analogous to those of benzene. The C-N bond distances in pyridine and pyrazine, however, are slightly greater because of the high electronegativity of the nitrogen atom which probably leads to significant additional contributions to the resonance by structure **(31)**.

The electronegativity of the two nitrogen atoms would be expected to have a definite influence on both the basic and the aromatic properties of pyrazines.

Pyrazine is a low-melting solid and most of the lower homologs are liquids at room temperature. The pyrazines in general possess a narcotic odor, sublime readily and may be distilled with steam. Like many other amines, the pyrazines from hydrates and on removal of the water of often results. The lower members of the series are very soluble in water, and several are miscible in all proportions.

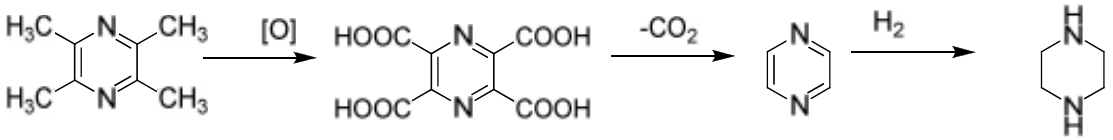
The preparation of 'amarone' in 1844 by Laurrent is the first recorded synthesis of a pyrazine. Laurent's method was obscure, however, and it was more than fifty years later that "amarone" was identified as tetraphenylpyrazine.[19] Meanwhile the systematic study of this series of compounds was initiated by Victor Meyer's students, Gutknecht and Treadwell, who found that the reduction of nitrosated ketones resulted in the formation of oxygen-free bases instead of the expected α-amino ketones as shown in Scheme 1.11.[20]



Scheme 1.11: Reduction of nitrosated ketones

The correct structure for the ring system of the product was first advanced by Wleugel[21], and the synthesis of pyrazine derivative by another method appeared to confirm this structure and established the correct positions of the substituents. Finally, in 1893 Wolff's conversion of tetramethylpyrazine to piperazine by the series of

reactions indicated in Scheme 1.12 provided unequivocal proof of the structure of pyrazines.[22]



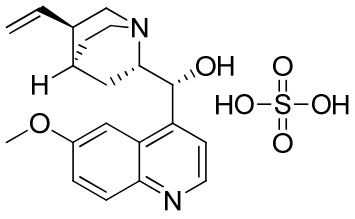
Scheme 1.12: Wolff's conversion of tetramethylpyrazine to piperazine

CHAPTER 2: FLUORESCENCE SPECTROSCOPY

2.1 Introduction

Fluorescence spectroscopy is a spectroscopic technique whereby fluorescent substances are being examined. Fluorescence spectral data are generally presented as emission spectra. A fluorescence emission spectrum is a plot of the fluorescence intensity versus wavelength (nanometers) or wavenumbers (cm^{-1}). There are two types of fluorescence sampling measurement which are in solid or solution.[23] In this study all samples were measured in solution. In solution, at normal temperatures, fluorescence occurs at a longer wavelength. It has a number of advantages over other forms of microscopy that offer high sensitivity and specificity. Because fluorescence is observed as luminosity on a dark background, particular constituents of the specimen can be seen even in extremely small amounts.[24]

The first observation of fluorescence is from a quinine solution in sunlight was reported by Sir John Frederick William Herschel in 1845.[25] He recognized the presence of an unusual phenomenon that could not be explained by the scientific knowledge of the time. The first known fluorophore, quinine was responsible for stimulating the development of the first spectrophotometers that appeared in 1950s. Nowadays quinine sulphate **(33)** and fluorescein **(34)** are widely used as references for the fluorescence.



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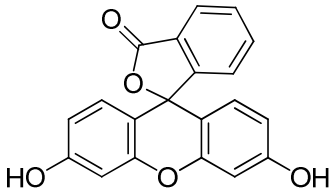

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The research was then reinvestigated by Stokes, who published a famous paper entitled 'On the Refrangibility of Light' in 1852.[26] The fluorescence normally observed in solution is called Stokes fluorescence. If thermal energy is added to an excited state or a compound has many highly populated vibrational energy levels, emission at shorter wavelengths than those of absorption can occurs.

2.2 Interaction of light with a molecule

When a molecule is placed in an oscillating electromagnetic field (light is shone on the molecule), the oscillating fields can push and pull the molecule around. In particular, charged parts of the molecule are affected by the oscillating electric field of light; the effect of the oscillating field is much weaker. If the charges on the molecule can oscillate in synchrony with the oscillating field (this is called resonance), the molecule can absorb energy from the field.

Molecules have specific resonance frequencies. For example, a typical C-H bond in a molecule vibrates about 10^{14} times per second (10^{14} Hz), while a C-C bond vibrates at about 3 x 10^{13} Hz. Electrons are over 1000 times lighter than nuclei and oscillate at even higher frequencies. A typical frequency of light absorbed by valence electrons is 10^{15} Hz, which is 30 times faster than the C-C bond vibration. Light with this frequency corresponds to the near-UV region of the spectrum. More generally, the range of wavelengths absorbed by valence electrons varies from about 1000 nm i.e near IR through the visible and UV down to about 100 nm i.e far UV.

Absorption of electromagnetic radiation and excitation of electrons take more or less instantaneously (~10^{-18} s) relative to nuclear motion (~10^{-15} s), according to the

Franck-Condon Principle. Despite this difference in times scales, excitation of electrons in a molecule can also cause a change in molecular structure. The absorbed energy leads to a redistribution of the electron cloud of the molecule, resulting in altered vibrational levels, an altered dipole moment and a change in the shape of the molecule. Quite simply, the bonds are not the same after an electron has been removed and more into a different orbital. Consequently, the electronic absorption is often accompanied by vibrational motion as the atoms move to their new positions[23-25].

Excited states of molecules are unstable. They relax (lose their energy) by a number of mechanisms including collisions with other molecules, for example, the solvent, or react with other species for example dissolved oxygen. The excited molecule may also relax by emitting a photon of light to return to a lower state, though not always the same lower state from which it came. The emitted photon was an energy corresponding to the difference in energy between the initial and final states of the molecule. This emission of a photon is known as fluorescence or some cases phosphorescence[23-25].

2.3 Jablonski diagram

Jablonski diagram is originally showing that the fluorescent state of a molecular entity is the lowest excited state from which the transition to the ground state is allowed, whereas the phosphorescent state is a metastable state below the fluorescent state, which is reached by a radiationless transition. In the most typical cases the fluorescent state is the lowest singlet excited state and the phosphorescent state the lowest triplet state, the ground state being a singlet. Presently, modified Jablonski diagrams are frequently used and are actually state diagrams in which molecular electronic states, represented by

horizontial lines displaced vertically to indicate relative energies, are grouped according to multiplicity into horizontially displaced columns. Excitation and relaxation processes that interconvert states are indicated in the diagrams by arrows. Radiative transition are generally indicated with wavy arrows.[27]

Therefore, on the Perrin-Jablonski diagram, the absorption transition is shown as starting in the ground state. There is no such restriction on the excited state; therefore absorption may occur to a variety of vibrational states in the excited electronic states. The typical amount of vibrational excitation, as discussed above, depends on the change in the geometry of the molecule between the two different electronic states. Small changes in geometry are accompanied by small vibrational excitation (arrow 1) whereas large changes in geometry are accompanied by large vibrational excitation (arrow 2) as show in Figure 2.1.

Essentially, to be absorbed, the energy of the incident radiation must exactly match one of the available energy-level transitions. Given the many possible combinations of electronic and vibrational energy levels for a polyatomic molecule, a range of light energies may be absorbed. The energy of the light is proportional to its frequency (thus inversely related to its wavelength), so a given molecule will absorb a specific set of wavelengths of light, giving rise to its absorption spectrum.

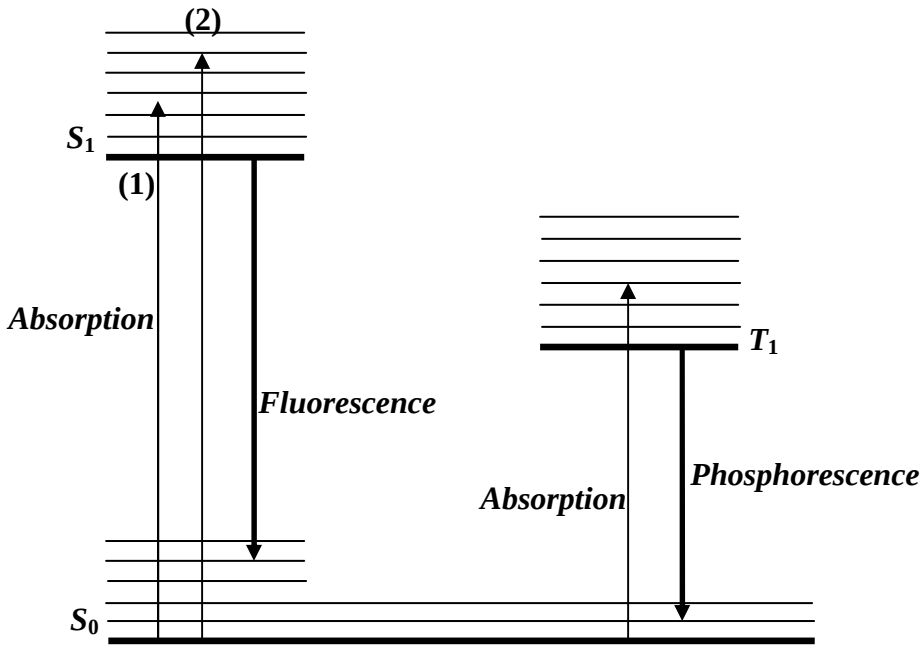


Figure 2.1: Simple Perrin-Jablonski diagram showing three electronic states, several vibrational states, absorption and emission of fluorescence or phosphorescence

The Perrin-Jablonski diagram in Figure 2.1 shows absorption to both S_1 and T_1. In reality, the transition from S_0 to T_1 is weaker than S_0 to S_1. Absorption into triplets states, as shown in the Figure 2.1 is therefore practically unimportant in most cases and is only observed in specialized situations in spectroscopy. The population of triplet states is one of the main mechanisms for photobleaching. It is simple and fortuitous, but triplets are not populated to any great extent by absorption of light by molecules commonly used in fluorescence spectroscopy and microscopy.

Emission of light is shown on a Perrin-Jablonski diagram as an arrow from the excited state back to the ground state. Emission that does not change electron spin, just like absorption, is much preferred over emission in which the electron spin is flipped. This spin-conserving emission is called fluorescence. Since the process is favourable, it happens readily and quickly, as a result the excited electronic states survive for only a very short period of time, typically a few nanoseconds before emitting. Emission

between triplet and singlet states is called phosphorescence. This emission is weak and therefore involves a slow process. As the result the molecule remains excited much longer, typically milliseconds to seconds. The process is slow compared to molecular events. It give rise to an unusual chemistry in the excited state leading to the reduction in fluorescence efficiency, photobleaching and other processes.

2.4 Instrumentation

A schematic representation of a fluorimeter is shown in Figure 2.2. The light source produces light photons over a broad energy spectrum, typically ranging from 220 to 900 nm. Photons impinge on the excitation monochromator, which selectively transmits light passes through adjustable slits that control magnitude and resolution by further limiting the range of transmitted light. The filtered light passes through the sample cell causing fluorescent emission by fluorophores within the sample. Emitted light enters the emission monochromator, which is positioned at 90° angle from the excitation light path to eliminate background signal and minimize noise due to stray light. Again, emitted light is transmitted in a narrow range centered about the specified emission wavelength and exits through adjustable slits, finally entering the photomultiplier tube (PMT). The signal is amplified and creates a voltage that is proportional to the measured emitted intensity. Noise in the counting process arises primarily in the PMT. Therefore, the spectral resolution and the signal-to-noise ratio is directly related to the selected slit widths. Since the source intensity may vary over time, most research-grade fluorimeters are equipped with an additional ‘reference PMT’ which measures a fraction of the source output just before it enters the excitation monochromator, and used to ratio the signal from the sample PMT.

Not all fluorimeters are configured as described above. Some instruments employ sets of fixed band pass filters rather than variable monochromators. Each filter can transmit only a select range of wavelengths. Units are usually limited to 5 to 8 filter and are therefore less flexible. Fiber optics are also employed for “surface readers”, to transmit light from the excitation monochromators to the sample surface and then transport emitted light to the emission monochromators. This setup has the advantage of speed, but has the signal to noise ratio is increased, due to the inline geometry, and smaller path length which increase the probability of quenching.

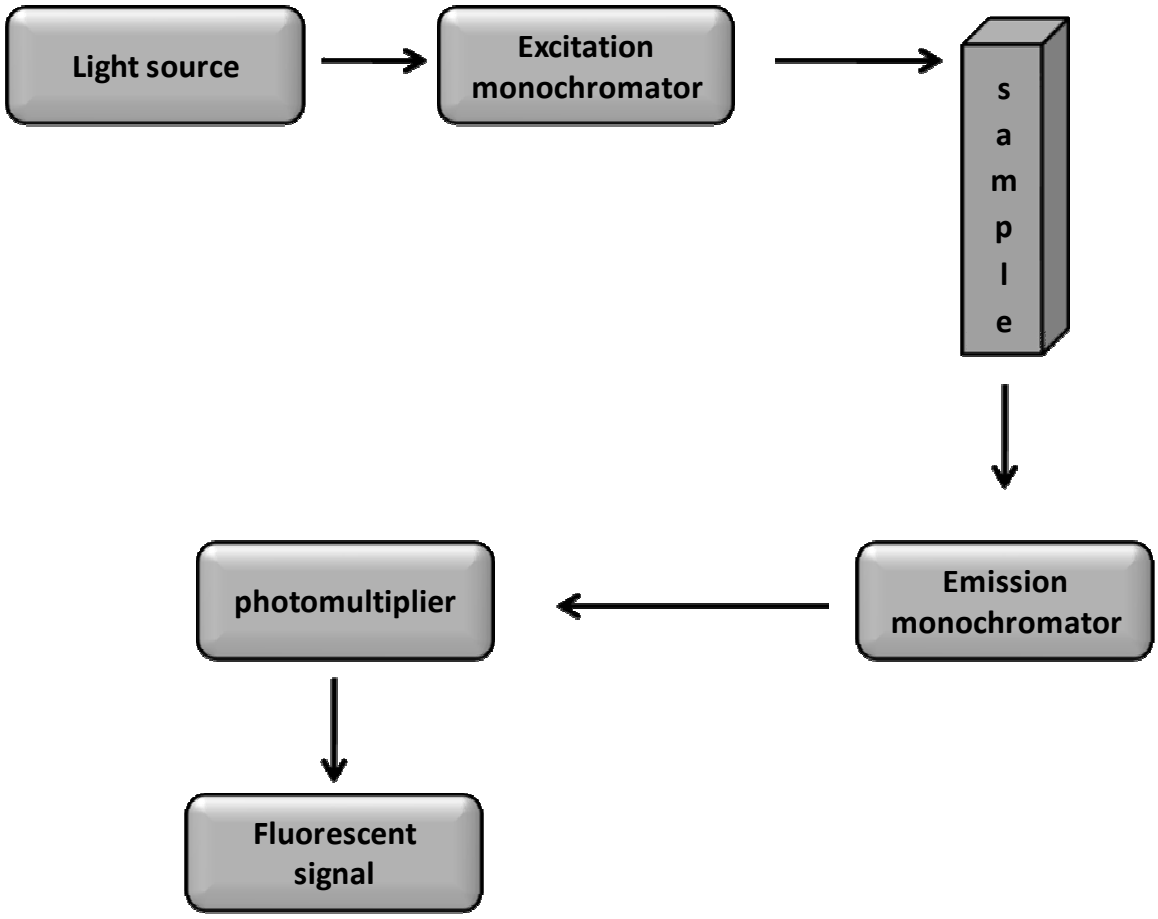


Figure 2.2: Schematic representation of a fluorescence spectrophotometer.

Fluorescent methods have two significant advantages over absorption spectroscopy. First, two wavelengths are used in fluorimetry, but only one in absorption spectroscopy. Emitted light from each fluorescent color can be easily separated because each color has a unique and narrow excitation spectra. This selectivity can be further

enhanced by narrowing the slit width of the emission monochromator so that only emitted light within a narrow spectral range is measured. Multiple fluorescent colours within a single sample can be quantified by sequential measurement of emitted intensity using a set of excitation and emission wavelength pairs specific for each color. The second advantage is that fluorescent methods have a greater range of linearity. Because of these differences, the sensitivity of fluorescence is approximately 1,000 times greater than absorption spectrophotometric methods.[28]

2.4.1 Perkin Elmer LS-50B

In this study all fluorescence data were measured with a Perkin Elmer LS-50B Luminescence Spectrometer. To obtain accurate data, it is necessary to understand several key aspects of fluorescence spectrophotometry and how these pertain to the use of the LS-50B spectrometer.

All fluorescence instruments contain three basic elements: a source of light, a sample holder, and a detector. To be of analytical utility, a system must be equipped with adjustable monochromators that can accurately select excitation and emission wavelengths. It is also essential to monitor and correct any fluctuations in the source intensity. The Perkin Elmer LS-50B Luminescence Spectrometer measure the fluorescence intensity of samples in either a continuous scan over a range of wavelength or at select excitation and emission wavelength pairs. Sections 2.4.1.1 to 2.4.1.6 explain the fluorescence instrument basic elements.

2.4.1.1 Preparation of sample

Before any analytical experiment is carried out, the compounds must be pure. Since fluorescence technique is a very sensitive technique, it is extremely susceptible to interference by contamination of trace level of organic chemicals. Thus, the solvents used are at highest level of purity and commercially obtained.

2.4.1.2 The Xenon source

In this study the source that has been employed is a pulsed Xenon flash lamp. It produces a high output using a low voltage, 9.9 watts, resulting in longer lamp life with minimal ozone and heat production. Equally important, the pulsed source reduces potential photobleaching of the pyrimidines and pyrazines sample, during analysis, by several orders of magnitude over continuous sources. Xenon flash lamp produces a 10 μsec pulse of radiation in 16 msec. In fluorescence mode, the photomultiplier tube detector is gated for an 80 msec period in synchronization with the lifetime of the lamp pulse.

2.4.1.3 Photomultiplier tube

A photomultiplier dark current is acquired prior to the onset of each lamp pulse and is substracted from pulse for correction of phototube dark current. The instrument measures and corrects every flash of the lamps to improve sensitivity at low levels of fluorescence[25], making it possible to measure samples at room light.

2.4.1.4 Determining fluorescence ratios

The intensity of emitted light depends on a number of factors, including intensity of incident exciting light i.e the more powerful the exciting light, the stronger the emitted fluorescence intensity. All light sources currently used in the fluorescence instrumentation normally lack of stability over long periods. This causes the output of a xenon lamp to fluctuate at a function of time, in which affects the measured fluorescence intensity of a given sample with all other conditions being equal. In order to perform accurate quantitative analyses, these fluctuations must be monitored and corrected to the measured fluorescence intensity. The LS-50B can automatically make this correction by determining the ratio of real-time lamp intensity over sample intensity. The lamp intensity is then monitored continuously with a beam splitter to divert a portion of the exciting light to a reference photomultiplier tube.

2.4.1.5 Signals processing

When operated in wavelength programming mode, the instrument automatically sets the excitation and emission wavelength for each sample and dwell time for the specified integration time. The instrument then averages the appropriate number of lamp pulse cycles for the specified integration time. Longer integration time reduces the signal-to-noise ratio for the sample fluorescence intensity. When calculating the optimal sample integration, there are 60 lamp pulses per sec and the noise in a sample measurement is reduced by the square-root of the number of lamp pulse used. Due to this, relationship between noise reduction and pulse number, there is a point of diminishing return for long integration times. An integration time exceeding 2 sec is only necessary when small fluorescence intensities are being measured.

2.4.1.6 Slit setting

An important feature of the LS-50B is the availability of continuous variable slit adjustment with 0.1 nm increments on both the excitation and emission monochrometers. The flexibility allows the user to 'fine–tune' the instrument for both selectivity and sensitivity in dye discrimination and measurement. The slits can best be described as volume controls for the fluorescence intensity. For optimal instrumental performance, the excitation slit width automatically controls the sample photomultiplier tube voltage. This provides an optimum signal-to-noise ratio as a function of sample intensity.

In general, a wider slit setting causes higher fluorescence signal measurements. However, because of the fluorescence ratio system used in the LS-50B, widening of the excitation slit width will not increase the reported fluorescent signal ratio, but will increase sample fluorescence signal, resulting in an improved signal-to-noise ratio.

2.5 Environmental effects

2.5.1 Solvent polarity

Emission from fluorophores generally occurs at wavelengths that are longer than those at which absorption occurs. This loss of energy is due to a variety of dynamic processes that occur following the light absorption. The fluorophore is typically excited to the first singlet state (S_1) usually to an excited vibrational level within S_1. The excess vibrational energy is rapidly lost to the solvent. If the fluorophore is excited to the second singlet state (S_2), it rapidly decays to the S_1 state in 10^{-12} sec due to internal conversion. Solvent effects shift the emission to lower energy due to the stabilization of

the excited state by the polar solvent molecules. Typically, the fluorophore has a larger dipole moment in the excited state than in the ground state. Following the excitation the solvent dipoles can re-orient or relax around which lowers the energy of the excited state. As the solvent polarity is increased, this effect becomes larger, resulting in the emission at lower energies or longer wavelengths. In general, only fluorophores that are themselves polar display a large sensitivity to solvent polarity. Nonpolar molecules, such as unsubstituted aromatic hydrocarbons are much less sensitive to solvent polarity.

Fluorescence lifetime (1-10 nsec) is usually much longer than the time required for solvent relaxation. For fluid solvents at room temperature, solvent relaxation occurs in 10-100 psec. For this reason, the emission spectra of fluorophores are representative of the solvent relaxed state. Absorption of light occurs in about 10^{-15} sec, a time too short of motion for fluorophore or solvent. Absorption spectra are less sensitive to solvent polarity because the molecule is exposed to the relaxed environment, which contain solvent molecules oriented around the dipole moment of the excited state.

The theory for solvent effect is often inadequate to explain the detailed behaviour of fluorophores in a variety of environment. This is because fluoropores often display multiple interactions with their local environment, which can shift the spectra by certain wavelength comparable to general solvent effects.

In addition to specific solvent-fluorophore interactions, many fluorophores can form an ‘Internal Charge Transfer’ (ICT) state, or a ‘Twisted Internal Charge Transfer’ (TICT) state. For instance, suppose the fluorophore contains both an electron-donating and an electron-accepting group. Such group could be amino and carbonyl groups, respectively, but numerous other groups are known. Following the excitation, there can be an increase in charge separation within the fluorophore. If the solvent is polar, then a

species with charge separation (the ICT state) may become the lowest energy state. In a non-polar solvent the species without charge separation, so-called 'Locally Excited' (LE) state, may have the lowest energy. Hence, the role of solvent polarity is not only affect the energy of the excited state due to general solvent effects, but also to govern which state has the lowest energy. In some cases, formation of the ICT state requires rotation of groups on the fluorophore to form the TICT state. Formation of the ICT states is not contained within the theory of general solvent effects. Additionally, a fluorophore may display a large spectral shift due to excimer or exciplex formation. The fluorophore may be fluorescent or nonfluorescent in these different states. The quantum yield can change due to change in the rate of non-radioactive decay or due to a conformational change in the fluorophore.

In summary, no single theory can be used for a quantitative interpretation of the effects of environment on fluorescence. Interpretation of these effects relies not only on polarity consideration, but also on the structure of the fluorophore and the types of chemical interactions it can undergo with other nearby molecules. The trends observed for solvent polarity follow the theory for general solvent effects, which may give the impression that the solvent polarity is the only factor to consider. In reality, multiple factors affect the emission of any given fluorophore.[25]

2.5.2 Oxygen

The intensity of fluorescence can be decreased by a wide variety of processes. Such decreases in intensity are called quenching. Quenching can occur by different mechanisms. Collisional quenching occurs when the excited-state fluorophore

is deactivated upon contact with some other molecule in solution, which is called the quencher. The molecules are not chemically altered in the process.

A wide variety of molecules can act as collisional quenchers. Examples include oxygen, halogens, amines and electron-deficient molecules like acrylamide. In this dissertation the focus is on the effect of the presence of oxygen in the fluorescence sample. The mechanism of quenching varies with the fluorophore-quencher pair. For instance, quenching of indole by acrylamide is probably due to the electron transfer from indole to acrylamide, which does not occur in the ground state. Quenching by halogen[29-30] and heavy atoms[31-33] occur due to spin-orbital coupling and intersystem crossing to the triplet state.

Aside from collisional quenching, fluorescence quenching can occur by a variety of other processes. Fluorophores can form nonfluorescent complexes with the quenchers. This process is referred to as static quenching[34] since it occurs in the ground state and[25].

2.5.3 pH

The addition of Bronsted acids or bases to the solvents in which absorbing, fluorescing or phosphorescing molecules are studied can affect the electronic spectra in two ways. If the acidity of the medium after the addition of acid or base is insufficient to protonate lone or non-bonded electron pairs or to abstract a proton from a dissociable group, the acid or base may form hydrogen bonds with the basic or acidic groups of the molecule of spectroscopic interest. The effects of these types of hydrogen bonding upon

the electronic spectra are similar to those described for hydrogen bond donor and acceptor solvents.

In some cases, aromatic molecules having non-bonded electron pairs fail to fluoresce in a non-hydrogen-bonding solvent because the lowest excited singlet state is of the *n*, π* types and favors radiationless intersystem crossing as a mode of deactivation of the lowest excited singlet state. The addition of small amount of acid results in the formation of hydrogen bonding with the non-bonded pairs often raising the energy of the *n*, π* state to such a degree that the lowest π, π* states become the lowest excited singlet state, making fluorescence likely. In this regard, several nitrogen heterocyclics, such as quinoline and acridine and some aromatic carbonyl compounds such as 2-acetonaphthone and pyrene-3-aldehyde do not fluoresce but phosphoresce. This addition of small amounts of acids such as trifluoroacetic acid or trichloroacetic acid, which are fairly soluble in hydrocarbons, results in appearance and decrease in the intensity of phosphorescence from these molecules.

If the acidity of the medium is sufficient to protonate functional groups having lone or non-bonded electron pairs, or to abstract a proton from acidic functional groups, the effects on the electronic spectra are more dramatic but qualitatively similar to the effects produced by hydrogen bonding. Protonation of a basic molecule, or dissociation of an acidic molecule, produce a chemical species whose reactivity and electronic structure are different from that of the original molecule. However, protonation is similar to the interaction with a hydrogen-bond donor solvent in that a positive polarizing influence is affected at the protonated functional group, while dissociation is similar to interaction with a hydrogen-bond acceptor solvent in that the removal of a

positively charged proton is equivalent to a negative polarizing influence at the dissociated group.

Following the lines of reasoning developed for hydrogen-bonding effects on electronic spectra, some generalization can be made. Protonation of non-bonded pairs on functional groups in the excited state enhances the acceptor properties of these groups and results in stabilization of the excited states relative to the ground state. Protonation of these types of functional groups therefore produces shifting of the intramolecular, electronic, charge-transfer spectra to longer wavelengths. However, the *n*, π* states giving rise to *n*, π* transitions (which are usually seen only in the absorption spectra) of these molecules are raised in energy to such an extent by protonation that they disappear completely from the absorption spectra. Protonation of lone pairs on functional groups that are charge-transfer donors in the excited states (e.g $–NH_2$) inhibits the donor properties of these groups and results in shifting of the electronic spectra to shorter wavelengths[8].

2.6 The chemical structure and the fluorescence

The nature of substituents (especially chromophoric ones) plays an important role in the nature and extent of a molecule's fluorescence. Substituent effects on the chemical and physical properties of organic molecules in their ground electronic states constitute a lively area of investigation at present. Furthermore, only little is known about the influence of substituents on the behaviour of the excited states. Both effects must be understood before generalizations concerning the effect of various substituent groups can be made.

A simple generalization is that *ortho-para*-directing substituents often enhance fluorescence, whereas *meta*-directing group repress it as shown in Table 2.1. Many of the common *meta*-directing substituents, possess low-lying (n, π^*) singlets. The $-NO_2$ group is especially notorious for repressing fluorescence. Carbonyl substituents (ketone, aldehyde, ester, carboxylic acid), which are *meta*-directing, repress fluorescence because carbonyl-substituted aromatic possess low-lying (n, π^*) singlets.[35]

The –CN substituent is *meta*-directing, yet cyno-substituted aromatics often fluoresce more intensely than the parent hydrocarbon. Evidently, (n, π^*) singlet states in cynoaromatics are sufficiently higher in energy than the lowest (π, π^*) singlet for the former to have no significant perturbing effect.

Some *ortho-para*-directing substituents (-OH, $-NH_2$, $-OCH_3$) tend to enhance the fluorescence of aromatic compounds. Great care must be exercised in discussing the effect of these substituents because they have a strong tendency to form hydrogen-bond with the solvent or occasionally with other solute. For example, the dissociated –OH group ($-O^-$) is a strongly *ortho-para*-directing group, yet most phenolates are less fluorescent than their conjugated acids. In most cases ionized phenols interact very strongly with the solvent, increasing the efficiency of $S_1^* \rightarrow S_0$ internal conversion. In other words, for aromatic compounds with acidic or base functional groups, it is inherently impossible to separate ‘structural” from “environmental” effects on their luminescence behaviour.

Table 2.1: The effect of substituents on the fluorescence of aromatics[36]

Substituent	Effect on frequency of emission	Effect on intensity
Alkyl	None	Very slight increase or decrease
-OH, -OCH_3, -OC_2H_5	Decrease	Increase
CO_2H	Decrease	Large decrease
NH_2,NHR, NR_2	Decrease	Increase
NO_2	Large decrease	Large decrease
CN	None	Increase
SH	Decrease	Decrease
F	Decrease	Decrease
Cl	Decrease	Decrease
Br	Decrease	Decrease
I	Decrease	Decrease
SO_3H	none	none

2.7 Objectives of study

The main objectives of this study is first to synthesize a series of phenoxy derivatives of pyrimidine and pyrazine. The second objective is to study the fluorescence characteristic of all compounds prepared with respect to:

i. solvents
ii. substituents
iii. concentrations
iv. pH
v. effect of oxygen

CHAPTER 3: RESULTS AND DISCUSSION

3.1 Synthesis of the compounds studied

In this study, eleven compounds have been synthesized which consist of nine phenoxypyrimidines and two phenoxypyrazines. Details of synthesis are described in chapter five. Reaction equation of 2-chloropyrimidine **(35)** with a phenol and its derivatives are as shown in Figure 3.1

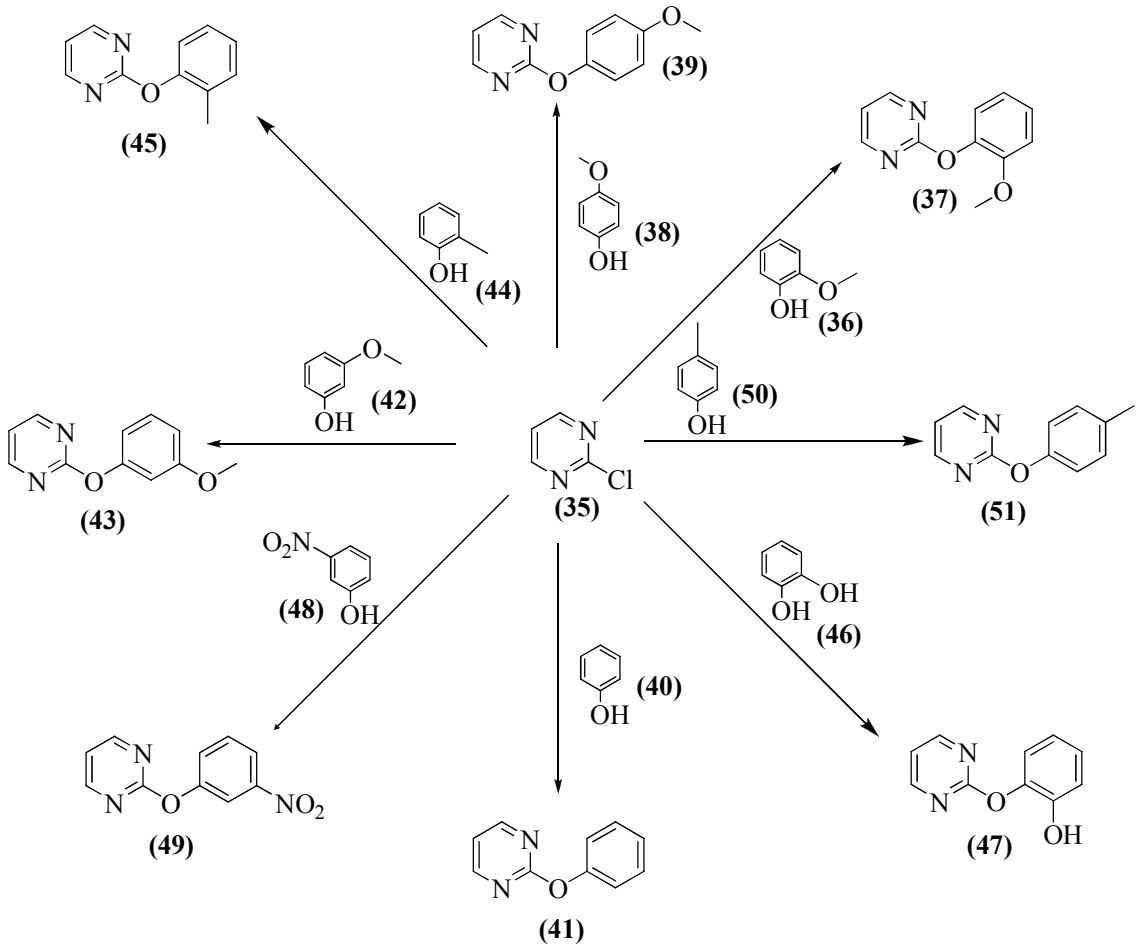


Figure 3.1: Reactions of 2-chloropyrimidine (35) with phenol and its derivatives

Reaction of 2-chloropyrazine **(54)** with *o*-methoxyphenol **(36)** and *p*-methoxyphenol **(38)** were as shown in Figure 3.2

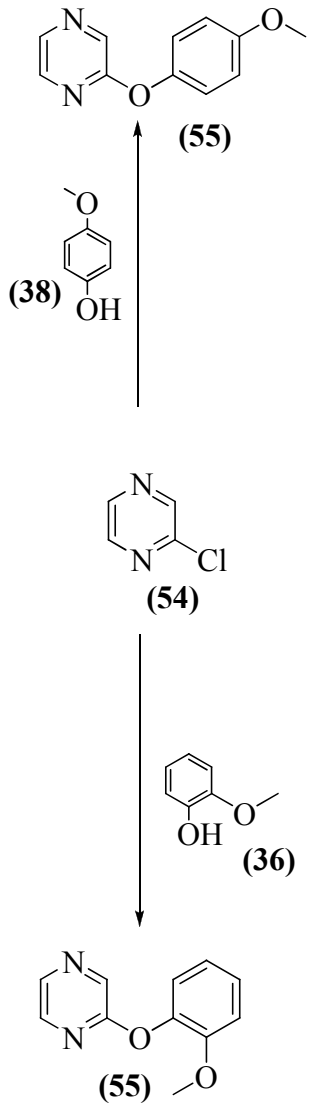
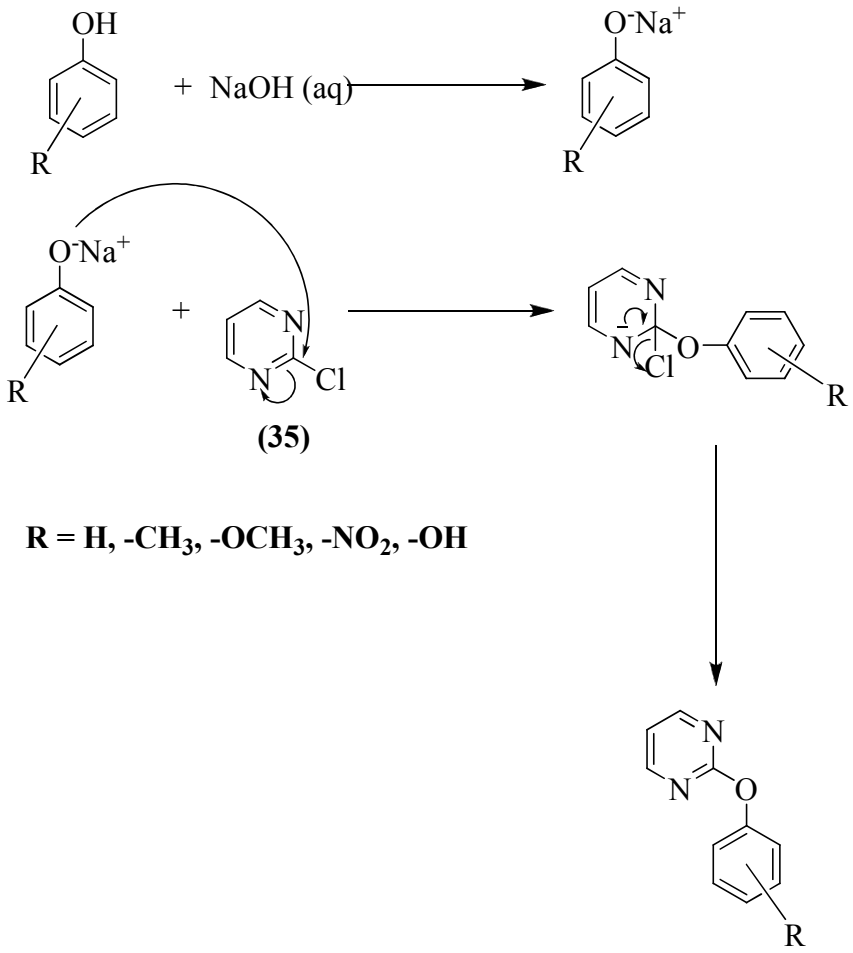


Figure 3.2: The reaction of 2-chloropyrazine (54) with *o*-methoxyphenol (36) and *p*-methoxyphenol (38).

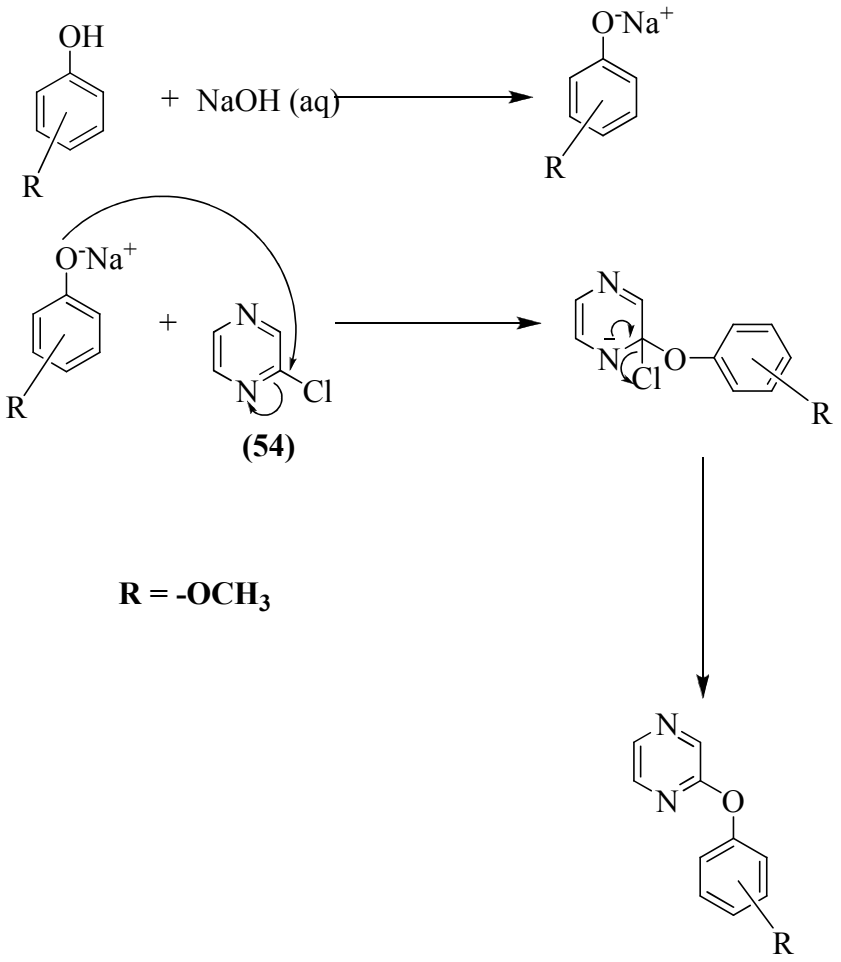
The structures of all prepared compounds were confirmed by IR, ^{1}H NMR, ^{13}C NMR and GC-mass spectra. The detailed spectra are attached in Appendices section.

Reaction of 2-chloropyrimidine **(35)** with *o*-methoxyphenol **(36)**, *p*-methoxyphenol **(38)**, phenol **(40)**, *m*-methoxyphenol **(42)**, *o*-cresol **(44)**, 1,2-dihydroxybenzene **(46),** *m*-nitrophenol **(48)** and *p*-cresol **(50)** were carried out using classical Williamson ether synthesis.[37] The Williamson ether synthesis is one of the best methods for preparing ethers. The reactions mechanism of this reaction is as shown in Scheme 3.1



Scheme 3.1: The reaction mechanism of 2-chloropyrimidine (35) with phenol and its derivatives

Similarly, 2-chloropyrazine **(54)**, reacted with either *o*-methoxyphenol **(36)** or *p*-methoxyphenol **(38)** via William ether synthesis. The reaction mechanism of 2-chloropyrazine **(54)** with phenol derivatives is as shown in Scheme 3.2.



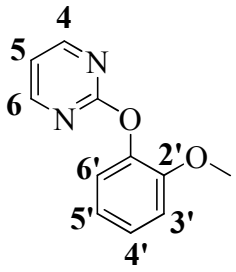
Scheme 3.2: The reaction mechanism of 2-chloropyrazine (54) with phenol derivatives

3.2 Synthesis of phenoxypyrimidines

3.2.1 Reactions of 2-chloropyrimidine with various phenols

Reactions of 2-chloropyrimidine **(35)** with *o*-methoxyphenol **(36)**, *p*-methoxyphenol **(38)**, phenol **(40)**, 3-methoxyphenol **(42)**, *o*-cresol **(44),** 1, 2-dihydroxybenzene **(46)**, 3-nitrophenol **(48)** and *p*-cresol **(50)** were studied as shown in

Figure 3.1. 2-(2-Methoxyphenoxy)pyrimidine **(37)** was obtained when *o*-methoxyphenol **(36)** was added to sodium hydroxide and 2-chloropyrimidine **(35)**. 60% of the pure product was obtained after recrystallisation from ethyl acetate. The structure of **(37)** was confirmed by IR, ^{1}H NMR, ^{13}C NMR and GC mass spectra.



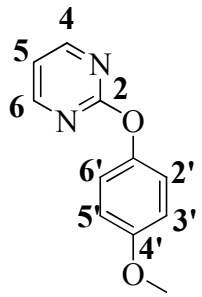
(37)

The mass spectrum showed an [M^{+}] peak at *m/z* 202 corresponding to the molecular formula of $C_{11}H_{10}N_2O_2$. The ^{1}H NMR spectrum showed a doublet with coupling constant of 4.9 Hz at δ 8.54 which represented H-4 and H-6, while a multiplet at δ 7.22 was assigned to H-5. Two sets of multiplets at δ 7.01 for H-3', H-4' and H-5' but H-6' at δ 7.22 while hydrogen of the methoxy group was observed as a singlet at δ 3.74.

The ^{13}C NMR spectrum showed a total of ten signals attributable to eleven carbons which consist of methoxy carbon, 6 methine carbons and 3 quaternary carbons, which are in agreement with the corresponding molecular formula of **(37)**. The relatively low intensity of quaternary carbon at δ 165.2 was assigned to C-2 of the pyrimidine ring, while signal at δ 159.5 was assigned to carbons C-4 and C-6. Two signals at δ 151.5 and δ 141.8 were assigned to C-2' and C-1' of quaternary carbons, while signal at δ 112.7 was attributable to C-5 of pyrimidine ring. The signal at δ 122.7 – δ 112.7 were assigned to C-3', C-4', C-5' and C-6' of the *o*-methoxyphenoxide moiety. The upfield signal at δ 55.8 is notable for the presence of a methoxy group.

The infrared spectrum showed a strong absorption band at 1569 and a medium absorption bands at 1498 and 1404 which were due the presence of C=N stretching and aromatic C=C stretching respectively. A strong band observed at 1302 and 1023 were typical of C-O stretching bands.

Reaction of 2-chloropyrimidine **(35)** with 4-methoxyphenol **(38)** gave 50% yield of colourless crystal of **(39)**. The structure of **(39)** was confirmed by spectroscopic methods. The mass spectrum displayed an [M^+] peak at *m/z* 202 which is consistent with the molecular formula $C_{11}H_{10}N_2O_2$.

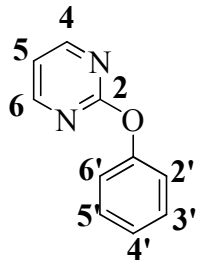


(39)

The ^{1}H NMR spectrum of **(39)** showed similar profiles with those of **(37)**. The differences were observed as two doublets (J= 9.3 Hz) at δ 7.14 and δ 6.96, which were assigned for H-2'/H-6' and H-3'/H-5' respectively.

The ^{13}C NMR spectrum showed a total of 8 signals which represented 11 carbons. Out of 8 peaks, six peaks showed similar profiles as compared to **(37)**. The differences were observed for signals at δ 122.5 and δ 114.7, each represented 2 aromatic of C-2'/C-6' and C-3'/C-5' respectively. The IR spectrum of (39) displayed similar absorptions to that of (**37)**.

2-Phenoxypyrimidine **(41)** was obtained when phenol **(40)** was allowed to react with 2-chloropyrimidine **(35)**. The GC-mass spectrum displayed the [M^+] peak at *m/z* 172 which is consistent with the molecular formula $C_{10}H_8N_2O$.



(41)

The ^{1}H NMR spectrum of **(41)** showed a downfield doublet at δ 8.5 which attributable to H-4 and H-6 of **(37)**. A triplet at δ 7.42 with coupling constant of 6.6 Hz was due to H-3' and H-5' while a doublet at δ 7.23 with coupling constant of 5.8 Hz was assigned to H-4'while another doublet (J= 7.6 Hz) at δ 7.18 was attributable to H-2' and H-6'. A downfield triplet (J= 4.9 Hz) at δ 7.01 was consistent to H-5 of the pyrimidine ring.

A total of seven signals which represented 10 carbon atoms were observed in the ^{13}C NMR spectrum of **(41)**. However, only three signals, δ 165 (C-2), δ 160 (C-4/C-6) and δ 153 (C-1') were similar as compound **(37)**. In addition, two signals at δ 129.6 and δ 116.1 were attributable to C-3'/C-5' and C-2'/C-6' respectively. The remaining two signals at δ 125.5 and δ 121.6 were assigned to C-4' and C-5 respectively. The IR spectrum showed similar absorption bands as compounds **(37)**.

Ultimately, the correct structure of **(41)** was determined by X-ray crystallography analysis. The crystal system was found to be monoclinic and the refinement data are as shown in Table 3.1, while Figure 3.3 showed the ORTEP diagram of **(41)**.

Table 3.1: The crystal system and refinement data of (41)

Crystal data and structure refinement for 2-phenoxypyrimidine (41).	
Chemical formula	$C_{10}H_8N_2O$
Molecular weight	172.18
Crystal system	Monoclinic,
T (K)	100 (2)
Space group	*P*21/*c*
a (Å)	10.859 (1)
b (Å)	20.181 (2)
c (Å)	8.1339 (8)
β (º)	106.637 (2)
V (Å^3)	1707.8 (3)
Z	8
*D*calc Mg m^{-3}	1.339
Absorption coefficient μ (mm^{-1})	0.09
F_{000}	720
Crystal size (mm)	0.25 × 0.20 × 0.15
θ range for data collection	2.2–28.2º
Index ranges	(-11, -26, -10) to (14, 26, 10)
Reflections collected	9752
Independent reflection	3901
Data / parameters	235
Goodness-of-fit on F^2	0.102
Final R indices $R[F^2 > 2\sigma(F^2)]$	= 0.037

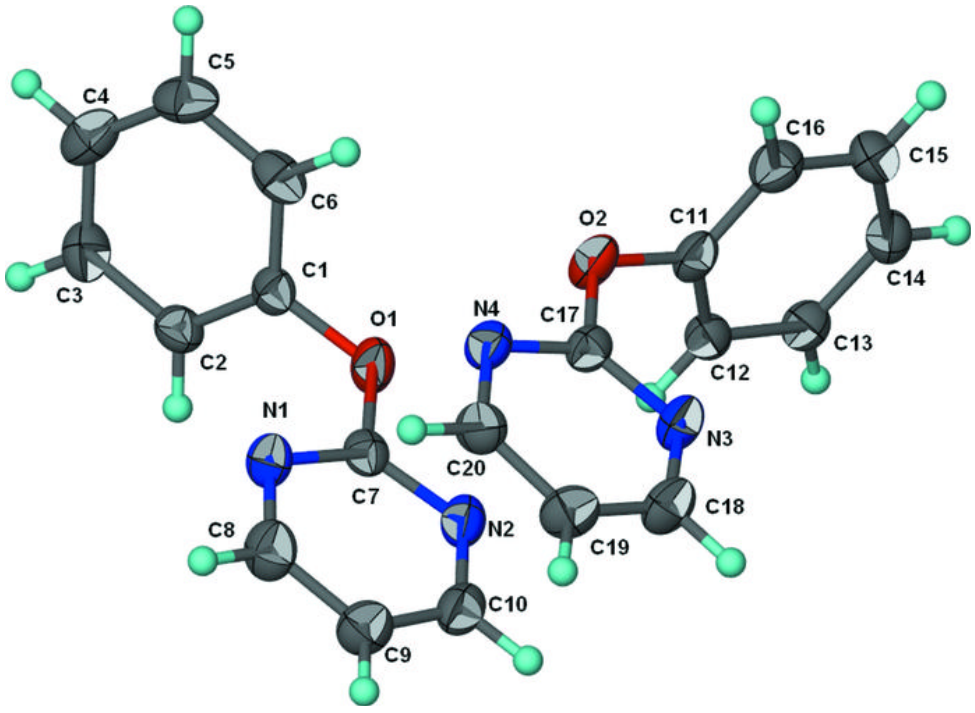
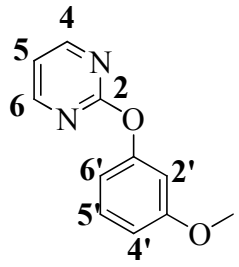


Figure 3.3: ORTEP diagram of 2-phenoxypyrimidine (41)[38]

Treatment of 2-chloropyrimidine **(35)** with 3-methoxyphenol **(42)** gave 36% yield of colourless crystal **(43)**. The mass spectrum displayed an [M^+] peak at *m/z* 202 which is consistent with the molecular formula $C_{11}H_{10}N_2O_2$.



(43)

The ^{1}H NMR spectrum of **(43)** also showed similar profile for protons of pyrimidine ring of **(37)**. In addition two triplets were observed at δ 7.33 and δ 7.04 with coupling constant of 4.6 Hz was assigned to H-5' and H-2' respectively. A multiplet at δ 6.79 were attributable to H-4', H-5 and H-6'. The remaining singlet at δ 3.81 indicated the presence of a methoxyl.

The ^{13}C NMR spectrum showed a total of 10 signals consist one methoxy, 3 quaternary and 6 methine representing 11 carbon atoms which agree with the molecular formula of **(43)**. Two carbon peaks were similar with compound **(37)** for C-2 and methoxy group. The low intensity of quaternary carbons recorded at δ 160.7 and δ 153.9 were assigned to C-1' and C-3'. A signal at δ 158.7 was assigned to C-4/C-6 where as five signals at δ 130.0 – δ 100.5 were assigned due to carbon C-5', C-5, C-6', C-4' and C-2'. The IR spectrum displayed similar absorption bands as **(37)** in the earlier discussion.

The structure of **(43)** was also determined by X-ray crystallography analysis. The crystal system was found as monoclinic and the refinement data of **(43)** are as shown in Table 3.2 while Figure 3.4 showed the ORTEP diagram of **(43)**.

Table 3.2: The crystal system and refinement data of compound (43)

Crystal data and structure refinement for 2-(3-Methoxyphenoxy)pyrimidine (43)	
Chemical formula	$C_{11}H_{10}N_2O_2$
Molecular weight	202.21
Crystal system	Monoclinic
T (K)	293
Space group	*Cc*
a = (Å)	8.8120 (16)
b (Å)	18.215 (3)
c (Å)	7.2094 (10)
β (º)	119.380 (2)
V (Å^3)	1008.4 (3)
Z	4
*D*calc Mg m^{-3}	1.332
Absorption coefficient μ (mm^{-1})	0.09
F_{000}	424
Crystal size (mm)	0.40 × 0.30 × 0.08
θ range for data collection	2.2–21.9
Index ranges	(−11, −23, −9) to (11, 23, 9)
Reflections collected	4725
Independent reflection	1165
Data / parameters	138
Goodness-of-fit on F^2	0.086
Final R indices $R[F^2 > 2\sigma(F^2)]$	0.032

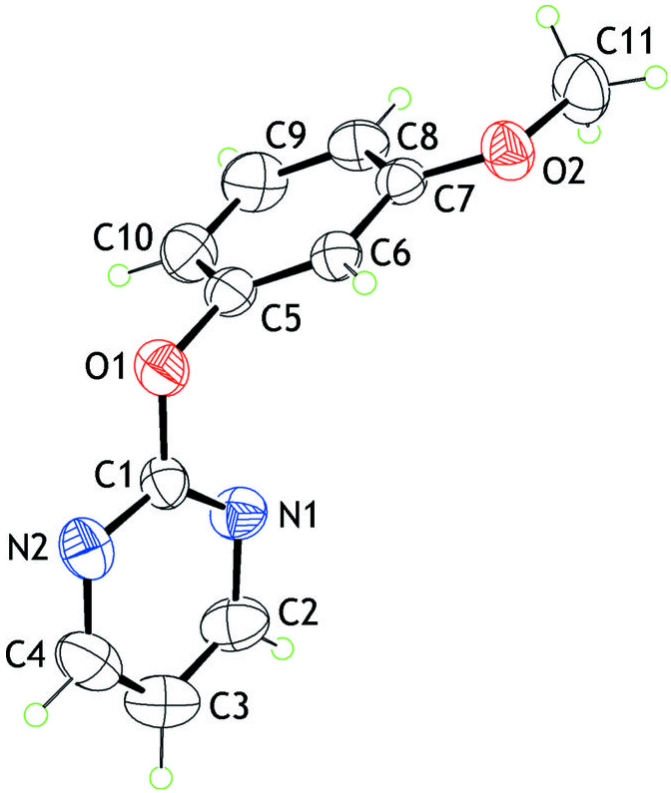
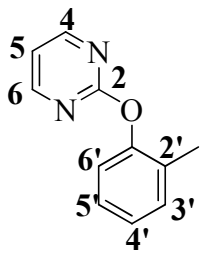


Figure 3.4: ORTEP diagram of 2-(3-Methoxyphenoxy)pyrimidine (43)[39]

Colourless crystal of 2-(*o*-tolyloxy)pyrimidine **(45)** was obtained when 2-chloropyrimidine **(35)** was reacted with *o*-cresol **(44)** in 40% yield. The GC-mass spectrum displayed an [M^+] at *m/z* 186 which in agreement with the molecular formula $C_{11}H_{10}N_2O$



(45)

The ^{1}H NMR spectrum of **(45)** showed a triplet at δ 7.30 was due to H-3' and H-6'. A triplet was also observed at δ 7.19 with coupling constant 6.1 Hz was due to H-4'. A doublet and a triplet were observed at δ 7.12 and δ 7.01 which were due to H-5' and H-5 respectively. For proton H-4 and H-6 the doublet peak was similar to compound **(37)**.

The ^{13}C NMR spectrum of **(45)** showed a total of 10 carbon peaks, which consist of one methyl, 3 quaternary and 6 methine carbons. One signal for C-2 was similar to **(37)** carbon peak. Signal at δ 159.7 and δ 151.3 were assigned to carbons C-4/C-6 and C-1' while six signals at δ 131.3 - δ 159.7 were due to C-2', C-3', C-5', C-4', C-6' and C-5. The peak recorded at δ 16.2 was assigned to carbon of methyl group. IR spectrum displayed similar absorption bands as compound **(37)** as discussed earlier.

The structure of **(45)** was also determined by X-ray crystallography analysis. The crystal system was found to be orthorhombic and the refinement data of **(45)** are as shown in Table 3.3 while Figure 3.5 showed the ORTEP diagram of **(45)**.

Table 3.3: The crystal system and refinement data of compound (45)

Crystal data and structure refinement for 2-(*o*-Tolyloxy)pyrimidine (45)	
Chemical formula	$C_{11}H_{10}N_2O$
Molecular weight	186.21
Crystal system	Orthorhombic
T (K)	153
Space group	Pca21
a = (Å)	7.5197(2)
b (Å)	12.7997 (3)
c (Å)	20.3238 (4)
V (Å3)	1956.16 (8)
Z	8
*D*calc Mg m^{-3}	1.265
Absorption coefficient μ (mm^{-1})	0.08
F_{000}	784
Crystal size (mm)	0.35 x 0.25 x 0.15
θ range for data collection	2.6 – 27.9
Index ranges	(-9,-16, -26) to (9, 16, 26)
Reflections collected	12792
Independent reflection	2317
Data / parameters	255
Goodness-of-fit on F^2	0.088
Final R indices $R[F^2 > 2\sigma(F^2)]$	0.033

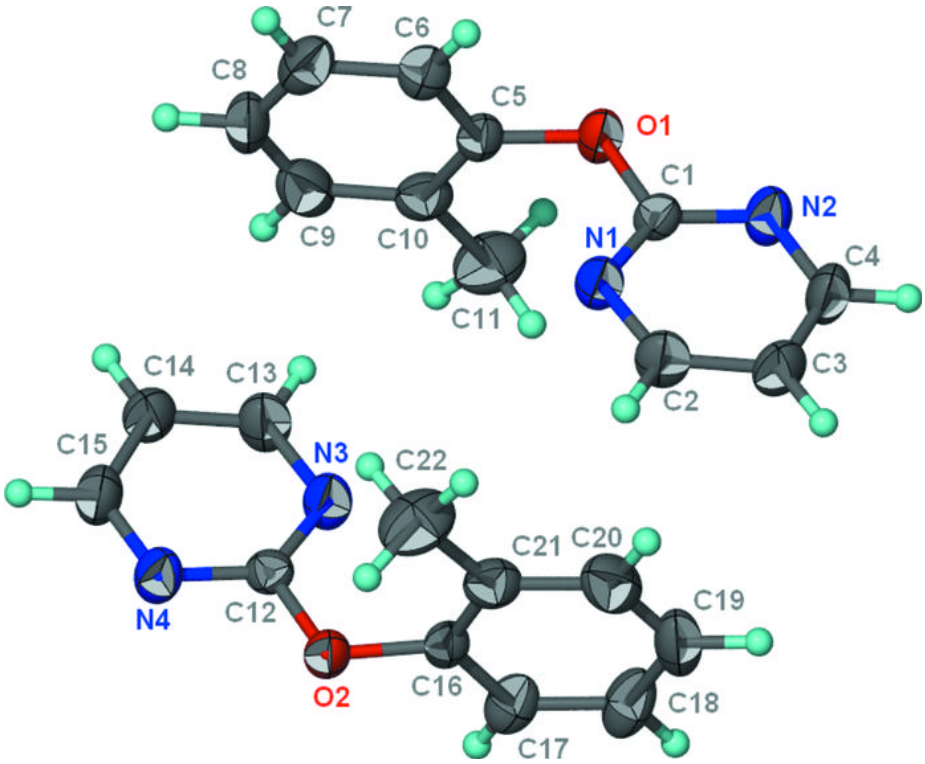
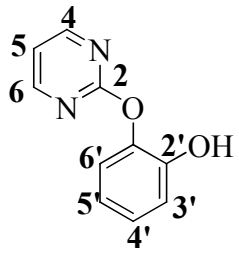


Figure 3.5: ORTEP diagram of 2-(*o*-tolyloxy)pyrimidine (45)[40]

Reactions of 2-chloropyrimidine **(35)** with 1,2-dihydroxybenzene **(46)** gave 25% yield of colourless crystal **(47)**. The structure of 2-(pyrimidin-2-yloxy)phenol **(47)** was confirmed by spectroscopic methods. The mass spectrum displayed an [M^+] at *m/z* 188 which agree with the molecular formula $C_{10}H_8N_2O_2$.



(47)

The ^{1}H NMR spectrum of **(47)** showed a singlet at δ 9.55 was assigned to O-H. Triplet were also observed on the benzene ring at δ 6.92 and δ 6.80 with coupling constant 6.3 Hz and 5.9 Hz respectively were assigned to H-4' and H-5'. The proton peaks for the pyrimidine ring were similar to compound **(37)**.

The ^{13}C NMR spectrum showed a total of nine carbon peaks consisting three quaternary carbons and six methine carbons which agreement with molecular formula of **(47)**. The rest of four carbon peaks were similar to the compound **(37)**. Meanwhile signals δ 123.1 – δ 116.7 were due to C-3', C-4', C-5' and C-6'.

The IR spectrum displayed a strong absorption bands at 3297 cm^{-1} which was due to OH group. Others displayed absorption bands were similar to **(37)** as discussed earlier. The structure of compound **(47)** was also determined by X-ray crystallography analysis. The crystal system is monoclinic and the refinement data of **(47)** are as shown in Table 3.4 while Figure 3.6 showed the ORTEP diagram of compound **(47)**.

Table 3.4: The crystal system and refinement data of compound (47)

Crystal data and structure refinement for 2-(Pyrimidin-2-yloxy)phenol (47)	
Chemical formula	$C_{10}H_8N_2O_2$
molecular weight	188.18
Crystal system	Monoclinic
T (K)	293
Space group	*C*2/*c*
a = (Å)	18.0849 (18)
b (Å)	7.3293 (8)
c (Å)	13.3983 (14)
β (º)	92.521 (1)°
V (Å^3)	1774.2 (3)
Z	8
*D*calc Mg m^{-3}	1.409
Absorption coefficient μ (mm^{-1})	0.10
F_{000}	784
Crystal size (mm)	0.32 × 0.30 × 0.10
θ range for data collection	3.0–26.9°
Index ranges	(−23, −9, −17) to (23, 9, 15)
Reflections collected	2048
Independent reflection	2048 R_{int} = 0.027
Data / parameters	130
Goodness-of-fit on F^2	0.112
Final R indices $R[F^2 > 2\sigma(F^2)]$	0.039

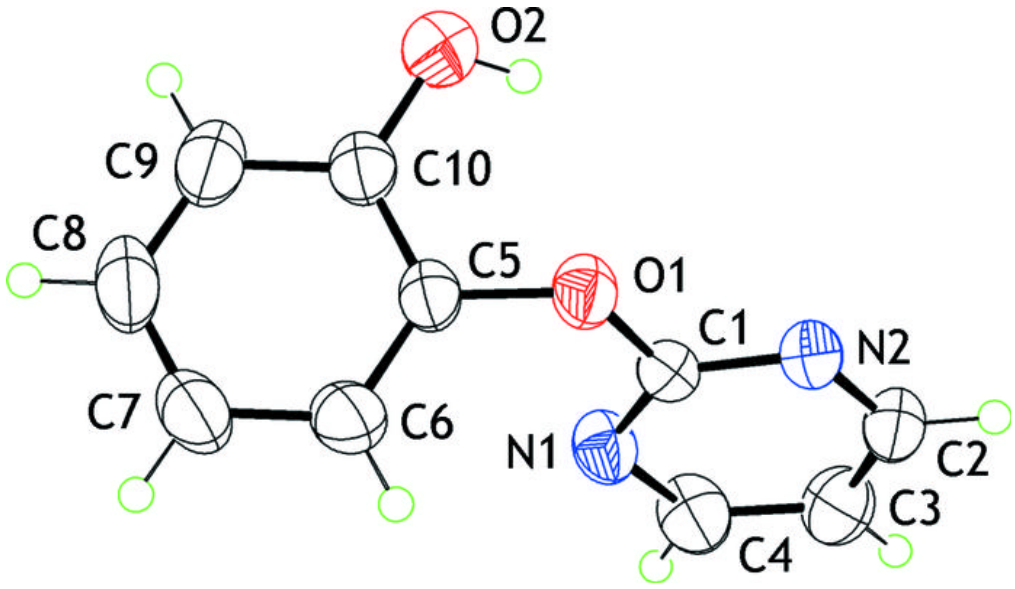
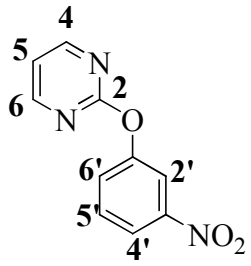


Figure 3.6: ORTEP diagram of 2-(Pyrimidin-2-yloxy)phenol (47)[41]

Reactions of 2-chloropyrimidine **(35)** with *m*-nitrophenol **(48)** gave 39 % yield of yellow crystals **(49)**. The GC-mass spectrum gave an [M$^+$] at *m/z* 217 which is consistent with the molecular formula $C_{10}H_7N_3O_3$.



(49)

The ^{1}H NMR spectrum of **(49)** showed a doublet at δ 8.53 with coupling constant 4.9 Hz which was assigned to H-4 and H-6, while a multiplet at δ 8.05 was due to H-2' and H-4'. Another multiplet at δ 7.54 was assigned to H-5' and H-6. The remaining signal is a triplet with coupling constant 4.9 Hz was observed at δ 7.07 which was due to H-5.

The ^{13}C NMR spectrum showed a total of 9 signals representing 10 carbons which agree with the molecular formula of 2-(3-nitrophenoxy)pyrimidine **(49)**. The relative low intensity signal at δ 164.6 was assigned to C-2. A signal at δ 159.9 was assigned to carbons C-4, C-5 and C-6. The signals at δ 153.0 and δ 130.2 were due to C-1' and C-3' respectively. Signals δ 128.1 – δ 117.1 were assigned to C-2', C-5', C-6' and C-4'.

The IR spectrum displayed similar absorption bands as **(37)** which have been discussed earlier. However, additional band at 1353 cm^{-1} was due to NO_2 group. The structure of **(49)** was also determined by X-ray crystallography analysis. The crystal system is orthorhombic and the crystal refinement data of **(49)** are as shown in Table 3.5, while Figure 3.7 showed the ORTEP diagram of compound **(49)**.

Table 3.5: The crystal system and refinement data of compound (49)

Crystal data and structure refinement for 3-Nitrophenyl pyrimidin-2-yl ether (49)	
Chemical formula	$C_{10}H_7N_3O_3$
Molecular weight	217.19
Crystal system	Orthorhombic,
T (K)	118
Space group	*Pbcn*
a = (Å)	18.1360 (3)
b (Å)	7.3355 (1)
c (Å)	14.5986 (3)
V (Å^3)	1942.15 (6)
Z	8
*D*calc Mg m^{-3}	1.486
Absorption coefficient μ (mm^{-1})	0.11
F_{000}	896
Crystal size (mm)	0.40 × 0.20 × 0.15
θ range for data collection	2.8–28.2º
Index ranges	(−23, −9, −18) to (23, 9, 18)
Reflections collected	12785
Independent reflection	2242
Data / parameters	145
Goodness-of-fit on F^2	0.102
Final R indices $R[F^2 > 2\sigma(F^2)]$	0.037

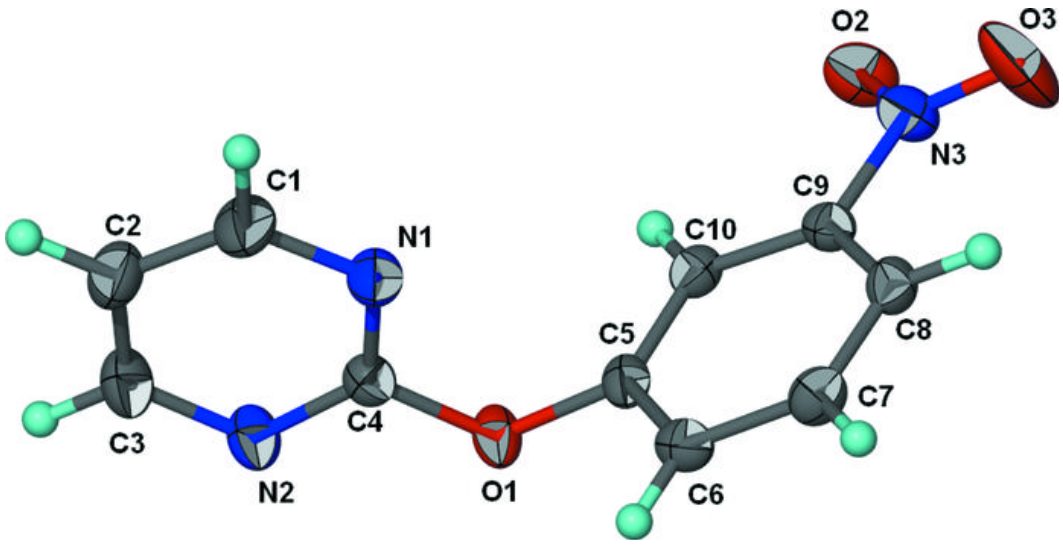
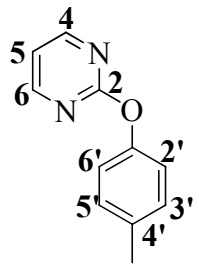


Figure 3.7: ORTEP diagram of 3-nitrophenylpyrimidin-2-yl ether (49)[42]

2-(*p*-Tolyloxy)pyrimidine **(51)** was formed when 2-chloropyrimidine **(35)** was treated with *p*-cresol **(50)**. 33 % yield of colourless crystals was obtained. The GC-mass

spectrum gave an [M^+] at *m/z* 186 which is consistent with the molecular formula $C_{11}H_{10}N_2O$.



(51)

The ^{1}H NMR spectrum of **(51)** showed similar signals attributable to H-4/H-6 and H-5 as of **(37)**, while another doublet with coupling constant 8.8 Hz at δ 7.28 was assigned to H-3' and H-5'. Another doublet (J=6.8 Hz) at δ 6.97 was due to H-3' and H-5'. An upfield singlet at δ 2.9 indicated to the presence of methyl group.

The ^{13}C NMR spectrum showed a total of eight signals represent three quaternary, seven methine and one methyl carbons which in agreement with the molecular formula of **(51)**. The relative low intensity signals at δ 160.6, δ 157.0 and δ 146.2 were assigned to quaternary carbons C-2, C-1' and C-4'. The carbons of pyrazine ring were recorded at δ 141.0, δ 138.1 and δ 135.7 which were assigned to C-3, C-5 and C-6. The signals at δ 122.3 was assigned to C-2' and C-6' while a signal at δ 114.8 was due to C-5' and C-3'. Meanwhile a signal at δ 55.6 was due to carbon of a methyl group. The IR spectrum of **(51)** was similar to that of **(37)** as discussed earlier.

The structure of compound **(51)** was determined by X-ray crystallography method. The crystal system is orthorhombic and the refinement data of **(51)** are as shown in Table 3.6, while Figure 3.8 showed the ORTEP diagram of compound **(51)**.

Table 3.6: The crystal system and refinement data of compound (51)

Crystal data and structure refinement for 2-(*p*-tolyloxy)pyrimidine (51)	
Chemical formula	$C_{11}H_{10}N_2O$
Molecular weight	186.21
Crystal system	Orthorhombic
T (K)	153
Space group	*Pbca*
a (Å)	11.2918 (2)
b (Å)	7.2275 (1)
c (Å)	23.3359 (5)
V (Å^3)	1904.48 (6)
Z	8
*D*calc Mg m^{-3}	1.299
Absorption coefficient μ (mm^{-1})	0.09
F_{000}	784
Crystal size (mm)	0.35 × 0.35 × 0.35
θ range for data collection	2.8–28.2
Index ranges	(−14, −9, −30) to (13, 9, 30)
Reflections collected	12308
Independent reflection	2189
Data / parameters	128
Goodness-of-fit on F^2	0.109
Final R indices $R[F^2 > 2\sigma(F^2)]$	0.038

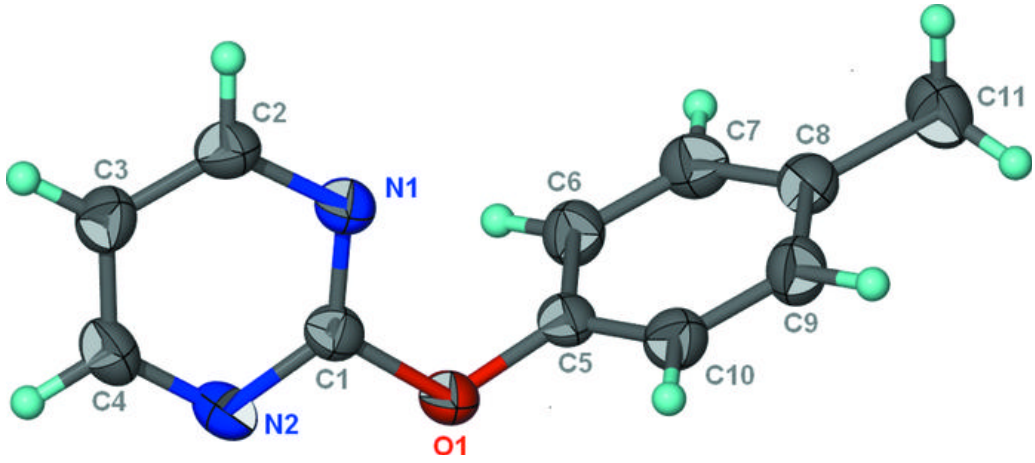
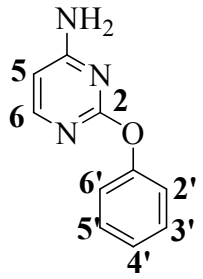


Figure 3.8: ORTEP diagram of 2-(*p*-tolyloxy)pyrimidine (51)[43]

3.2.2 Reactions of 2-chloropyrimidin-4-amine with phenol

Reactions of 2-chloropyrimidin-4-amine **(52)** with phenol **(40)** gave 47 % yield of colourless crystal of **(53)**. The GC-mass spectrum displayed an [M$^+$] at *m/z* 217 which consistent with the molecular formula $C_{10}H_9N_3O$



(53)

The ^{1}H NMR spectrum of **(53)** showed a doublet at δ 8.02 with coupling constant of 5.6 Hz was assigned to H-6, while a triplet at δ 7.38 was attributable to H-3' and H-5'. A multiplet was also observed at δ 7.17 which was due to H-2', H-4', H-6', while a doublet with coupling constant 5.6 Hz were observed at δ 6.14 was assigned to H-5. A broad upfieldsinglet at δ 5.00 indicated the presence of NH_2 group.

The carbon peaks of the ^{13}C NMR spectrum showed a total of eight peaks representing three quaternary and seven methine carbons which in agreement with the molecular formula of **(53)**. The peaks for C-2, C-4 and C-6 were similar to carbon peak of compound **(37)**. The signals at δ 153.0 and δ 130.2 were due to C-1' and C-3' respectively. Signals recorded at δ 128.1 – δ 117.1 were assigned to C-2', C-5', C-6' and C-4'.

IR spectrum displayed similar absorption bands to those **(37)**. Strong absorption recorded at 3130 cm^{-1} which was due to NH_2- stretching vibration. The structure of compound **(53)** was determined by X-ray crystallography analysis. The crystal system is orthorhombic and the refinement data of **(53)** are as shown in Table 3.7, while Figure 3.9 showed the ORTEP diagram of compound **(53)**.

Table 3.7: The crystal system and refinement data of compound (53)

Crystal data and structure refinement for 4-Amino-2-phenoxypyrimidine (53)	
Chemical formula	$C_{10}H_9N_3O$
Molecular weight	187.20
Crystal system	Monoclinic
T (K)	120
Space group	*P*21/*n*
a = (Å)	8.8443 (3)
b (Å)	12.1214 (3)
c (Å)	9.0415 (2)
β (º)	96.751 (2)
V (Å^3)	962.58 (5)
Z	4
*D*calc Mg m^{-3}	1.292
Absorption coefficient μ (mm^{-1})	0.09
F_{000}	392
Crystal size (mm)	0.40 × 0.20 × 0.10
θ range for data collection	2.3–27.9
Index ranges	(−10, −15, −10) to (11, 15, 11)
Reflections collected	6375
Independent reflection	2178
Data / parameters	136
Goodness-of-fit on F^2	0.163
Final R indices $R[F^2 > 2\sigma(F^2)]$	0.055

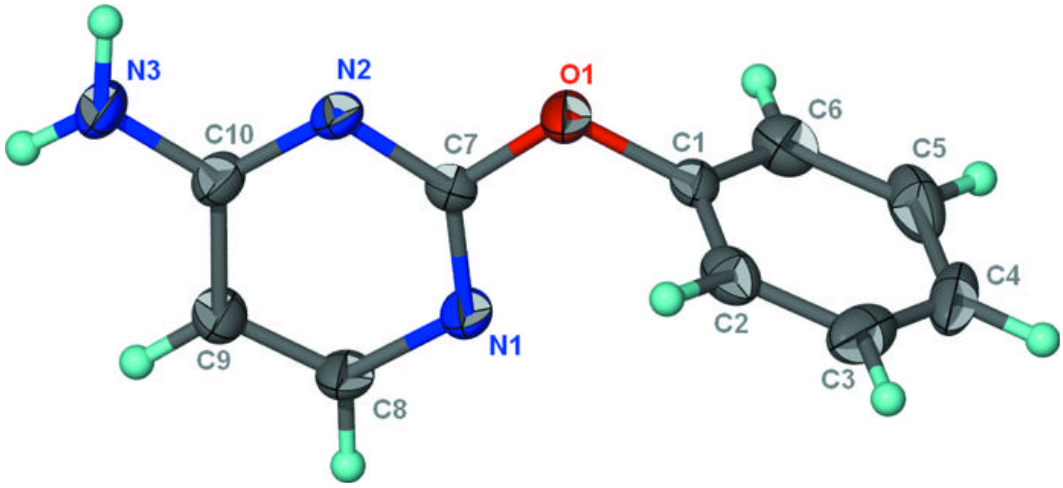
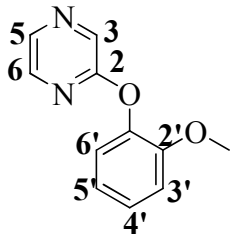


Figure 3.9: ORTEP diagram of 4-Amino-2-phenoxypyrimidine (53)[44]

3.3 Synthesis of pyrazine derivatives

Reactions of 2-chloropyrazine **(54)** with *o*-methoxyphenol **(36)** gave 41 % yield of colourless crystal of compound **(55)**. The GC-mass spectrum gave an [M^+] at *m/z* 202 which is consistent with the molecular formula $C_{11}H_{10}N_2O_2$

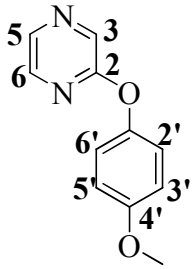


(55)

The ^{1}H NMR spectrum of **(55)** showed singlets at δ 8.43, δ 8.22 and δ 8.06 which were due to H-3, H-5 and H-5 respectively. A doublet at δ 7.23 with coupling constant 8.08 Hz, was assigned to H-6'. Another doublet was also recorded at δ 7.16 with coupling constant 6.6 Hz which was due to H-2'. A triplet with coupling constant of 8.28 Hz was recorded at δ 7.03 which was due to H-3'and H-4'.

The ^{13}C NMR spectrum showed a total of eleven signals which consist of three quaternary, seven methine and one methoxy carbons which in agreement with the molecular formula of **(55)**. The relative low intensity signals recorded at δ 160.1, δ 151.5 and δ 141.5 were assigned to C-2, C-2' and C-1'respectively. Signals at δ 141.0, δ 138.1 and δ 135.2 were assigned to C-6, C-3 and C-5 of the pyrazine ring. Meanwhile, signals at δ 126.7, δ 122.9, δ 121.1 and δ 112.8 were due to C-4,', C-6', C-5' and C-3' respectively. One upfield signal at δ 55.7 was due to a methoxy carbon. The IR spectrum displayed similar absorption bands as compared to **(37)**.

2-(4-Methoxyphenoxy)pyrazine **(56)** was obtained in 42% as colorless crystal when 2-chloropyrazine **(54)** was reacted with *p*-methoxyphenol **(38)**. The GC-mass spectrum displayed an [M^+] at *m/z* 202 which is consistent with the molecular formula $C_{11}H_{10}N_2O_2$



(56)

The ^{1}H NMR spectrum of **(56)** showed similar protons profiles for pyrazine as compared to **(55)**. In addition, a doublet (J= 10.5 Hz) at δ 7.10 was attributable to H-3' and H-5'. Another doublet was also observed with coupling constant 6.8 Hz at δ 6.97 which was due to H-2' and H-6'.

The ^{13}C NMR spectrum showed a total of nine which representing peaks three quaternary, seven methine carbons and one methoxy carbons which in agreement with the molecular formula of **(56)**. The relative low intensity signals recorded at δ 160.6, δ 157.0 and δ 146.2 were assigned to C-2, C-4' and C-1' respectively. The methine carbons of pyrazine ring were recorded δ 141.0, δ 138.1 and δ 135.7 which was assigned to C-6, C-5 and C-3 respectively. The signals at δ 122.3 was attributable to C-2' and C-6' while a signal at δ 114.8, was assigned to C-5' and C-3'. Meanwhile, signal at δ 55.6 was due to the methoxy carbon. IR spectrum displayed similar absorption bands ac compared to those of **(37)** as discussed earlier.

The structure of **(56)** was also determined by X-ray crystallography analysis. The crystal system is monoclinic and the refinement data of **(56)** are as shown in Table 3.8, while Figure 3.10 showed the ORTEP diagram of compound **(56)**.

Table 3.8: The crystal system and refinement data of compound (56)

Crystal data and structure refinement for 2-(4-methoxyphenoxy)pyrazine (56)	
Chemical formula	$C_{11}H_{10}N_2O_2$
Molecular weight	202.21
Crystal system	Monoclinic
T (K)	293
Space group	*P*21/*c*
a = (Å)	5.8783 (2)
b (Å)	10.9298 (4)
c (Å)	15.6430 (6)
β (º)	97.109 (2)
V (Å^3)	997.32 (6)
Z	4
*D*calc Mg m^{-3}	1.347
Absorption coefficient μ (mm^{-1})	0.10
F_{000}	424
Crystal size (mm)	0.35 × 0.20 × 0.10
θ range for data collection	2.3–22.4
Index ranges	(−6, −12, −18) to (6, 12, 18)
Reflections collected	5515
Independent reflection	1743
Data / parameters	138
Goodness-of-fit on F^2	0.100
Final R indices $R[F^2 > 2\sigma(F^2)]$	0.036

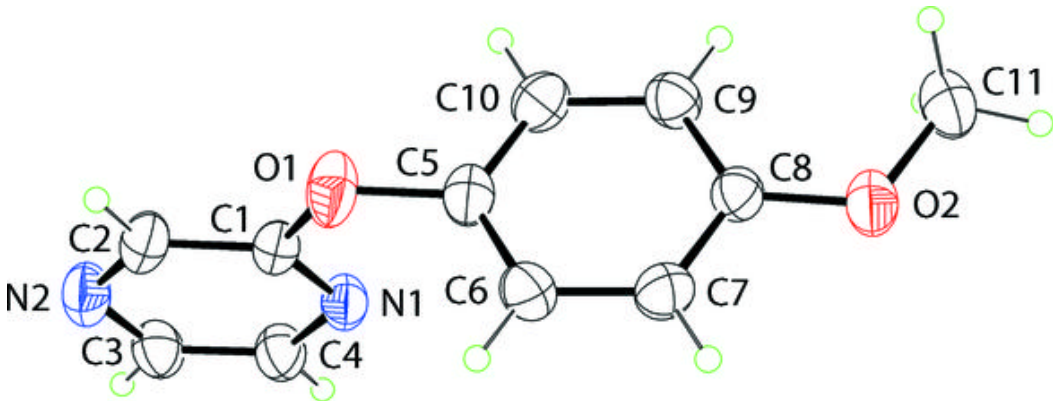


Figure 3.10: ORTEP diagram 2-(4-Methoxyphenoxy)pyrazine (56)[45]

3.4 Fluorescence characteristics of synthesised compounds

Figure 3.11 shows a histogram of the fluorescence intensity of 2-(2-methoxyphenoxy)pyrimidine **(37)**, 2-(4-methoxyphenoxy)pyrimidine **(39)**, 2-phenoxypyrimidine **(41)**, 2-(3-methoxyphenoxy)pyrimidine **(43)**, 2-(*o*-tolyloxy)pyrimidine **(45),** 2-(pyrimidin-2-yloxy)phenol **(47)**, 2-(3-nitrophenoxy)pyrimidine **(49),** 2-(*p*-tolyloxy)pyrimidine **(51)**, 2-phenoxypyrimidin-4-amine **(53)**, 2-(2-methoxyphenoxy)pyrazine **(55)**, and 2-(4-methoxyphenoxy)pyrazine **(56)** in various of solvents.

Figure 3.11: Fluorescence characteristic of synthesis compound in various solvents

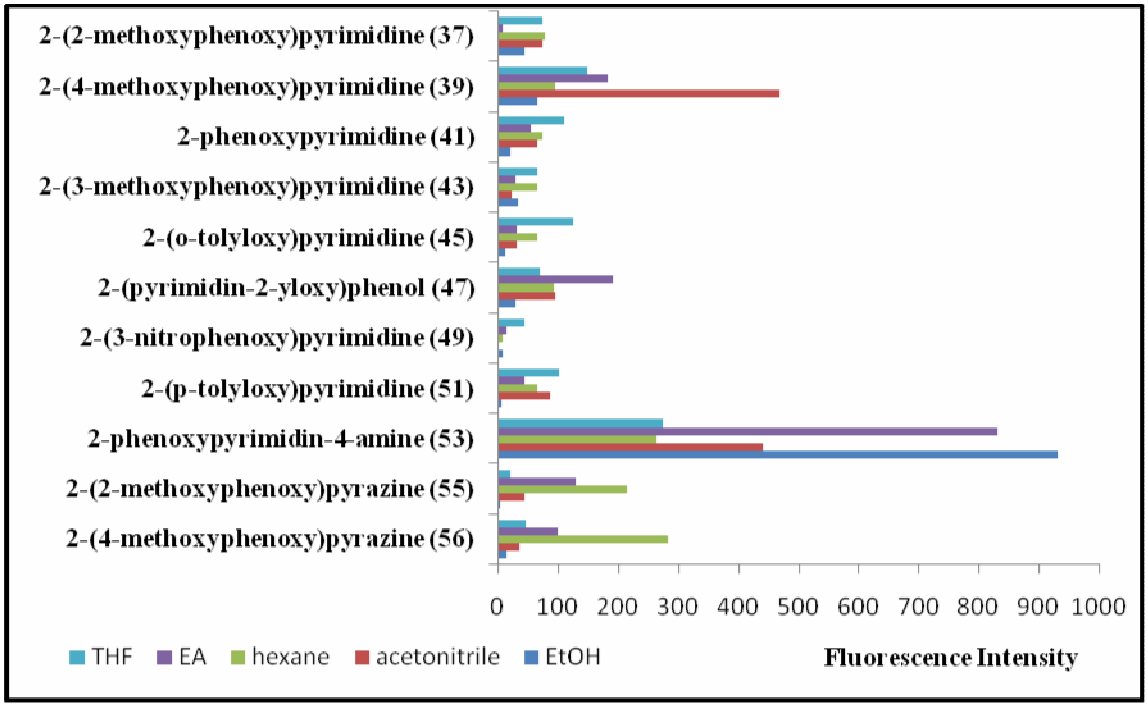


Table 3.9 shows the fluorescence characteristic of 2-(2-methoxyphenoxy)pyrazine **(55)** and 2-(4-methoxyphenoxy)pyrazine **(56)** in various solvents in capped conditions.

Table 3.9: Fluorescence characteristic of 2-(2-methoxyphenoxy)pyrazine (55) and 2-(4-methoxyphenoxy)pyrazine (56) in various solvents. (concentration: 4.95 x 10^{-4} M)

Compound	Solvent	Excitation wavelength (nm)	Fluorescence wavelength (nm)	Intensity
2-(2-methoxyphenoxy)pyrazine **(55)**	Hexane	345	355	215.63
	Ethanol	214	362	3.71
	Acetonitrile	203	325	45.14
	Ethyl acetate	344	437	130.55
	Tetrahydrofuran	203	333	21.60
2-(4-methoxyphenoxy)pyrazine **(56)**	Hexane	349	377	283.47
	Ethanol	200	376	13.95
	Acetonitrile	201	347	37.05
	Ethyl acetate	347	446	100.07
	Tetrahydrofuran	204	373	46.35

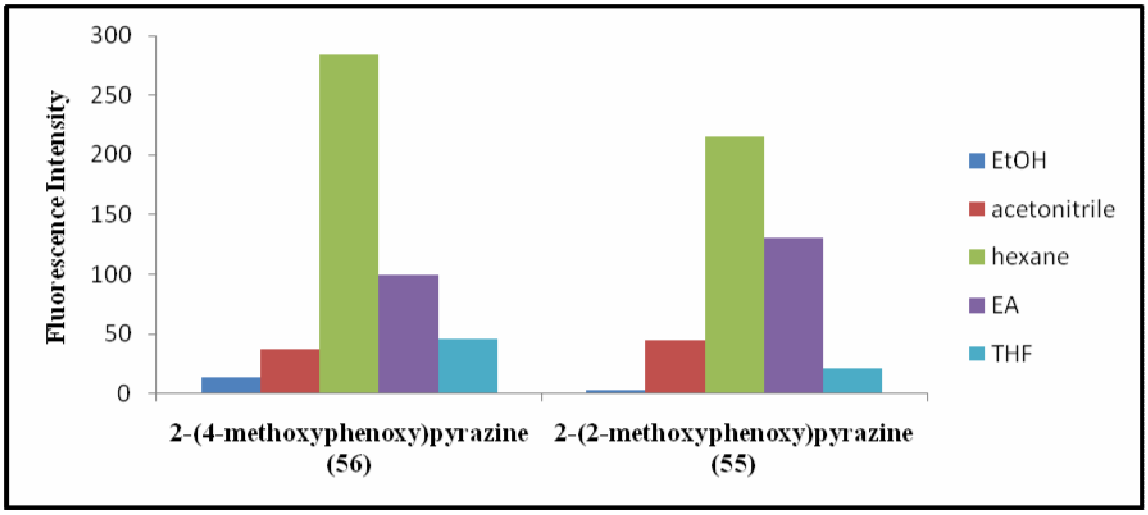


Figure 3.12: Fluorescence characteristic of compound (55) and (56) in various solvents.

The fluorescence characteristic of the compounds **(55)** and **(56)** were carried out in hexane, ethanol, acetonitrile, ethyl acetate and tetrahydrofuran as show in Figure 3.12. Compounds **(55)** and **(56)** showed the lowest fluorescence intensities in ethanol.

The reason of low fluorescence intensity observed is due to solvent effects whereby it is believed that compound (**55)** and **(56)** formed a complex with the ethanol as shown in Figure 3.13.

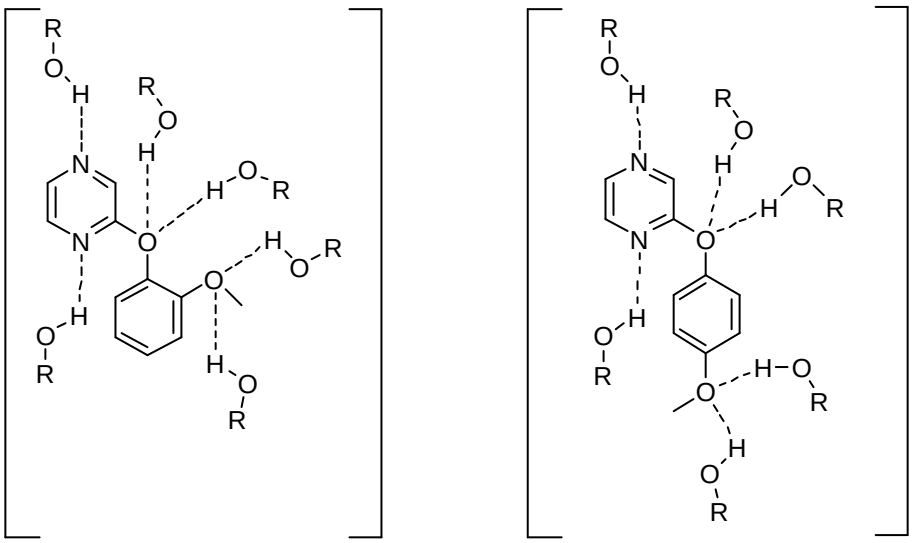


Figure 3.13: Formation of hydrogen bonded complexes

The formation of hydrogen bonds which is capable of conjugating with the π-electron hence been disturbed and caused the fluorescence intensity to be reduced. This phenomenon favours the low lying n → π* transitions which refers to the excitation of a nonbonding electron to an antibonding orbital. It was reported that n → π* transition[46] is forbidden in fluorescence spectra and when it present the intensity is weak. As a result, a decrease in fluorescence intensity was observed.

A change in the ability of a solvent to form hydrogen bonds can affect the nature of n → π* and π → π* of the lowest singlet state. Inversion of these two states can be observed when the polarity and the hydrogen-bonding power of the solvent increases, because the n → π* state shifts to higher energy whereas the π → π* state shifts to

lower energy. This results in decrease fluorescence intensity because radiative emission from n → π* states is known to be less efficient than from π → π* states.

However in Figure 3.12, compounds (**55)** and **(56)** exhibit at the highest fluorescence intensity in hexane which is a non-polar solvent. It is believe that the occurrence of an electronic transition in a solute requires a finite transition dipole which polarizes the surrounding solvent shell.[47] As a result high fluorescence intensity was observed.

Table 3.10 shows the fluorescence characteristic of 2-(2-methoxyphenoxy)pyrimidine **(37),** 2-(4-methoxyphenoxy)pyrimidine **(39)**, 2-(2-methoxyphenoxy)pyrazine **(55)** , and 2-(4-methoxyphenoxy)pyrazine **(56)** in various solvents in capped condition.

Table 3.10: Fluorescence characteristic of 2-(2-methoxyphenoxy)pyrimidine (37), 2-(4-methoxyphenoxy)pyrimidine (39), 2-(2-methoxyphenoxy)pyrazine (55), and 2-(4-methoxyphenoxy)pyrazine (56) in various solvents in capped condition. (Concentration: 4.95 x 10^{-4} M)

Compound	Solvent	Excitation wavelength (nm)	Fluorescence wavelength (nm)	Intensity
2-(4-methoxyphenoxy)pyrimidine **(39)**	ethanol	201	388	61.91
	acetonitrile	203	323	469.05
	tetrahydrofuran	207	380	149.08
2-(2-methoxyphenoxy)pyrimidine **(37)**	ethanol	260	312	43.99
	acetonitrile	201	355	50.97
	tetrahydrofuran	203	389	41.57
2-(2-methoxyphenoxy)pyrazine **(55)**	ethanol	214	359	2.70
	acetonitrile	203	361	49.61
	tetrahydrofuran	203	381	18.78
2-(4-methoxyphenoxy)pyrazine **(56)**	ethanol	200	377	12.15
	acetonitrile	201	379	31.65
	tetrahydrofuran	204	401	37.68

Figure 3.14 and Figure 3.15 show the histogram of fluorescence intensity between phenoxypyrimidines and phenoxypyrazines respectively.

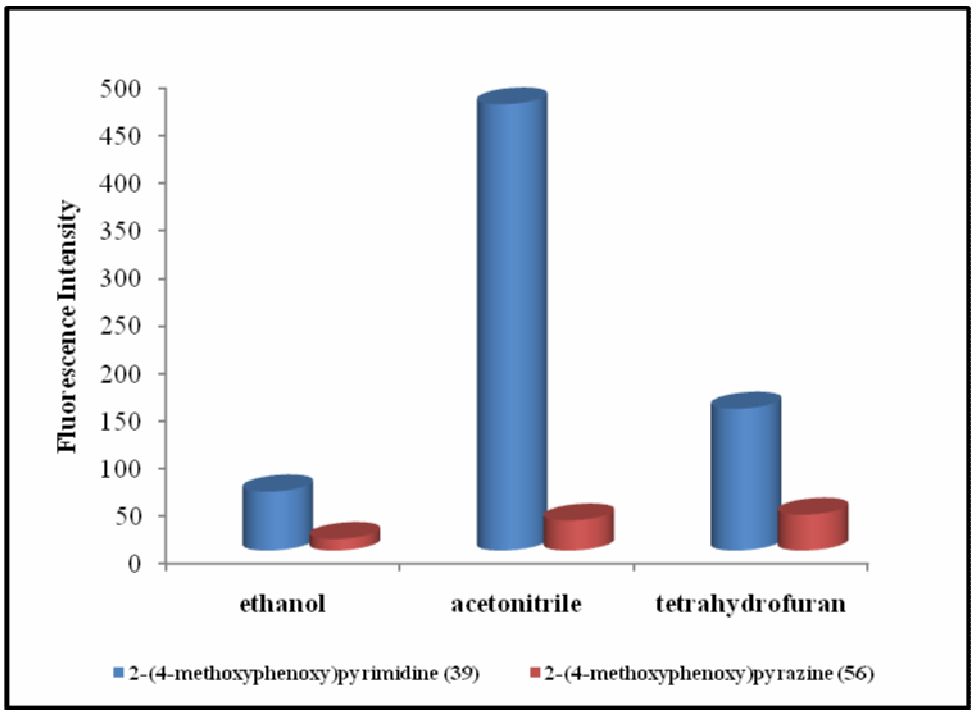


Figure 3.14: Fluorescence of 2-(4-methoxyphenoxy)pyrimidine (39) and 2-(4-methoxyphenoxy)pyrazine (56) in ethanol, acetonitrile and tetrahydrofuran.

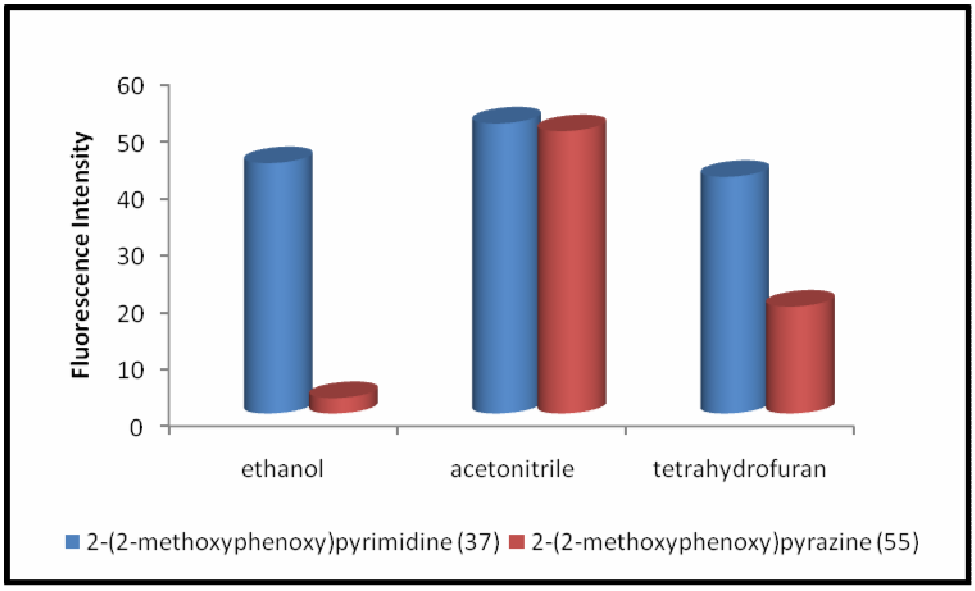


Figure 3.15: Fluorescence of 2-(2-methoxyphenoxy)pyrimidine (37) and 2-(2-methoxyphenoxy)pyrazine (55) in ethanol, acetonitrile and tetrahydrofuran.

2-(4-Methoxyphenoxy)pyrimidine **(39)** gave higher fluorescence intensity than 2-(4-methoxyphenoxy)pyrazine **(56)** in ethanol, acetonitrile and tetrahydrofuran

respectively as shown in Figure 3.14. The same pattern observed for 2-(2-methoxyphenoxy)pyrimidine **(37)** and 2-(2-methoxyphenoxy)pyrazine **(55).** From the results obtained, 1, 3 methoxyphenoxydiazine derivatives gave a higher fluorescence intensity than 1, 4 methoxyphenoxydiazine i.e pyrazine derivatives.

The possible explanation for this result might be due to the position of the nitrogen atoms in the heterocyclic ring as shown in Figure 3.16. In pyrimidine, oxygen atom binds to carbon which is *ortho* to two nitrogen atoms of pyrimidine ring. Since oxygen is an electron donor, thus it activated both *ortho* nitrogen atoms of pyrimidine. On the other hand, in pyrazine, the oxygen is bind to carbon which is *meta* and *ortho* to nitrogen atoms of pyrazine ring. Thus, the position of nitrogen atoms in the ring plays an important factor to be considered in studying the fluorescence behavior of organic compounds.

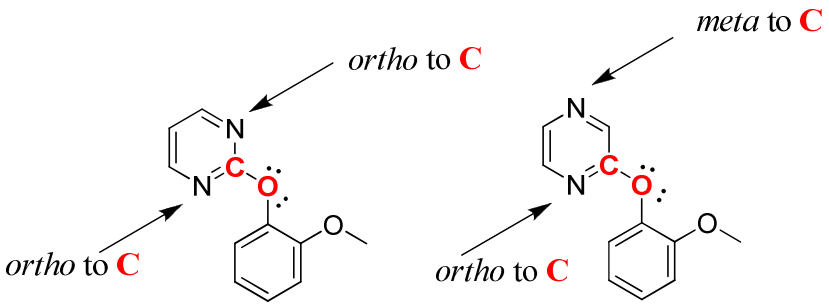


Figure 3.16: The position of the nitrogen atoms in compound (37) and (55)

Table 3.10 also shows compound **(39)** gave a higher fluorescence intensity than compound **(37)**. The low fluorescence intensity recorded for compound **(37)** is possibly due to interference between the solvent and the *ortho* methoxy substituent as shown in Figure 3.17. This interference can result in the steric hindrance, and such interference did not occur in compound **(39)**. The steric hindrance created by the *ortho* methoxy

group enhanced by the formation of hydrogen bonding with the solvent as shown in Figure 3.17.[48]

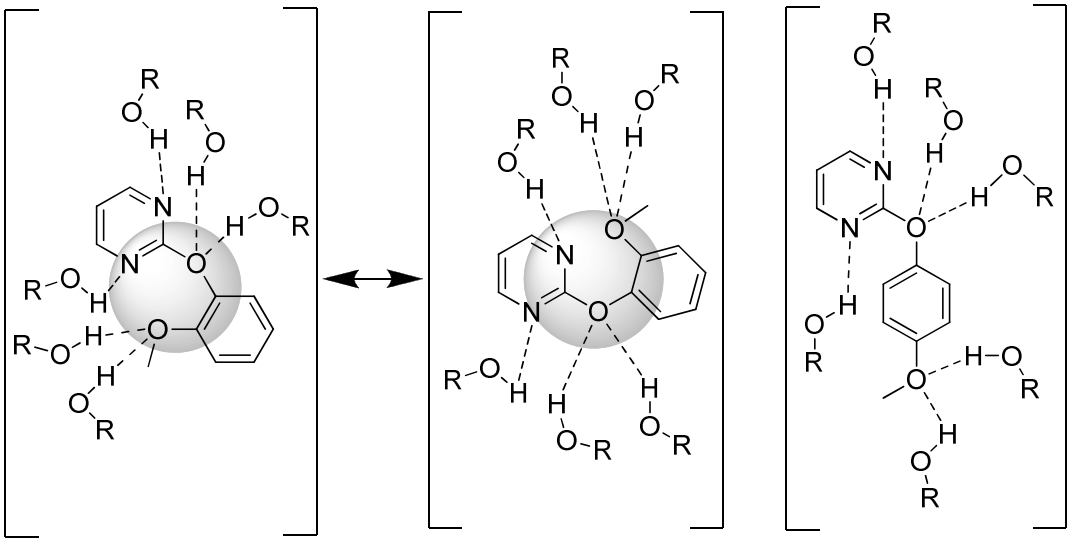


Figure 3.17: Steric hindrance effect by *ortho* and *para* methoxy substituent

Similar observations were recorded for compounds **(55)** and **(56),** except when acetonitrile was used as the solvent. Different observation with acetonitrile was due to the non-hydrogen bonding character of acetonitrile.

In order to support the previous result on the steric hindrance effect, 2-(*o*-tolyloxy)pyrimidine **(45)** and 2-(*p*-tolyloxy)pyrimidine **(51)** were synthesized. The fluorescence characteristics of **(45)** and **(51)** were as shown in Table 3.11 and Figure 3.18.

Table 3.11: Fluorescence characteristic of 2-(*o*-tolyloxy)pyrimidine (45) and 2-(*p*-tolyloxy)pyrimidine (51) in ethyl acetate and acetonitrile in capped condition. (concentration: 5.376 x 10^{-4} M)

Compound	Solvent	Excitation wavelength (nm)	Fluorescence wavelength (nm)	Intensity
2-(*o*-tolyloxy)pyrimidine **(45)**	Ethyl acetate	210	351	13.51
	acetonitrile	205	389	15.88
2-(*p*-tolyloxy)pyrimidine **(51)**	Ethyl acetate	200	358	35.31
	acetonitrile	204	366	29.67

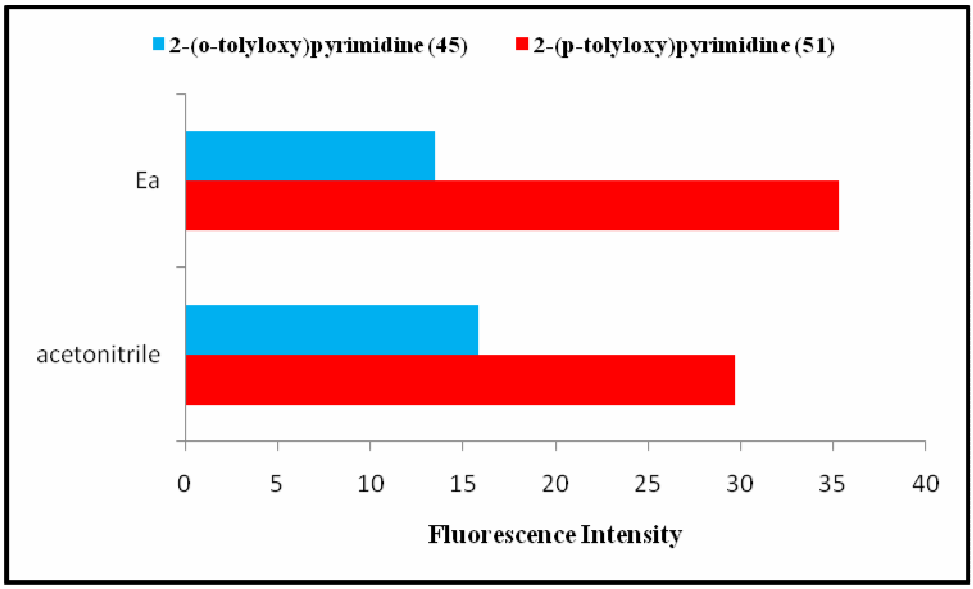


Figure 3.18: Fluorescence characteristic of 2-(*p*-tolyloxy)pyrimidine (51) and 2-(*o*-tolyloxy)pyrimidine (45) in ethyl acetate and acetonitrile in capped condition.

It can be seen from Table 3.11 and Figure 3.18 that compound **(51)** showed higher fluorescence intensity than compound **(45)** in ethyl acetate and acetonitrile. Thus the observation is in the agreement with previously recorded for compounds **(37)** and **(39)**.

Table 3.12 and Figure 3.19 show fluorescence characteristics of 2-(*p*-methoxyphenoxy)pyrimidine **(39)** and 2-(*m*-methoxyphenoxy)pyrimidine **(43)** in various of solvents. Compound **(39)** showed a higher fluorescence intensity compare to compound **(43).**

Table 3.12: Fluorescence characteristic of 2-(4-methoxyphenoxy)pyrimidine (39) and 2-(3-methoxyphenoxy)pyrimidine (43) in various solvents in capped condition. (concentration: 4.95 x 10^{-4} M)

Compound	Solvent	Excitation wavelength (nm)	Fluorescence wavelength (nm)	Intensity
2-(4-methoxyphenoxy)pyrimidine **(39)**	Hexane	350	380	95.38
	Ethanol	201	388	61.91
	Acetonitrile	203	323	469.05
	Ethyl acetate	204	392	130.11
	Tetrahydrofuran	207	380	149.08
2-(3-methoxyphenoxy)pyrimidine **(43)**	Hexane	201	359	59.55
	Ethanol	213	379	15.04
	Acetonitrile	204	364	10.39
	Ethyl acetate	209	349	28.84
	Tetrahydrofuran	202	344	61.83

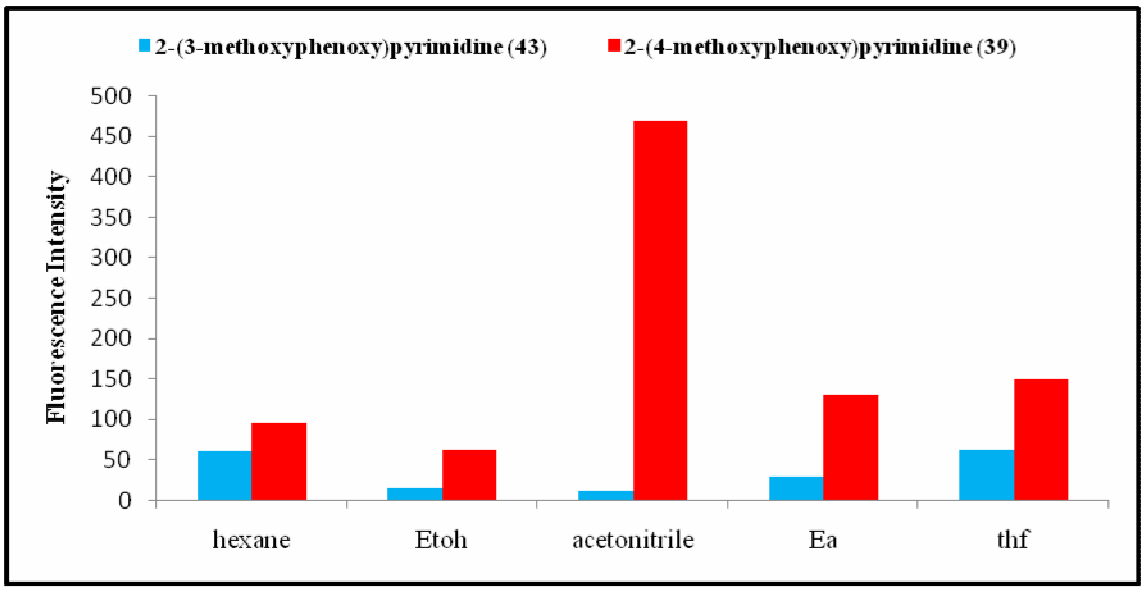


Figure 3.19: Fluorescence characteristic of 2-(4-methoxyphenoxy)pyrimidine (39) and 2-(3-methoxyphenoxy)pyrimidine (43) in various solvents in capped condition.

It seems that methoxyphenoxypyrimidine with a *para* substituent gave a higher fluorescence intensity than with *meta* substituent. As shown in Figure 3.20, the methoxy group which is an electron donating at the *para* position**,** is more effective at transferring electron to the pyrimidine ring which in turn increasing its hydrogen-bond basicity and retention, i.e *para* methoxy group has more negative value of the Hammet σ-parameter[49] than does a *meta* methoxy group. As the result, compound **(39)** gave higher fluorescence intensity than compound **(43)**.

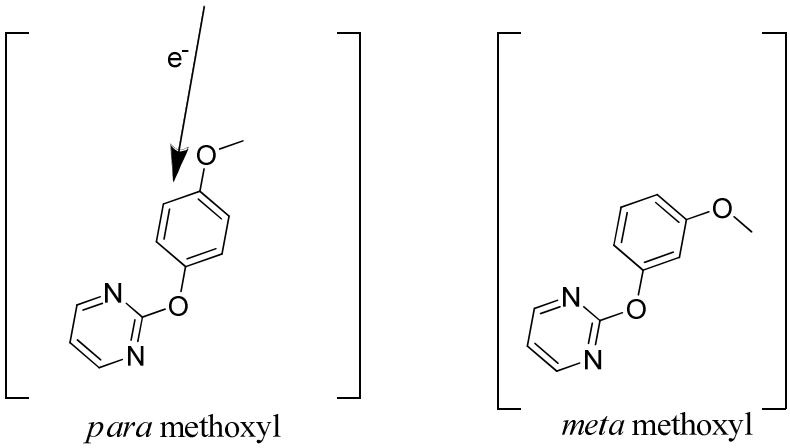
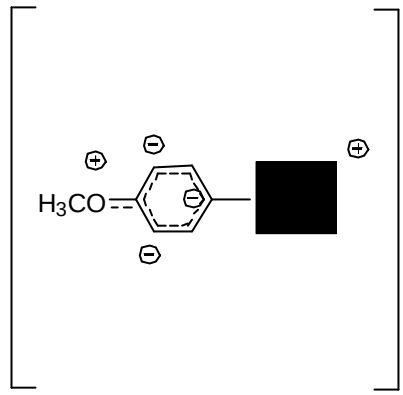
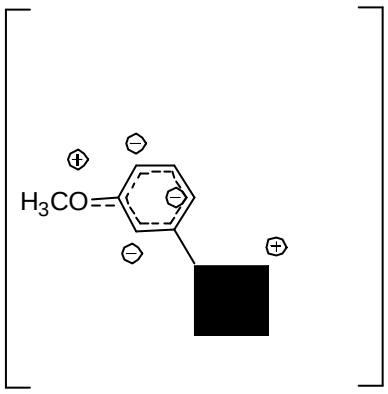


Figure 3.20: *Para* position is more effective than *meta* position in transferring electron to the pyrimidine ring

Apart from the effectiveness in transferring electron to pyrimidine system, a resonance electron-donating engenders partial negative charge at position *ortho* and *para* to itself as shown in Figure 3.21. The *para* charge stabilized a positive charge at the pyrimidine ring.[50] But the resonance effect of a *meta* methoxy is very much less compared to *para* position, thus *meta* methoxy in compound **(43)** gave low fluorescence intensity.



resonance effect at para position



resonance effect at meta position

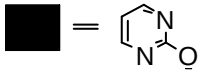


Figure 3.21: Resonance effect at *para* and *meta* position

Table 3.13 and Figure 3.22 show the fluorescence characteristic of 2-phenoxypyrimidin-4-amine **(53)** and 2-phenoxypyrimidine **(41)** in various of solvents. 2-Phenoxypyrimidin-4-amine **(53)** shows a higher fluorescence intensity than 2-phenoxypyrimidine **(41)** in ethanol, acetonitrile, tetrahydrofuran, hexane and ethyl acetate respectively.

Table 3.13: Fluorescence characteristic of 2-phenoxypyrimidin-4-amine (53) (5.348×10^{-4} M) and 2-phenoxypyrimidine (41) (5.814×10^{-4} M) in various of solvents.

Compound	Solvent	Excitation wavelength (nm)	Fluorescence wavelength (nm)	Intensity
2-phenoxypyrimidine **(41)**	Hexane	340	366	75.41
	Ethanol	201	381	16.61
	Acetonitrile	205	370	53.75
	Ethyl acetate	201	362	59.53
	tetrahydrofuran	345	369	111.00
2-phenoxypyrimidin-4-amine **(53)**	Hexane	203	358	274.44
	Ethanol	328	360	916.56
	Acetonitrile	212	372	431.18
	Ethyl acetate	204	324	830.94
	tetrahydrofuran	226	332	274.35

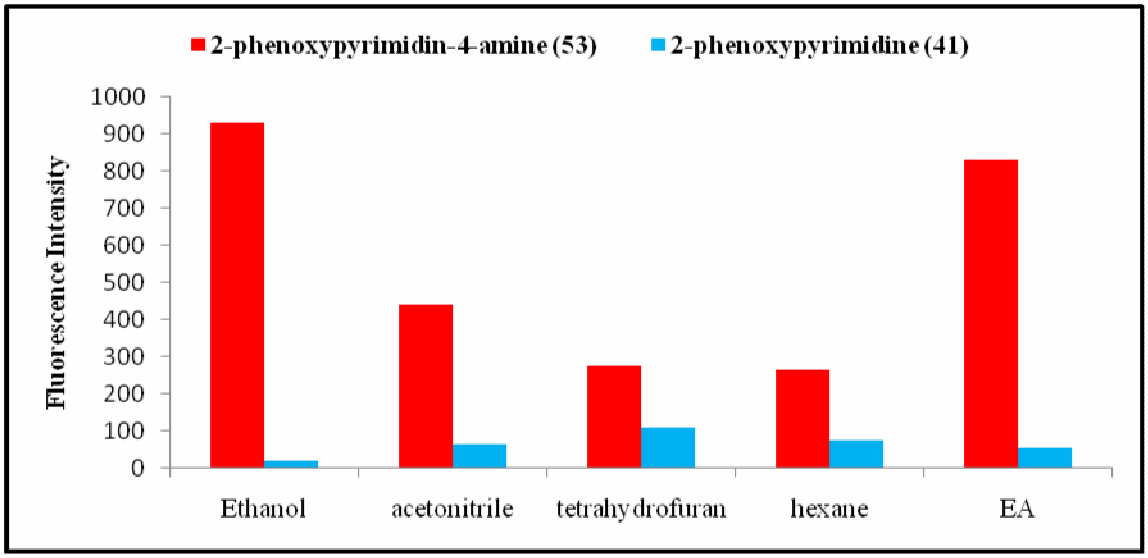


Figure 3.22: Fluorescence characteristic of 2-phenoxypyrimidine (41) and 2-phenoxypyrimidin-4-amine (53) in various of solvents.

In this study, most of the synthesised compounds do not have any substituent on the diazine ring. However, only compound **(53)** has an amino substituent on the pyrimidine ring. Generally, heterocyclic compound is electron-riched compound. The

presence of amino substituent, which is a very strong electron donating group gave a very significant result in fluorescence intensity in comparison with compound **(41)**.

Figure 3.22 shows compound **(53)** has higher fluorescence intensity than compound **(41)**. This observation is due to the hyperchromic effect, which leads to an increase in emission intensity. The introduction of an amino group as auxochrome in compound **(53)** causes the hyperchromic shift.[51]

The $\pi \rightarrow \pi^*$ transition of polar compound **(53)** are shifted to longer wavelengths and generally towards higher intensity with an increase in solvent polarity. The excited state in this transition is more polar than the ground state. The dipole-dipole interaction with polar solvent lowers the energy of the excited state. Thus, there is a bathochromic shift on-going from hexane (358 nm) to acetonitrile (372 nm) as a result of increasing solvent polarity as shown in Table 3.13.

High fluorescence intensity which was recorded for 2-phenoxypyrimidin-4-amine **(53)** as compared to 2-phenoxypyrimidine **(41)** is may also due to the effect of twisted intramolecular charge transfer (TICT).[52] In ground state, **(53)** is believed to be planar, thus the conjugation between the amino group and the pyrimidine ring is at a maximum. This geometry is retained in the excited states. However, there is also a special excited state in which the amino group is twisted at a right angle so that conjugation is totally lost in this TICT state, thus there is total charge separation between the amino group and the pyrimidine ring as shown in Figure 3.23.

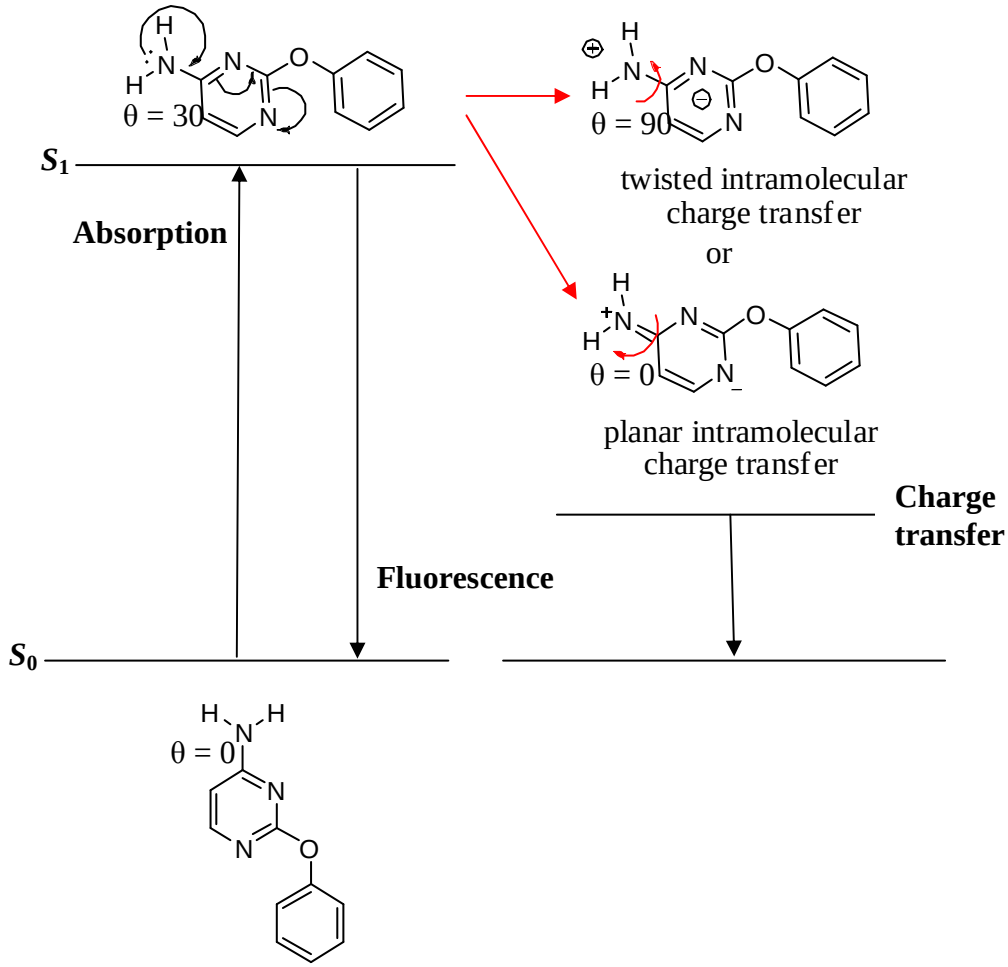


Figure 3.23: Twisted Intramolecular Charge Transfer (TICT) effect on compound (53)

The TICT state cannot be reached by direct light absorption since its geometry is totally different from that of ground state. It was formed by the 'slow' twisting of the two parts of the molecule from planar S_1 state. The TICT state has large dipole moment. Electrostatic interaction between the molecular dipole moment and polar solvents stabilize the twisted form and new emission with high intensity appears which is not observed in non-polar solvent.

Table 3.14: Fluorescence characteristic of 2-(3-methoxyphenoxy)pyrimidine (43) (4.95×10^{-4} M) and 2-(3- nitrophenoxy)pyrimidine (49) (4.608×10^{-4} M) in various solvents.

Compound	Solvent	Excitation wavelength (nm)	Fluorescence wavelength (nm)	Intensity
2-(3-methoxyphenoxy)pyrimidine **(43)**	Hexane	201	359	59.55
	Ethanol	213	379	15.04
	Acetonitrile	204	364	10.39
	Ethyl acetate	209	349	16.69
	tetrahydrofuran	202	344	61.83
2-(3- nitrophenoxy)pyrimidine **(49)**	Hexane	205	382	6.34
	Ethanol	382	398	8.72
	Acetonitrile	**X**	**X**	**X**
	Ethyl acetate	208	352	5.73
	tetrahydrofuran	205	404	25.41

X = not fluorescent

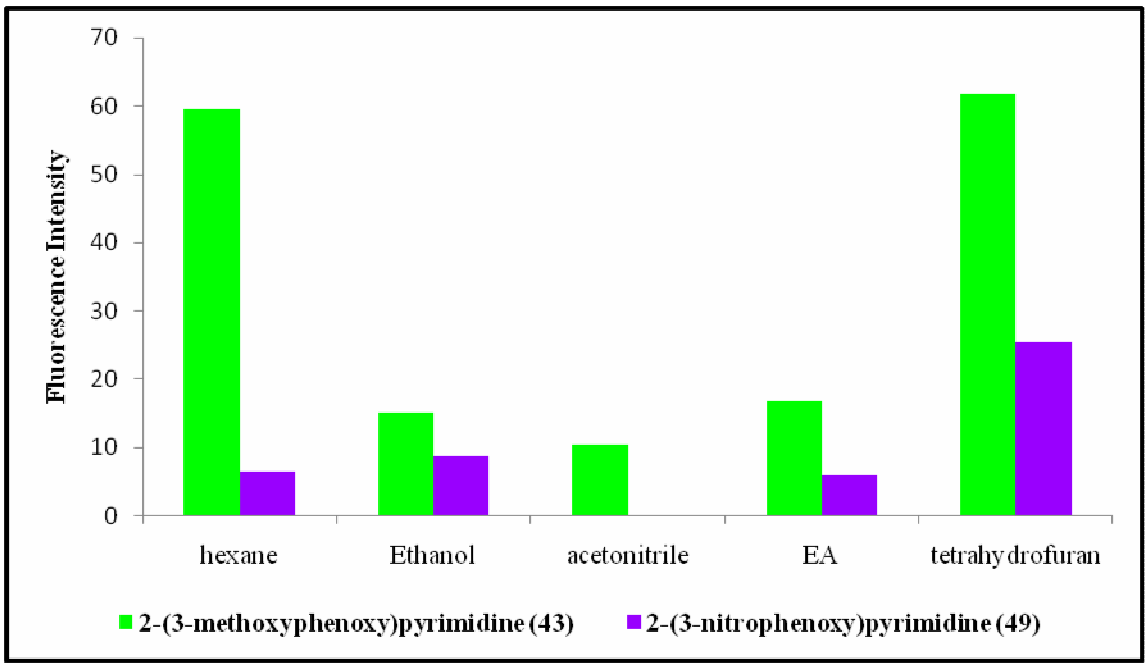


Figure 3.24: Fluorescence characteristic of 2-(3-methoxyphenoxy)pyrimidine (43) and 2-(3- nitrophenoxy)pyrimidine (49) in various solvents.

Table 3.14 and Figure 3.24 show fluorescence intensity 2-(3-methoxyphenoxy)pyrimidine **(43)** and 2-(3-nitrophenoxy)pyrimidine **(49)** in various solvents. Compound **(43)** showed a high fluorescence intensity in all solvents whilst compound **(49)** showed low fluorescence intensities in all solvents.

In general, substitution with electron-donating groups induces an increase in the molar absorption coefficient and shift in both absorption and fluorescence spectra. The presence of lone pairs of electrons on the oxygen and nitrogen atoms does not change the $\pi \rightarrow \pi^*$ nature of the transitions of the parent molecule. These lone pairs are indeed involved directly in π bonding with the aromatic system.

Compound **(43)** gave a high fluorescence intensity which is believed to be due to the hyperchromic shift.[53] The introduction of the auxochromes, [54] i.e methoxy group, leads to an increase in intensity. Other than that, methoxy group which is an electron donating group observed enhances the electron density of the aromatic system hence,

high intensity is observed. Low fluorescence intensity was observed with compound **(49)** is due to hypochromic effect. The presence of a nitro group, an electron withdrawing in compound **(49)** distorted the chromophore by forcing the rings out of coplanarity resulting in the loss of conjugation.

Table 3.15 and Figure 3.25 show fluorescence characteristic of compound **(35)**, **(37)**, **(45)** and **(47)** in various solvents. Compound **(37)** showed the highest fluorescence intensity followed by compound **(47)** and compound **(45)** showed the lowest fluorescence intensity. The entire compounds showed this pattern in ethanol, acetonitrile and ethyl acetate.

Table 3.15: Fluorescence characteristic of 2-chloropyrimidine (35) (8.772×10^{-4} M), 2-(*o*-tolyloxy)pyrimidine (44) (5.3763×10^{-4} M), 2-(2-methoxyphenoxy)pyrimidine (46) (4.95×10^{-4} M), and 2-(pyrimidin-2-yloxy)phenol (48) (5.3191×10^{-4} M) in various solvents.

Compound	Solvent	Excitation wavelength (nm)	Fluorescence wavelength (nm)	Intensity
2-chloropyrimidine **(35)**	Hexane	204	327	103.58
	Ethanol	205	370	460.50
	Acetonitrile	225	363	587.71
	Ethyl acetate	206	370	460.50
	tetrahydrofuran	203	364	29.43
2-(2-methoxyphenoxy)pyrimidine **(37)**	Hexane	326	358	79.94
	Ethanol	260	312	43.99
	Acetonitrile	201	316	75.67
	Ethyl acetate	210	327	7.96
	tetrahydrofuran	203	340	75.37
2-(*o*-tolyloxy)pyrimidine **(45)**	Hexane	324	361	66.52
	Ethanol	207	328	12.70
	Acetonitrile	205	318	32.98
	Ethyl acetate	210	313	31.81
	tetrahydrofuran	202	331	124.93
2-(pyrimidin-2-yloxy)phenol **(47)**	Hexane	201	359	92.87
	Ethanol	200	352	29.00
	Acetonitrile	202	357	96.78
	Ethyl acetate	201	322	191.87
	tetrahydrofuran	208	349	70.26

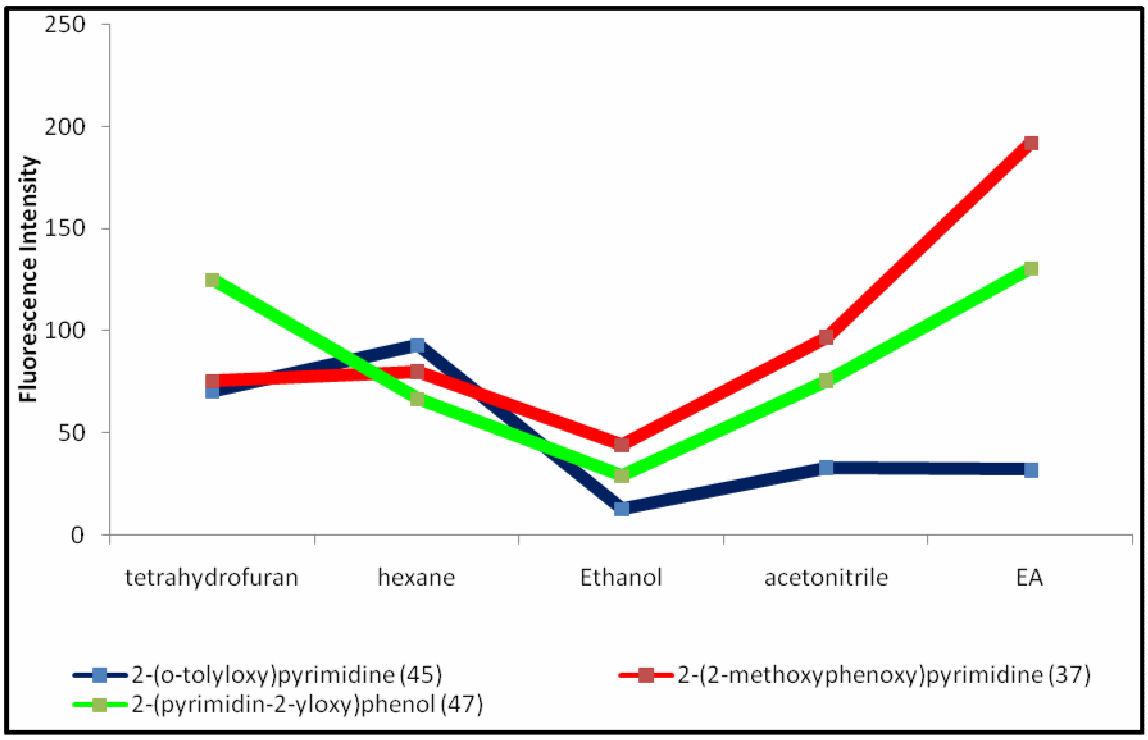


Figure 3.25: Fluorescence characteristic of 2-(2- methoxyphenoxy)pyrimidine (37), 2-(*o*-tolyloxy)pyrimidine (45), and 2-(pyrimidin-2-yloxy)phenol (47) in various solvents.

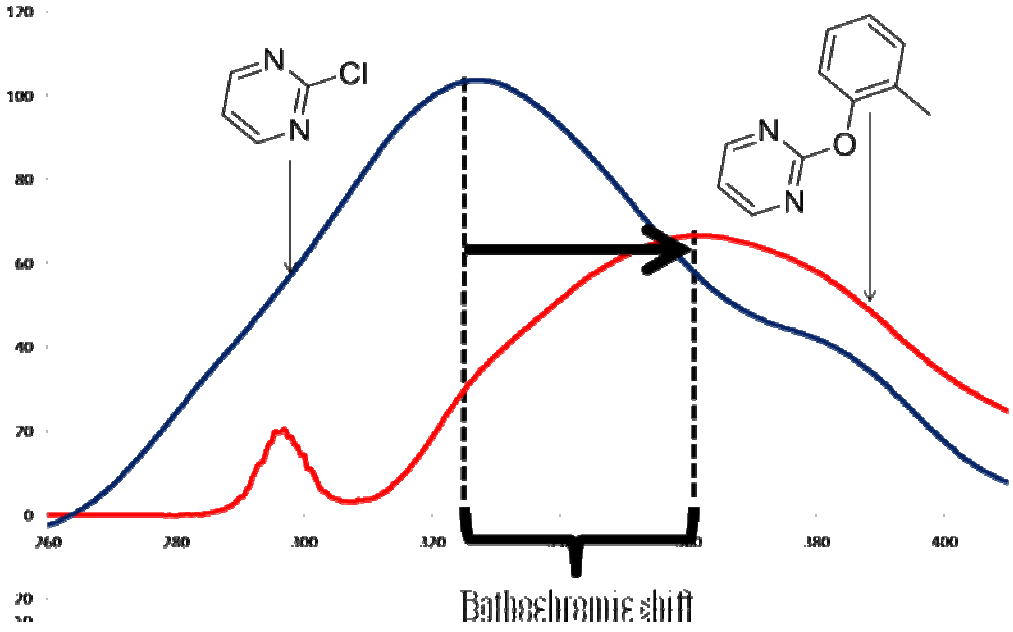


Figure 3.26: Bathochromic shift between 2-chloropyrimidine (35) (8.772 x 10^{-4} M) and 2-(*o*-tolyloxy)pyrimidine (45) (5.3763 x 10^{-4} M) in hexane.

Figure 3.26 showed a bathochromic shift occurred between 2-chloropyrimidine **(35)** and 2-(tolyloxy)pyrimidine **(45)**. This is due to the presence of an auxochrome which generally increases the value of excitation by extending the conjugation through resonance. This phenomena is also called 'colour enhancing groups'. [55]

The combination of chromophore and auxochrome sometimes behaves as a new chromophore having different values of emission maximum. Table 3.15 shows **(35)** in hexane shows emission wavelength at 327 nm whereas compounds **(37)**, **(45)**, and **(47)** show emissions wavelengths of 361 nm, 358 nm and 359 nm respectively. The shift of emission wavelength to a longer wavelength is due to a bathochromic shift.[56] The increase in the wavelengths proves that $-OCH_3$, -OH and $-CH_3$ substituents each as auxochrome which extends the conjugation, hence resulting in the increase values of emission wavelength.

This finding is supported by the work of Kiss, Molnar and Sandorfy, who have pointed out that the magnitude of the shift in the absorption bands produced by methoxy, hydroxyl and methyl substituents may correlated with the degree of conjugation of these groups.[57]

The effects of auxochrome on the fluorescence of the synthesised compound are listed in Table 3.15. There are exceptions to this table since a number of other factors must be considered. For example, molecules which are able to rotate, bend or twist have a tendency to lose energy from the excited state through molecular collision and other vibration processes. It is not possible to complete set rules for determining whether a molecule will fluoresce, as there are many anomalies to be considered.

Table 3.16 shows the fluorescence characteristic of compound **(37)**, **(41)**, **(55)** and **(56)** with time in THF. The measurements were taken immediately, 30 minutes and 60 minutes.

Table 3.16: Fluorescence characteristic of selected diazine derivatives with time in THF

Compound	Duration	Excitation Wavelength (nm)	Fluorescence Wavelenghth (nm)	Intensity
2-(2-methoxyphenoxy)pyrimidine **(37)**	Immediately	310	359	49.91
	30		358	45.21
	60		358	41.24
2-(2-methoxyphenoxy)pyrazine **(55)**	Immediately	316	437	75.84
	30		437	73.6
	60		436	71.46
2-(4-methoxyphenoxy)pyrazine **(56)**	Immediately	325	452	67.04
	30		450	63.01
	60		451	58.82
2-phenoxypyrimidine **(41)**	Immediately	389	438	20.81
	30		439	20.28
	60		439	19.46

The study on the possible delayed fluorescence was carried out by measuring the fluorescence characteristic of the selected compounds in capped condition with time. Four compounds i.e compounds **(37)**, **(41)**, **(55)**, and **(56)** were selected. The fluorescence measurements of these compounds were carried out immediately, after 30 minutes and after 60 minutes respectively as shown in Table 3.16

2-(2-Methoxyphenoxy)pyrimidine **(37)** and 2-(4-methoxyphenoxy)pyrazine **(56)** showed a decrease in fluorescence intensity with time as shown in Figure 3.27 and

Figure 3.28. Similar pattern was observed with compounds **(41)** and **(55)** as shown in Figures 3.29 and 3.30.

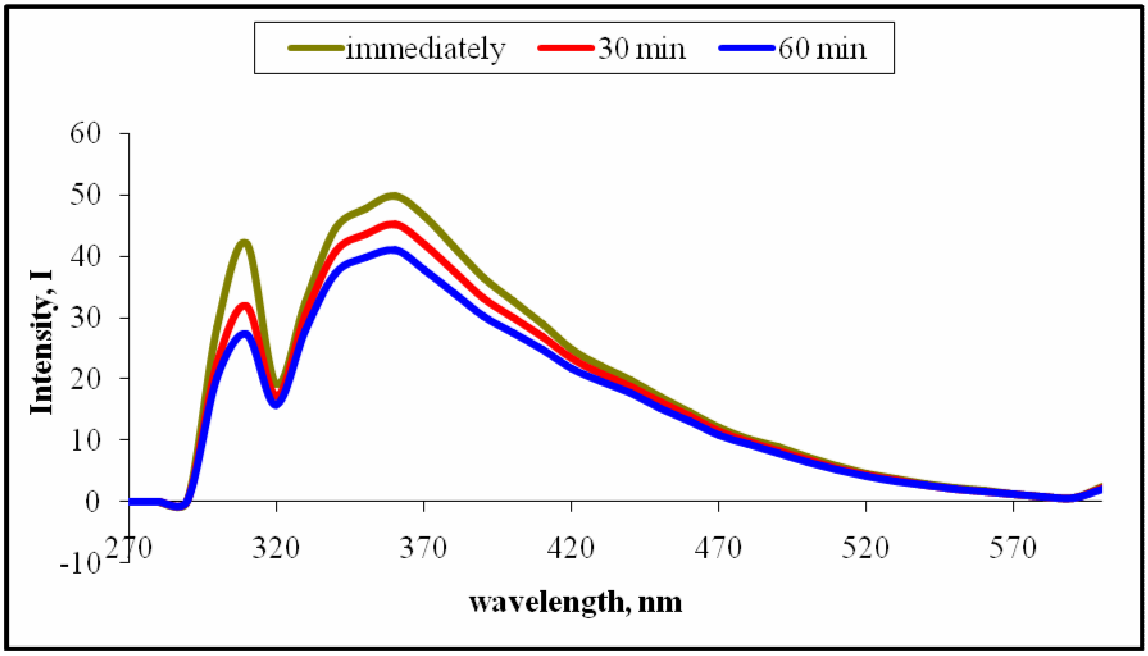


Figure 3.27: Fluorescence spectra of 2-(2-methoxyphenoxy)pyrimidine (37) in different time in tetrahydrofuran (4.9505 x 10^{-4} M)

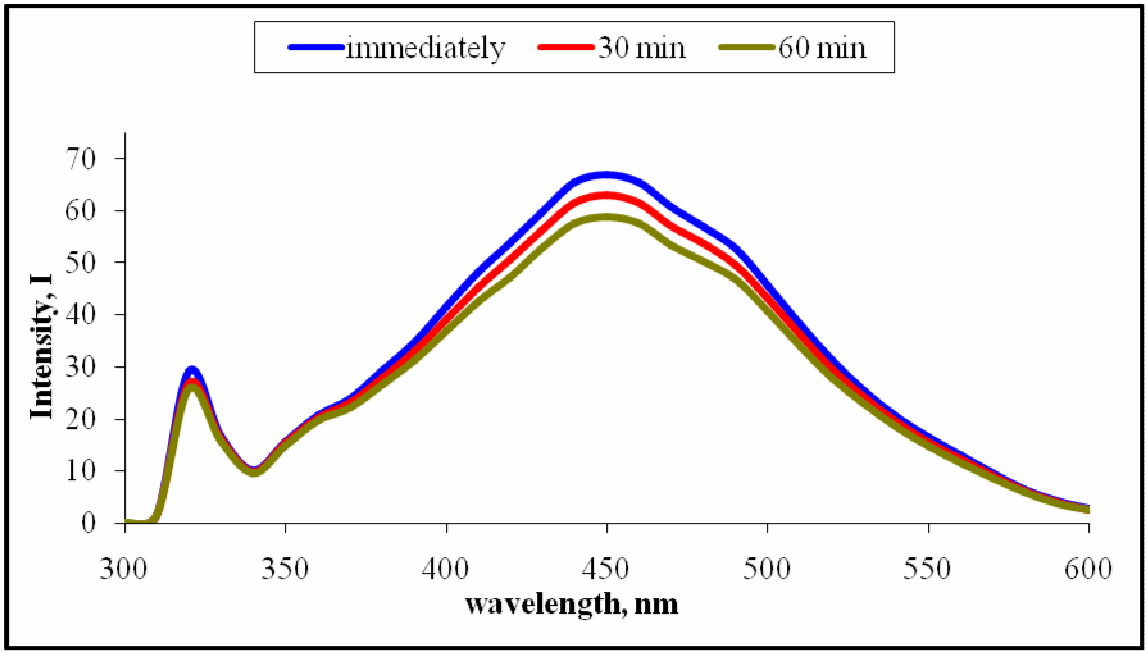


Figure 3.28: Fluorescence spectra of 2-(4-methoxyphenoxy)pyrazine (56) in different time in tetrahydrofuran (4.9505 x 10^{-4} M)

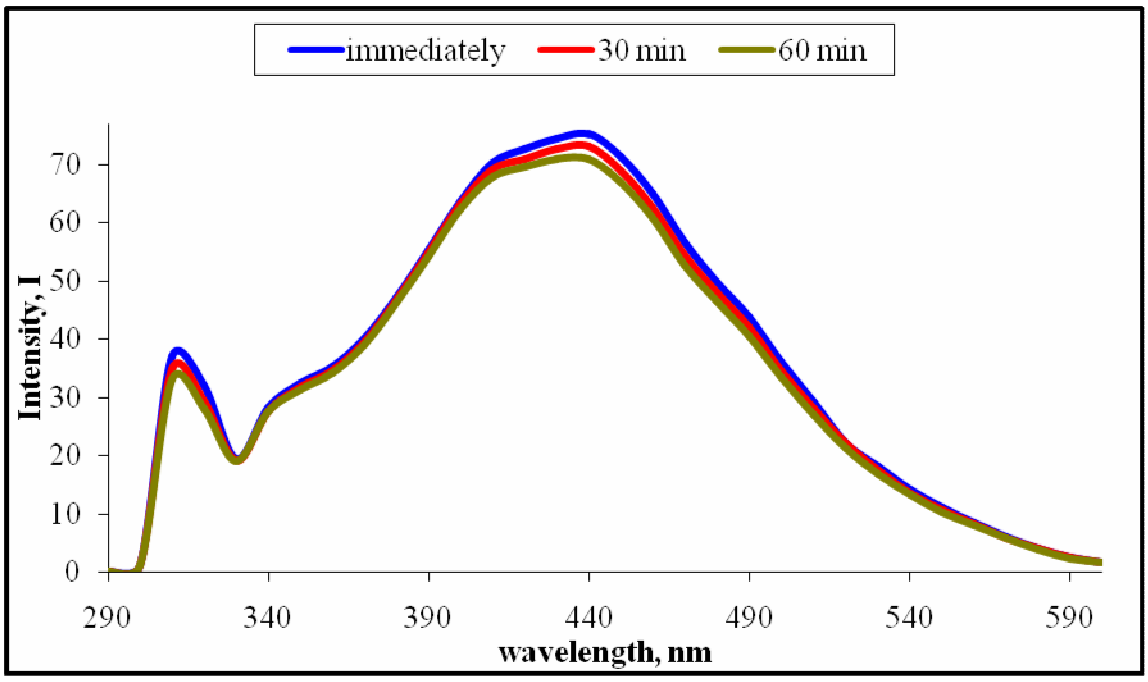


Figure 3.29: Fluorescence spectra of 2-(2-methoxyphenoxy)pyrazine (55) in different time in tetrahydrofuran (4.9505x 10^{-4} M)

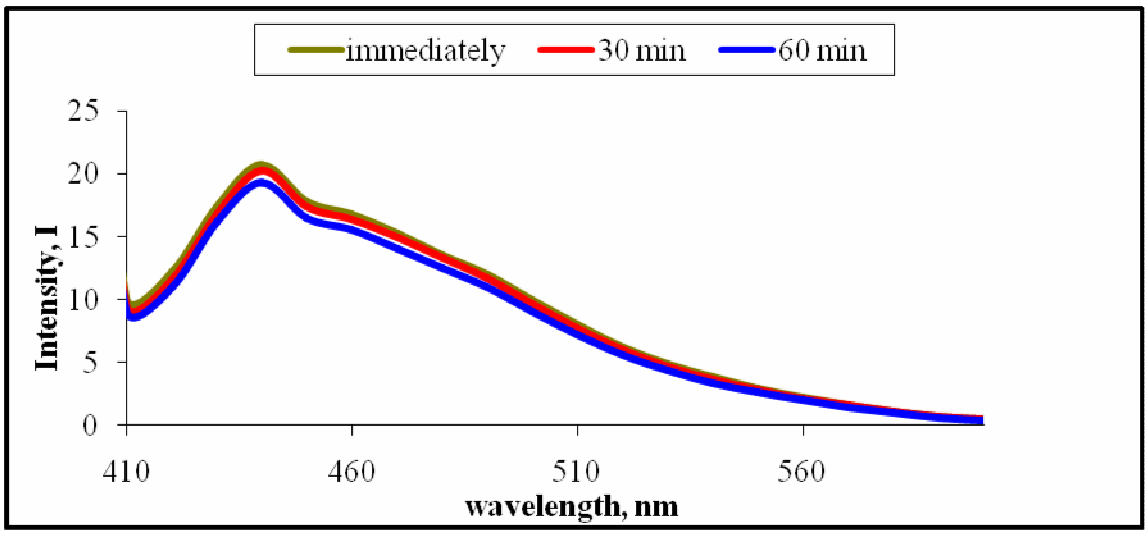


Figure 3.30: Fluorescence spectra of 2-phenoxypyrimidine (41) in different time in tetrahydrofuran (3.8314 x 10^{-4} M)

In liquid solutions, quenching of excited-singlet states of organic molecules by dissolved O_2 molecule has a very large diffusion co-efficient. As the solution was allowed to stand for 30 and 60 minutes, more oxygen entered in the solution and quenched the fluorescence further.

In this study, it is possible that 'chemical' quenching also occurred through the formation of a complex between solute and oxygen. Under atmospheric pressure, the concentration of oxygen in most solvents is $10^{-3} – 10^{-4}$ mol L^{-1}.[58]

Another possible explanation for the reduction of fluorescence intensity with time is the formation of a complex between oxygen and the ground state of the organic compound as the solution was allowed to stand for a certain period of time. When the emission process happened, the oxygen complex may enhance $S_1 \rightarrow S_0$ internal conversion hence quenched the fluorescence intensity. Tables 3.17, 3.18 and 3.19 show fluorescence characteristics of 2-(pyrimidin-2-yloxy)phenol **(47)**, 2-phenoxypyrimidine **(41)** and 2-(4-methoxyphenoxy)pyrimidine **(39)** with different concentrations.

Table 3.17: Fluorescence characteristic of 2-(pyrimidin-2-yloxy)phenol (47) in different concentrations

Solvent	Excitation wavelength (nm)			Fluorescence wavelength (nm)			Intensity		
	10^{-4} M	10^{-5} M	10^{-6} M	10^{-4} M	10^{-5} M	10^{-6} M	10^{-4} M	10^{-5} M	10^{-6} M
Hexane	201	202	**X**	360	349	**X**	91.63	162.78	**X**
EtOH	200	**X**	**X**	352	**X**	**X**	24.42	**X**	**X**
CH_3CN	202	202	**X**	356	356	**X**	91.73	25.14	**X**
EtOAc	201	201	201	377	381	**X**	182.77	43.37	**X**
THF	208	208	208	348	353	367	69.30	34.43	17.53

Concentration = 5.3191 x 10^m M, where 10^m M = 10^{-6} M, 10^{-5} M, 10^{-4} M
X = non-fluorescent

Table 3.18: Fluorescence characteristic of 2-phenoxypyrimidine (41) in different concentrations

Solvent	Excitation wavelength (nm)			Fluorescence wavelength (nm)			Intensity		
	10^{-4} M	10^{-5} M	10^{-6} M	10^{-4} M	10^{-5} M	10^{-6} M	10-4 M	10^{-5} M	10^{-6} M
Hexane	340	**X**	**X**	366	**X**	**X**	75.41	**X**	**X**
EtOH	201	201	201	381	374	358	16.61	31.66	67.07
CH_3CN	205	204	205	370	362	354	53.75	35.07	30.88
EtOAc	201	201	203	362	362	375	59.53	32.29	11.68
THF	345	344	345	369	353	**X**	111.00	77.07	**X**

Concentration = 3.8314 x 10^m M, where 10^m M = 10^{-6} M, 10^{-5} M, 10^{-4} M

X = non-fluorescent

Table 3.19: Fluorescence characteristic of 2-(4-methoxyphenoxy)pyrimidine (39) in different concentrations

Solvent	Excitation wavelength (nm)			Fluorescence wavelength (nm)			Intensity		
	10^{-4} M	10^{-5} M	10^{-6} M	10^{-4} M	10^{-5} M	10^{-6} M	10^{-4} M	10^{-5} M	10^{-6} M
Hexane	350	**X**	**X**	380	**X**	**X**	95.38	**X**	**X**
EtOH	201	202	201	388	381	**X**	61.91	35.00	**X**
CH_3CN	203	202	203	323	318	313	469.05	213.77	69.30
EtOAc	204	204	**X**	392	384	**X**	130.11	41.31	**X**
THF	207	**X**	**X**	380	**X**	**X**	149.08	**X**	**X**

Concentration = 4.9505 x 10^m M, where 10^m M = 10^{-6} M, 10^{-5} M, 10^{-4} M

X = non-fluorescent

Figure 3.31, 3.32 and 3.33 show fluorescence spectra of compounds **(39)**, **(41)** and **(47)** at different concentrations.

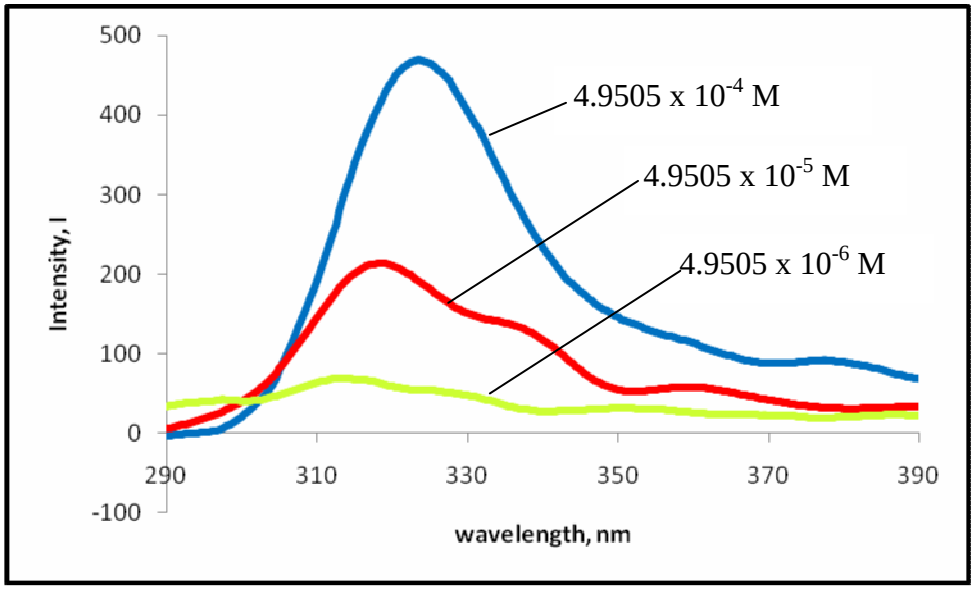


Figure 3.31: Fluorescence spectra of 2-(4-methoxyphenoxy)pyrimidine (39) in different concentration in acetonitrile

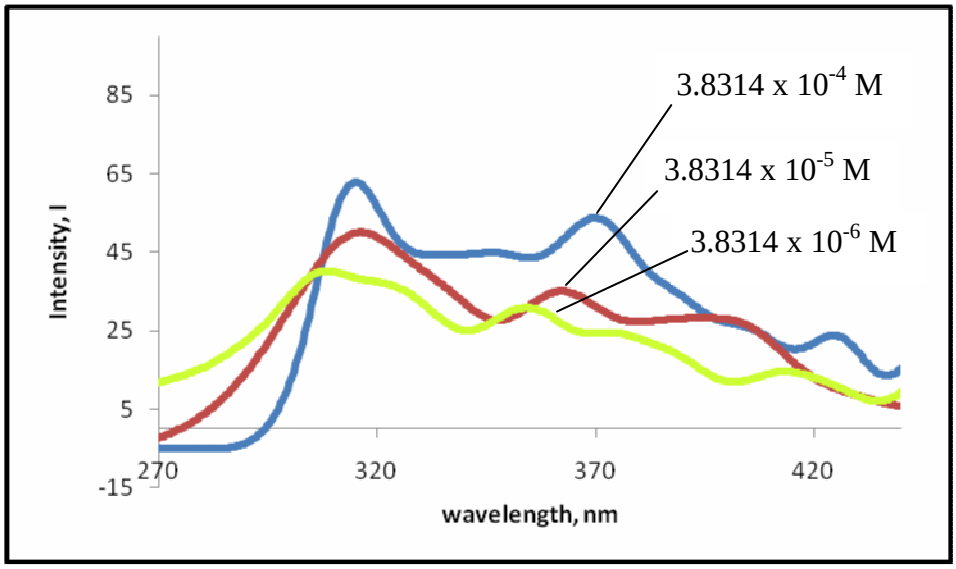


Figure 3.32: Fluorescence spectra of 2-phenoxypyrimidine (41) in different concentration in acetonitrile

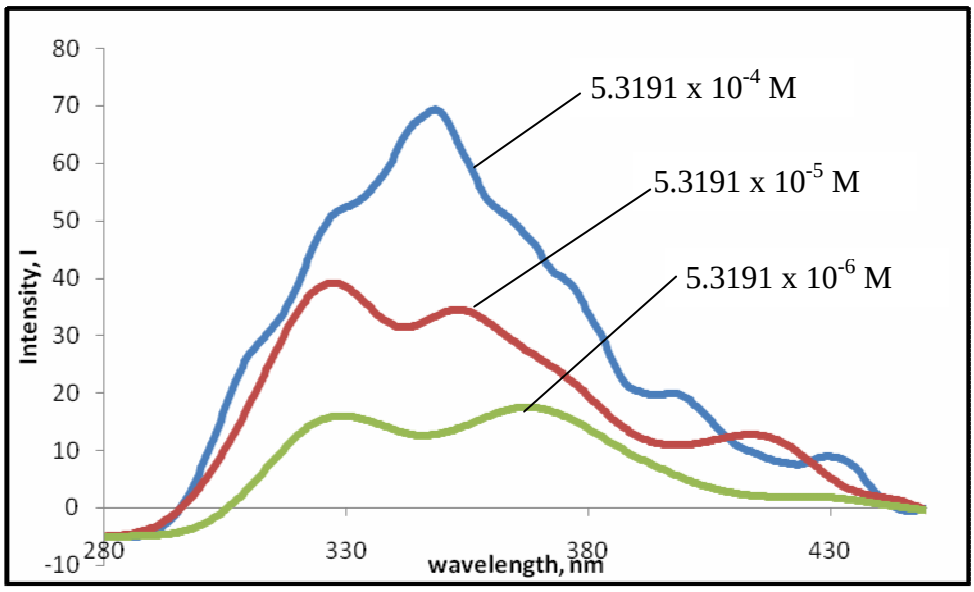


Figure 3.33: Fluorescence spectra of 2-(pyrimidin-2-yloxy)phenol (47) in different concentration in tetrahydrofuran

It has been reported that the fluorescence intensity of a given solute increases linearly with increasing concentration at relatively low concentration. At higher concentrations the fluorescence intensity reached a limiting value and even decrease with further increase in concentration. Several processes are responsible for these "concentration-quenching" effects. This is believed what happens to compounds **(39)**, **(41)** and **(47)** as shown in Figure 3.31, Figure 3.32 and Figure 3.33.

At higher concentrations, the fluorescence intensity of all compounds may reached a limiting value and resulted in concentration quenching which decreased with further increases in concentration.

This is because the low-frequency tail of the absorption spectrum of the compounds often overlaps with the high-frequency end of its fluorescence spectrum, thus fluorescence from electronic excited state molecule can be re-absorbed by a ground-state molecule of the same solute. The probability of such an event increases with increasing of solute concentration. "Self-absorption" distorted the shape of the

fluorescence spectrum, since only the higher frequencies in the spectrum are re-absorbed. Self-absorption ultimately reduced the fluorescence intensity.

The change of pH also affects the fluorescence intensity of the compounds studied. Selected data on fluorescence maxima and intensity with pH of the selected compounds are as summarized in Table 3.20 while their spectra in ethanol are shown in Figure 3.34 and Figure 3.35.

Table 3.20: Fluorescence characteristic of 2-phenoxypyrimidine (41) and 2-(3-methoxyphenoxy)pyrimidine (43) with variation of pH in ethanol

Compound	pH	Excitation wavelength (nm)	Fluorescence wavelength (nm)	Intensity
2-phenoxypyrimidine **(41)**	2	264	346	16.67
	3	206	355	67.29
	7	206	362	108.18
	11	201	360	129.34
	12	201	365	192.43
2-(3-methoxyphenoxy)pyrimidine **(43)**	2	201	365	130.32
	3	202	365	137.58
	7	202	363	170.88
	11	201	381	237.91
	12	202	365	365.48

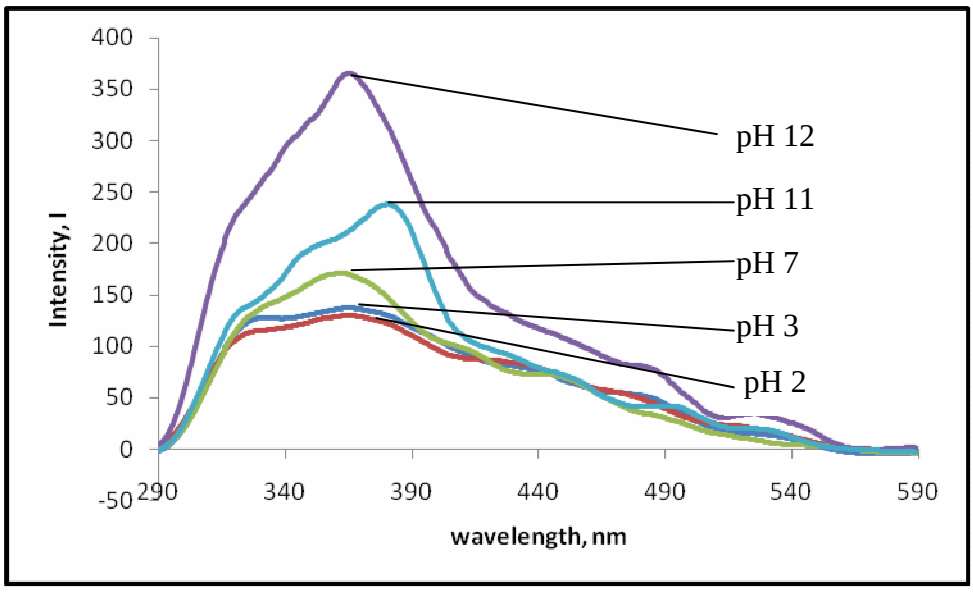


Figure 3.34: Fluorescence spectra of 2-(3-methoxyphenoxy)pyrimidine (43) with variation of pH in ethanol

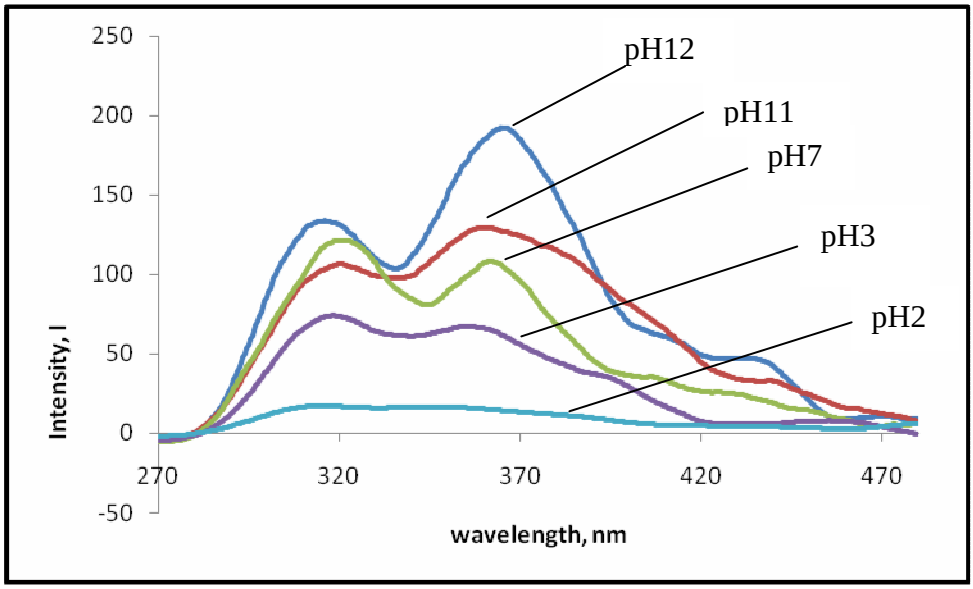


Figure 3.35: Fluorescence spectra of 2-phenoxypyrimidine (41) with variation of pH in ethanol

The fluorescence spectra for 2-phenoxypyrimidine **(41)** and 2-(3-methoxyphenoxy)pyrimidine **(43)** were measured in ethanol under neutral, acidic (0.1 M HCl) and basic (0.1 M NaOH) conditions. Table 3.20 shows that the fluorescence intensity increases with increases pH. The low fluorescence intensity observed in acidic medium is probably due to protonation of the compound. The protonated compound

shows lower fluorescence intensity because it involves the transferring of electron to the phenoxy ring as shown in Figure 3.36 and Figure 3.37.

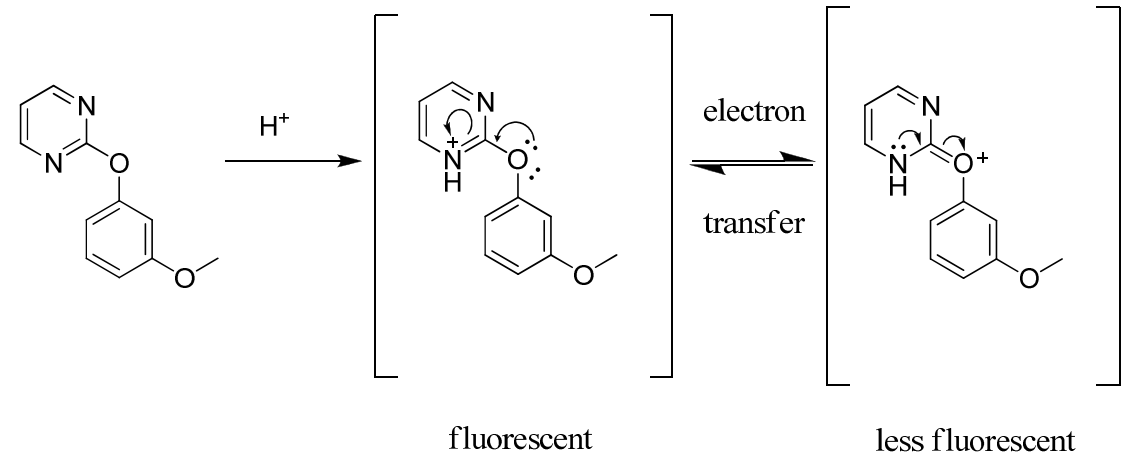


Figure 3.36: The electron transfer to the ring phenoxy of 2-(3-methoxyphenoxy)pyrimidine (43)

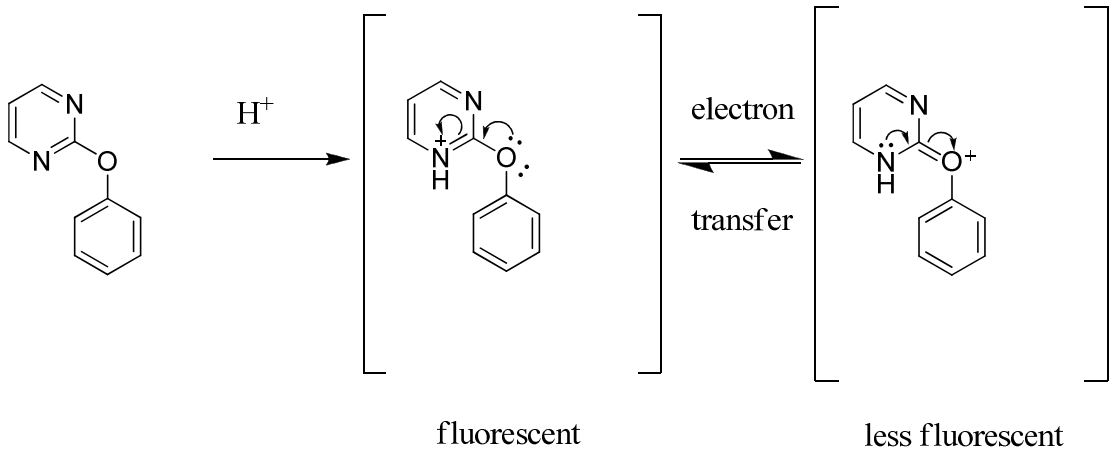


Figure 3.37: The electron transfer to the ring phenoxy of 2-phenoxypyrimidine (41)

As a result, the fluorescence intensity is completely quenched. The corresponding electrons phenomena created a non-conjugated system which resulting in non-fluorescent compounds.

CHAPTER 4: CONCLUSION

The objective of this study is to synthesize series of phenoxy derivatives of pyrimidine and pyrazine which then followed by the study of fluorescence characteristic of the synthesized compounds were successful. The NMR, IR and GC-MS analysis were carried out to confirm the structure of the synthesised compounds. Fluorescence studies shows a complete change in the intensity with a change of solvent, e.g. acetonitrile, ethanol, tetrahydrofuran, hexane and ethyl acetate.

2-Phenoxypyrimidin-4-amine **(53)** shows higher intensity than 2-phenoxypyrimidine **(41)**. The higher intensity observed was due to the presence of electron donating group on the pyrimidine ring. In the case of 2-(2-methoxyphenoxy)pyrimidine **(37)** and 2-(4-methoxyphenoxy)pyrimidine **(39)**, the fluorescence peak in compound **(37)** is lower than compound **(39)**. The steric hindrance effect in compound **(37)** is believed to be the reason of the low fluorescence intensity recorded.

While in case of concentration, the fluorescence intensity found to be increased with increasing concentration at 10^{-4} M. Studies in various pH shows that 2-phenoxypyrimidine **(41)** and 2-(3-methoxyphenoxy)pyrimidine **(43)** fluoresced at lower intensity in acid condition and fluoresced at higher intensity in neutral and basic condition.

CHAPTER 5: EXPERIMENTAL PROCEDURES

5.1 Introduction to experimental

All solvents used are AR Gred and were redistilled before use. Formation of compounds was routinely checked by Thin Layer Chromatography (TLC) on aluminium sheets, silica gel 60 F_{254}. Melting points were determined in an open capilary tube with electrothermal Melting point Apparatus and were not corrected.

Infrared spectra were recorded using Perkin Elmer 298 Infrared Spectrometer and FTIR Perkin Elmer 1600 Series in KBr for solid compounds and neat for liquid compounds.

The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on JEOL FT-NMR Lambda 400MHz and FT-NMR ECA 400 MHz spectrometer. Mass spectra were recorded with GC-MS Hewlett-Packard HP 6890 series with mass selective indicator and GCMS QP5050A Shimadzu.

Fluorescence spectra were recorded by Luminescence Spectrophotometer Perkin Elmer Model LS 50B and quartz cell were used. All starting materials were obtained from Sigma-Aldrich and Merck.

5.2 Preparation of pyrimidine and pyrazine derivatives

5.2.1 Pyrimidine derivatives

5.2.1.1 Preparation of 2-(2-methoxyphenoxy)pyrimidine (37)

o-Methoxyphenol **(36)** (2.3 mL, 0.02 moles) was added to sodium hydroxide pellet (0.8 g, 0.02 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-Chloropyrimidine **(35)** (2.28 g, 0.02 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration, evaporation of the organic layer and purification of the residue using chloroform gave the product.

M.p. 120-122 °C, (2.4 g, 60 %), IR ($\nu_{max,}$ cm^{-1}): 1569 (C=N), 1498 and 1404 (aromatic C=C), 1302 and 1023 (C-O); ^{1}H NMR $\delta_{H:}$ 8.54 (2H, d, *J*= 4.88 Hz, H-6, H-4), 7.22 (2H, m, H-5), 7.01 (3H, m, H-3', H-4', H-5', H-6'), 3.74 (3H, s, CH_3); ^{13}C NMR δ_C : 165.2 (C-2), 159.5 (C-4, C-6), 151.5 (C-1'), 141.8 (C-2'), 126.5 (C-5), 122.7 (C-3'), 121.0 (C-4'), 115.9 (C-5'), 112.7 (C-6'), 55.8 (OCH_3); MS: M^+ found =202.00; $C_{11}H_{10}N_2O_2$ requires M^+ = 202.07.

5.2.1.2 Preparation of 2-(*p*-methoxyphenoxy)pyrimidine (39)

p-Methoxyphenol **(38)** (1.49 g, 0.012 moles) was added to sodium hydroxide pellet (0.67 g, 0.012 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-Chloropyrimidine **(35)** (1.37 g, 0.012 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) and 5% sodium hydroxide solution (5 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform and recrystallization gave the product.

M.p. 50-52 °C, (1.2 g, 50 %), IR ($\nu_{max,}$ cm^{-1}): 1568 (C=N), 1509 and 1404 (aromatic C=C), 1308 and 1030 (C-O); ^{1}H-NMR $\delta_{H:}$ 8.56 (2H, d, *J*= 4.64 Hz, H-4, H-6), 7.14 (2H, d, *J*= 9.28, H-2', H-6'), 7.01 (2H, t, *J*= 4.88, H-5), 6.96 (2H, d, *J*=9.28, H-3', H-5'); ^{13}C NMR δ_{C} C: 165.8 (C-2), 159.7 (C-4, C-6), 157.0 (C-1'), 146.3 (C-4'), 122.5 (C-5), 116.0 (C-6', C-2'), 114.7 (C-5', C-3'), 55.6 (OCH_3); MS: M^+ found =202.00; $C_{11}H_{10}N_2O_2$ requires M^+ = 202.07.

5.2.1.3 Preparation of 2-phenoxypyrimidine (41)

Phenol **(40)** (1.04 mL, 0.0096 moles) was added to sodium hydroxide pellet (0.384 g, 0.0096 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-Chloropyrimidine **(35)** (1.49 g, 0.0096 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform gave the product.

M.p. 88-99 °C, (0.8 g, 50 %), IR ($\nu_{max,}$ cm^{-1}): 1576 (C=N), 1492 and 1404 (aromatic C=C), 1302 and 1023 (C-O); ^{1}H NMR $\delta_{H:}$ 8.55 (2H, d, *J*= 4.88 Hz, H-4, H-6), 7.42 (2H, t, *J*= 6.6 Hz, H-3', H-5'), 7.23 (2H, d, *J*= 5.84 Hz, H-2', H-6'), 7.18 (1H, d, *J*= 7.6 Hz, H-4'), 7.01 (1H, t, J= 4.88 Hz, H-5); ^{13}C NMR δ_{C} :165.4 (C-2), 159.7 (C-4, C-6), 152.8 (C-1'), 129.6 (C-5), 125.5 (C-2', C-6'), 121.6 (C-3', C-5'), 116.1 (C-4'); MS: M^{+} found =172.00; $C_{10}H_8N_2O$ requires M^{+} = 172.06.

5.2.1.4 Preparation of 2-(3-methoxyphenoxy)pyrimidine (43)

m-Methoxyphenol **(37)** (2.2 mL, 0.02 moles) was added to sodium hydroxide pellet (0.8 g, 0.02 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-Chloropyrimidine **(35)** (1.8 g, 0.02 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform and purification gave the product.

M.p. 78-80 °C, (1.45 g, 36 %), IR ($\nu_{max,}$ cm^{-1}): 1571 (C=N), 1483 and 1398 (aromatic C=C), 1279 and 1035 (C-O); ^{1}H NMR $\delta_{H:}$ 8.57 (2H, d, *J*= 4.64 Hz, H-4, H-6), 7.33 (1H, t, *J*= 8.28 Hz, H-5), 7.04 (1H, t, *J*= 4.64 Hz, H-2'), 6.78 (3H, m, , H-4', H-5', H-6'), 3.81 (3H, s, $-OCH_3$); ^{13}C NMR δ_C : 165.3 (C-2), 160.7 (C-1'), 159.7 (C-3'), 153.9 (C-4), 130.0 (C-6), 116.2 (C-5), 113.8 (C-2'), 111.3 (C-4'), 107.7 (C-5'), 100.5 (C-6'), 55.4 (CH_3); MS: M^+ found =202.00; $C_{11}H_{10}N_2O_2$ requires M^+ = 202.07.

5.2.1.5 Preparation of 2-(*o*-tolyloxy)pyrimidine (45)

o-Cresol **(44)** (2.16 mL, 0.02 moles) was added to sodium hydroxide pellet (0.8 g, 0.02 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-Chloropyrimidine **(35)** (2.28 g, 0.02 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform gave the product.

M.p. 77-78 °C, (1.5 g, 40 %), IR ($\nu_{max,}$ cm^{-1}): 1572 (C=N), 1489 and 1400 (aromatic C=C), 1303 and 1041 (C-O); ^{1}H NMR $\delta_{H:}$ 8.56 (2H, d, *J*= 4.88 Hz, C(4)-H, C(6)-H), 7.30 (2H, t, *J*= 7.32 Hz, C(3')-H, C(6')-H), 7.19 (1H, t, *J*= 6.12 Hz, C(4')-H), 7.12 (1H, d, 7.80, C(5')-H), 7.01 (1H, t, J= 4.64 Hz, C(5)-H); ^{13}C NMR δ_C :165.1 (C-2), 159.7 (C-4/C-6), 151.3 (C-1'), 131.3 (C-2'), 130.9 (C-3'), 127.1 (C-5'), 125.8 (C-4'), 121.8 (C-6'), 115.8 (C-5), 16.2 (-CH_3); MS: M^+ found =186.00; $C_{11}H_{10}N_2O$ requires M^+ = 186.08.

5.2.1.6 Preparation of 2-(pyrimidin-2-yloxy)phenol (47)

1, 2-Dihydroxybenzene **(46)** (12 g, 0.108 moles) was added to sodium hydroxide pellet (0.384 g, 0.04 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-Chloropyrimidine **(35)** (2 g, 0.018 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform gave the product.

M.p. 165-167 °C, (0.84 g, 25 %), IR ($\nu_{max,}$ cm^{-1}): 3297 (OH), 1575 (C=N), 1492 and 1409 (aromatic C=C), 1285 and 1223 (C-O); ^{1}H NMR $\delta_{H:}$ 9.55 (1H, s, O-H), 8.58 (2H, d, *J*= 5.36 Hz, H-4, H-6), 7.19 (1H, t, *J*= 4.16 Hz, H-5), 7.05 (2H, t, *J*= 7.06 Hz,, H-3', H-6'), 6.92 (1H, t, *J*= 6.32 Hz, H-4'), 6.80 (1H, t, *J*=5.88 Hz, H-5'); ^{13}C NMR δ_{C} : 164.8 (C-2), 160.0 (C-1', C-2'), 149.4 (C-4), 140.8 (C-6), 126.3 (C-5), 123.1 (C-3'), 119.6 (C-4'), 117.1 (C-5'), 116.7 (C-6') ; MS: M^{+} found =188.00; $C_{10}H_{8}N_{2}O_{2}$ requires M^{+} = 188.06.

5.2.1.7 Preparation of 2-(3-nitrophenoxy)pyrimidine (49)

m-Nitrophenol **(48)** (1.04 ml, 0.0096 moles) was added to sodium hydroxide pellet (0.384 g, 0.0096 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-Chloropyrimidine **(35)** (1.49 g, 0.0096 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration, evaporation of chloroform and recrystallization gave the product.

M.p. 100-103 °C, (0.8 g, 39 %), IR ($\nu_{max,}$ cm^{-1}): 1578 (C=N), 1525 and 1400 (aromatic C=C), 1353 (N=O), 1300 and 1075 (C-O); ^{1}H NMR $\delta_{H:}$ 8.54 (2H, d, *J*= 4.88 Hz, H-4, H-6), 8.05 (2H, m, H-2', H-4'), 7.55 (2H, m, H-5', H-6'), 7.07 (1H, t, *J*= 4.88 Hz, H-5); ^{13}C NMR δ_{C} : 164.6 (C-2), 159.9 (C-4, C-5, C-6) 153.0 (C-1'), 130.2 (C-3'), 128.1 (C-2'), 120.3 (C-5'), 117.4 (C-6'), 117.1 (C-4'); MS: M^{+} found =217.00 ; $C_{10}H_7N_3O_3$ requires M^{+} = 217.05.

5.2.1.8 Preparation of 2-(*p*-tolyloxy)pyrimidine (51)

p-Cresol **(50)** (2.00 mL, 0.02 moles) was added to sodium hydroxide pellet (0.8 g, 0.02 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-Chloropyrimidine **(35)** (2.28 g, 0.02 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform gave the product.

M.p. 65-68 °C, (1.2 g, 33 %), IR ($\nu_{max,}$ cm^{-1}): 1576 (C=N), 1509 and 1414 (aromatic C=C), 1300 and 1022 (C-O); ^{1}H NMR $\delta_{H:}$ 8.58 (2H, d, *J*= 4.88 Hz, H-4, H-6), 7.28 (2H, d, *J*= 8.76 Hz, H-2',H-6'), 7.12 (2H, d, *J*= 8.56 Hz, H-3', H-5'), 7.03 (1H, t, *J*= 4.64 Hz, H-5); ^{13}C NMR δ_{C} : 165.6 (C-2), 159.7 (C-4, C-6), 150.6 (C-1'), 135.1 (C-4'), 130.2 (C-2', C-6'), 121.3 (C-3', C-4'), 115.9 (C-5), 20.9 (CH_3); MS: M^+ found =186.00; $C_{11}H_{10}N_2O$ requires M^+ = 186.00

5.2.1.9 Preparation of 2-phenoxypyrimidin-4-amine (53)

Phenol **(40)** (0.94 mL, 0.01 moles) was added to sodium hydroxide pellet (0.4 g, 0.01 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 4-amino-2-chloropyrimidine (1.6 g, 0.01 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform gave the product. Recrystallization gave pure product.

M.p. 131-134 °C, (0.88 g, 47 %), IR ($\nu_{max,}$ cm^{-1}): 3130 (NH_2), 1590 (C=N), 1482 and 1375 (aromatic C=C), 1294 and 1022 (C-O); 1H-NMR $\delta_{H:}$ 8.02 (1H, d, *J*= 5.64 Hz, H-6), 7.38 (2H, t, *J*= 8.28 Hz, H-3', H-5'), 7.17 (3H, m, H-2', H-4', H-6'), 6.14 (1H, d, *J*= 5.64 Hz, H-5), 4.95 (2H, s, -NH_2); ^{13}C NMR δ_C : 165.4 (C-2), 165.0 (C-4), 157.8 (C-6), 153.0 (C-1'), 129.6 (C-5), 129.4 (C-2'), 125.0 (C-3'), 121.8 (C-4'), 115.3 (C-5'), 100.3 (C-6'); GCMS: M^+ found =187.00; $C_{10}H_9N_3O$ requires M^+ = 187.07.

5.2.2 Pyrazine derivatives

5.2.2.1 Preparation of 2-(2-methoxyphenoxy)pyrazine (55)

o-Methoxyphenol **(36)** (5.6 mL, 0.045 moles) was added to potassium hydroxide pellet (2.5 g, 0.045 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-Chloropyrazine **(52)** (4 mL, 0.045 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed. Water (10 mL) and was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform gave the product.

M.p. 79-80 °C, (3.7 g, 41 %), IR ($\nu_{max,}$ cm^{-1}): 1580 (C=N), 1500 and 1405 (aromatic C=C), 1279 and 1007 (C-O); ^{1}H NMR $\delta_{H:}$ 8.43 (1H, s, H-3), 8.22 (1H, s, H-5), 8.06 (1H, s, H-6), 7.23 (1H, d, *J*= 8.08 Hz, H-6'), 7.16 (1H, d, J= 6.6 Hz, H-2'), 7.03 (2H, t, J= 8.28 Hz, H-3', H-4'); ^{13}C NMR δ_{C} : 160.1 (C-2), 151.5 (C-1'), 141.5 (C-2'), 141.0 (C-3), 138.1 (C-5), 135.2 (C-6), 126.7 (C-4'), 122.9 (C-6'), 121.1 (C-5'), 112.8 (C-3'), 55.7 ($-OCH_3$) ; MS: M^+ found =202.00; $C_{11}H_{10}N_2O_2$ requires M^+ = 202.07.

5.2.2.2 Preparation of 2-(4-methoxyphenoxy)pyrazine (56)

p-Methoxyphenol **(38)** (5.6 g, 0.045 moles) was added to potassium hydroxide pellet (2.5 g, 0.045 moles) in minimum volume of water (5 mL). The mixture was heated until a dry solid was formed. 2-chloropyrazine **(52)** (4 mL, 0.045 moles) in THF (5mL) was then added to the dry white solid and refluxed for 5 hours. The mixture was cooled to room temperature and the solvent was removed under vacuo. Water (10 mL) was added to the reaction mixture followed by extraction with chloroform (3 x 10 mL). The organic layer was washed twice with water (2 x 10 mL) and dried over anhydrous sodium sulphate. Filtration and evaporation of chloroform gave the product.

M.p. 80-82 °C, (3.8 g, 42 %), IR ($\nu_{max,}$ cm^{-1}): 1584 (C=N), 1506 and 1408 (aromatic C=C), 1288 and 1005 (C-O); ^{1}H NMR $\delta_{H:}$ 8.40 (1H, s, H-5), 8.23 (1H, d, *J*= 2.68 Hz, H-6), 8.09 (1H, dd, *J*= 1.48 Hz, H-3), 7.10 (2H, d, *J*= 10.48 Hz, H-2', H-6'), 6.97 (2H, d, *J*= 6.8 Hz, H-3', H-5'); ^{13}C NMR δ_{C} : 160.6 (C-2), 157.0 (C-1'), 146.2 (C-4'), 141.0 (C-3), 138.1 (C-5), 135.7 (C-6), 122.3 (C-6', C-2'), 114.8 (C-5', C-3'), 55.6 (CH_3); MS: M^+ found =202.00; $C_{11}H_{10}N_2O_2$ requires M^+ = 202.07.

5.3 Fluorescence Measurements

All solvents (ethanol, tetrahydrofuran, ethyl acetate, hexane and acetonitrile) were purged with nitrogen gas before use.

5.3.1 Fluorescence measurement of pyrimidine and pyrazine derivatives

The fluorescence spectra of all the compounds studied were measured in various solvents. Samples were prepared from stock solution (10^{-4} M) of the corresponding compound in tetrahydrofuran (THF), acetonitrile (CH_3CN), ethyl acetate (EtOAc), ethanol (EtOH) and hexane to give concentrations of 10^{-5} M and 10^{-6} M

2-(2-Methoxyphenoxy)pyrimidine (37),

2-(2-Methoxyphenoxy)pyrimidine **(37)** (1.0 mg) was dissolved in solvents (10 ml)

Concentration = 4.9505 X 10^m M, where 10^m= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
Hexane	326	358	79.94	**X**	**X**	**X**	**X**
Ethanol	260	312	43.99	**X**	**X**	**X**	**X**
Acetonitrile	201	355	50.97	347	48.25	**X**	**X**
Ethyl acetate	210	329	6.51	**X**	**X**	**X**	**X**
THF	203	389	41.57	**X**	**X**	**X**	**X**

X = non-fluorescent

2-(4-Methoxyphenoxy)pyrimidine (39)

2-(4-Methoxyphenoxy)pyrimidine **(39)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 4.9505 X 10^m M, where 10^m= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
Hexane	350	380	95.38	**X**	**X**	**X**	**X**
Ethanol	201	388	61.91	381	35.00	**X**	**X**
Acetonitrile	203	323	469.05	318	213.77	313	69.30
Ethyl acetate	204	392	130.11	384	41.31	**X**	**X**
THF	207	380	149.08	**X**	**X**	**X**	**X**

X = non-fluorescent

2-Phenoxypyrimidine (41)

2-Phenoxypyrimidine **(41)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 5.814 X 10^m M, where 10^m= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
hexane	340	366	75.41	**X**	**X**	**X**	**X**
ethanol	201	381	16.61	374	31.66	358	67.07
acetonitrile	205	370	53.75	362	35.07	354	30.88
Ethyl acetate	201	362	59.53	362	32.29	375	11.68
THF	345	369	111.00	353	77.07	**X**	**X**

X = non-fluorescent

2-(3-Methoxyphenoxy)pyrimidine (43)

2-(3-Methoxyphenoxy)pyrimidine **(43)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 4.9505 X 10^m M, where 10^m= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
Hexane	201	359	59.55	356	67.22	**X**	**X**
Ethanol	213	379	15.04	373	8.06	**X**	**X**
Acetonitrile	204	364	10.39	385	12.29	374	20.80
Ethyl acetate	209	349	28.84	**X**	**X**	**X**	**X**
THF	202	344	61.83	372	68.62	**X**	**X**

X = non-fluorescent

2-(*o*-Tolyloxy)pyrimidine (45)

2-(*o*-Tolyloxy)pyrimidine **(45)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 5.3763 X 10^m M, where 10^m= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
Hexane	324	362	66.52	355	69.08	**X**	**X**
Ethanol	207	354	9.79	361	44.37	**X**	**X**
Acetonitrile	205	389	15.88	378	45.16	375	39.36
Ethyl acetate	210	351	13.51	**X**	**X**	**X**	**X**
THF	202	330	122.01	**X**	**X**	**X**	**X**

X = non-fluorescent

2-(Pyrimidin-2-yloxy)phenol (47)

2-(pyrimidin-2-yloxy)phenol **(47)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 5.3191 X 10^m M, where 10^m= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
Hexane	201	360	91.63	349	162.78	**X**	**X**
Ethanol	200	352	24.42	**X**	**X**	**X**	**X**
Acetonitrile	202	356	91.73	356	25.14	**X**	**X**
Ethyl acetate	201	377	182.77	381	43.37	**X**	**X**
THF	208	348	69.30	353	34.43	367	17.53

X = non-fluorescent

2-(3-Nitrophenoxy)pyrimidine (49)

2-(3-nitrophenoxy)pyrimidine **(49)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 4.6083 X 10^m M, where 10^m = 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
Hexane	205	382	6.34	**X**	**X**	**X**	**X**
Ethanol	382	398	8.72	**X**	**X**	**X**	**X**
Acetonitrile	**X**	**X**	**X**	**X**	**X**	**X**	**X**
Ethyl acetate	208	352	5.73	**X**	**X**	**X**	**X**
THF	205	404	25.41	363	66.27	**X**	**X**

X = non-fluorescent

2-(*p*-Tolyloxy)pyrimidine (51)

2-(*p*-Tolyloxy)pyrimidine **(51)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 5.3763 X 10^m M, where 10^m= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
Hexane	207	372	64.70	375	120.76	**X**	**X**
Ethanol	213	374	3.92	362	9.31	**X**	**X**
Acetonitrile	204	366	29.67	364	36.92	**X**	**X**
Ethyl acetate	200	358	35.31	373	11.95	**X**	**X**
THF	207	344	101.95	346	121.11	**X**	**X**

X = non-fluorescent

2-Phenoxypyrimidin-4-amine (53)

2-Phenoxypyrimidin-4-amine **(53)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 5.3476 X 10^m M, where 10^m= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
Hexane	203	358	274.44	374	97.48	**X**	**X**
Ethanol	328	360	916.56	364	347.01	362	87.28
Acetonitrile	212	372	431.18	358	145.44	**X**	**X**
Ethyl acetate	204	324	830.94	**X**	**X**	**X**	**X**
THF	226	332	274.35	339	44.80	**X**	**X**

X = non-fluorescent

2-(2-Methoxyphenoxy)pyrazine (55)

2-(2-Methoxyphenoxy)pyrazine **(55)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 4.9505 X 10^{m} M, where 10^{m}= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Iintensity	Emission	Intensity	Emission	Intensity
Hexane	345	355	215.63	351	78.88	**X**	**X**
Ethanol	214	359	2.70	372	11.72	**X**	**X**
Acetonitrile	203	361	49.61	362	53.60	**X**	**X**
Ethyl acetate	344	437	130.55	439	28.63	**X**	**X**
THF	203	381	18.78	367	35.86	**X**	**X**

X = non-fluorescent

2-(4-Methoxyphenoxy)pyrazine (56)

2-(4-Methoxyphenoxy)pyrazine **(56)** (1.0 mg) was dissolved in solvents (10 mL)

Concentration = 4.9505 X 10^{m} M, where 10^{m}= 10^{-4}, 10^{-5} and 10^{-6}

Excitation and emission slits = 5

Compound	*Excitation*	*Fluorescence*					
		10^{-4} M		10^{-5} M		10^{-6}M	
		Emission	Intensity	Emission	Intensity	Emission	Intensity
Hexane	349	377	283.47	380	111.98	383	50.04
Ethanol	200	377	12.15	354	22.52	**X**	**X**
Acetonitrile	201	379	31.65	350	40.78	369	98.13
Ethyl acetate	347	446	100.07	445	25.07	**X**	**X**
THF	204	401	37.68	399	29.14	**X**	**X**

X = non-fluorescent

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Journal articles (ISI)

1. Nasir Shah Bakhtiar, Maizathul Akmam A. Bakar, Zanariah Abdullah and Siek Weng Ng, 2-(2-Naphthyloxy)pyrimidine, *Journal of Acta Crystallographica*, **2009**, E65, o1881

2. Shah Bakhtiar Nasir, Zanariah Abdullah, Zainal A. Fairuz, Seik Weng Ng and Edward R. T. Tiekink, 2-(3-Methoxyphenoxy)pyrimidine, *Journal of Acta Crystallographica*, **2010**, E66, o2187

3. Shah Bakhtiar Nasir, Zanariah Abdullah, Azizah Mainal, Zainal A. Fairuz, Seik Weng Ng and Edward R. T. Tiekink, 2-(4-Methoxyphenoxy)pyrazine, *Journal of Acta Crystallographica*, **2010**, E66, o2303

4. Nasir Shah Bakhtiar, Zanariah Abdullah and Seik Weng Ng, 2-(o-tolyloxy)pyrimidine, *Journal of Acta Crystallographica*, **2009**, E65, o1880

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11. S. B. Nasir , Z. Abdullah, Z. A. Fairuz and E.R. T. Tiekink, "2-(4-methoxyphenoxy)-3-nitropyridine", *Journal of Acta Crystallographica*, **2010**, E66, o02426

Journal articles (Non-ISI)

1. Edura Badaruddin, Zaharah Aiyub, Zanariah Abdullah, Shah Bakhtiar Nasir, "Synthesis and Fluorometric Analysis of Selected Diazine Derivatives and Their Metal Complexes", *The Malaysian Journal of Analytical Sciences*, **2009**, vol 13, 129-135

CONFERENCE PROCEEDING

1. **22nd Malaysian Symposium on Analytical Science 2009 SKAM 22 (2009)** Phenoxypyrimidines: Fluorescence Characteristic.

2. **National Symposium on Organic Synthesis (NaSOS 2009)** – Phenoxypyrimidine: Synthesis and Fluorescence Characteristic

3. **International Conference for Young Chemist (ICYC 2010) –** Synthesis and Fluorescence Properties of Selected Methoxyphenoxypyrimidines and Methoxyphenoxypyrazines.

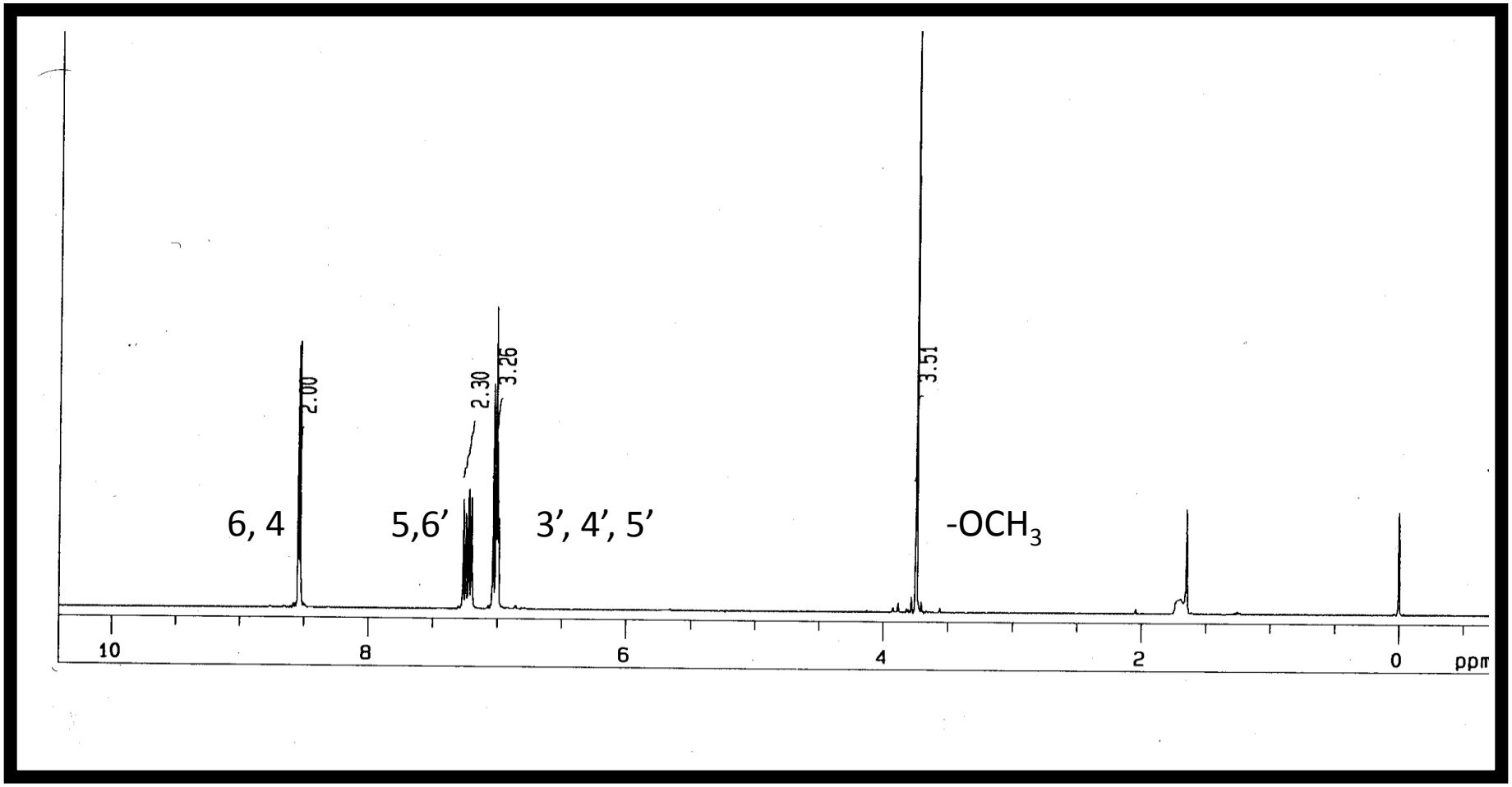
APPENDICES

Appendix 1: **^{1}H NMR, ^{13}C NMR, IR and GCMS spectra**

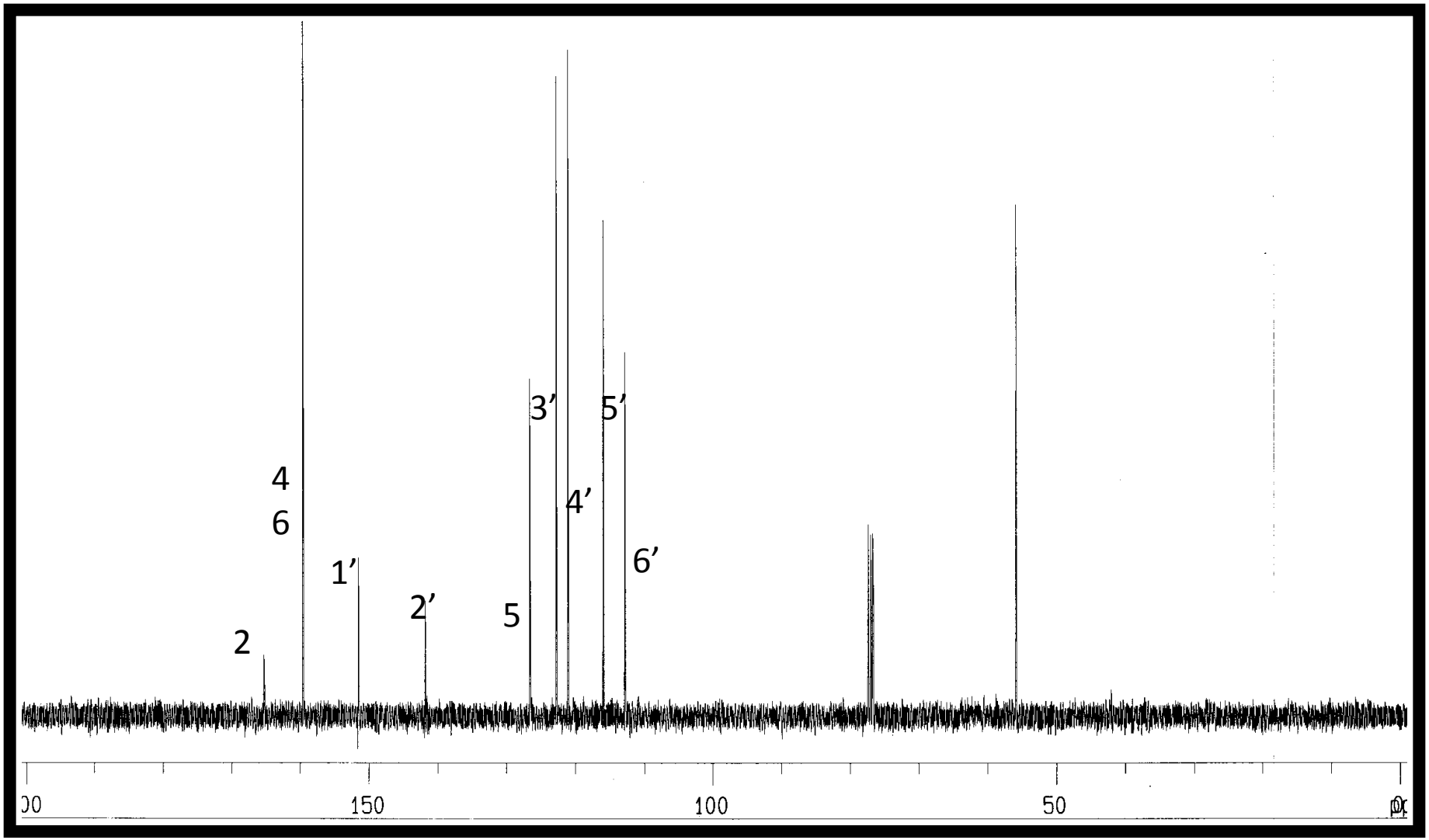
Appendix 2: **Publications**

APPENDIX 2: PUBLICATIONS

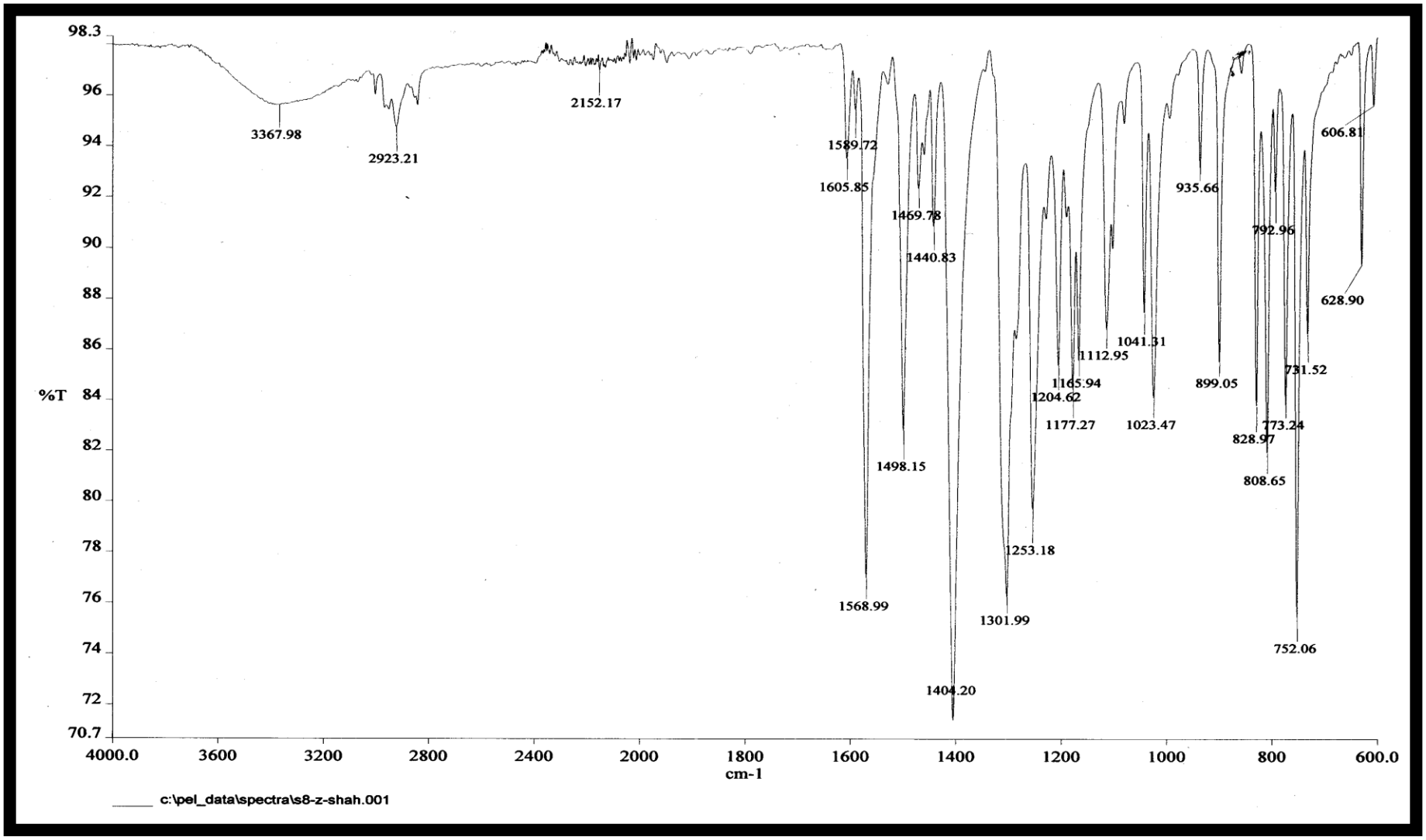
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



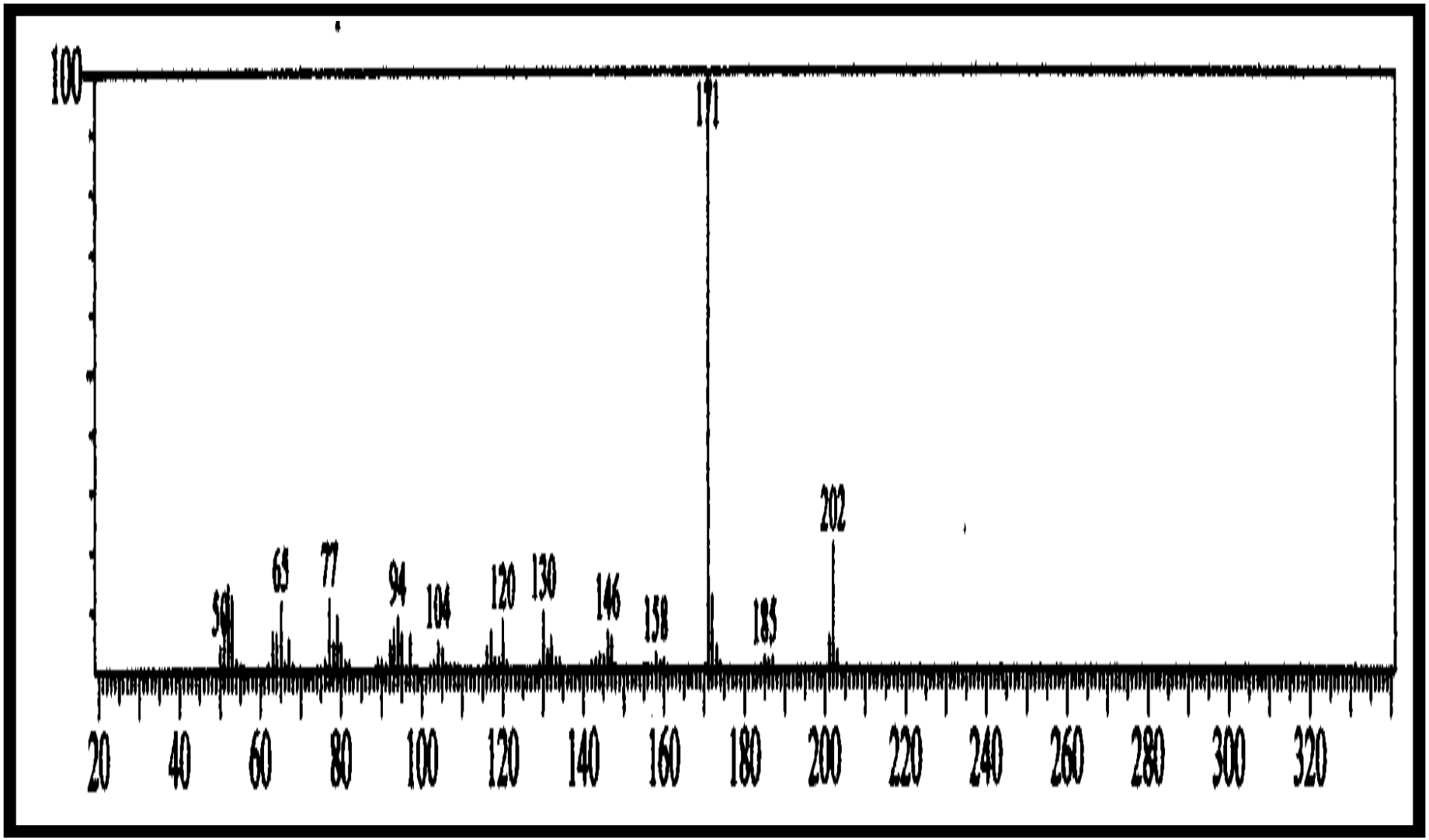
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-(2-methoxyphenoxy)pyrimidine (37)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-(2-methoxyphenoxy)pyrimidine (37)

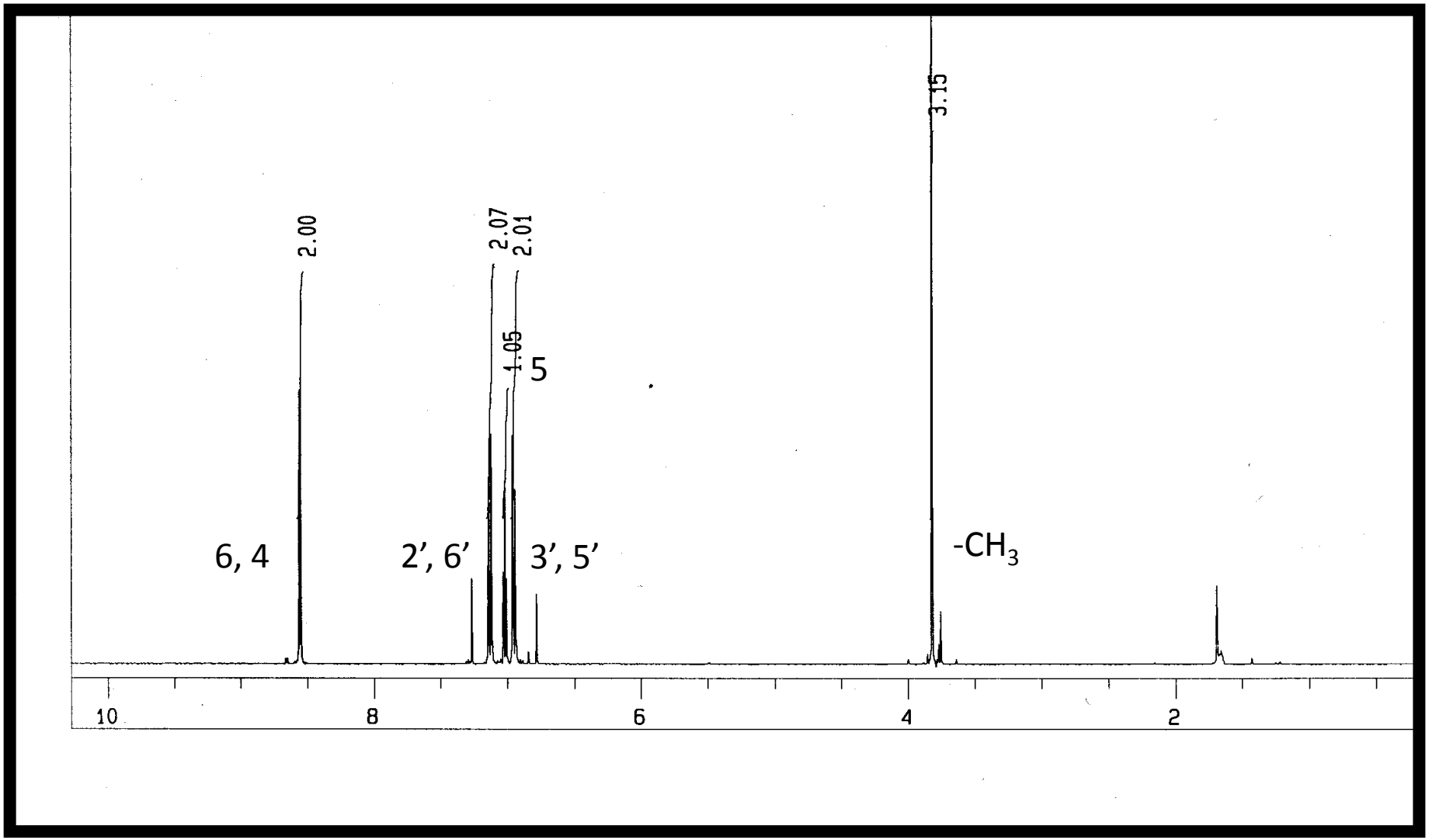


IR Spectrum of 2-(2-methoxyphenoxy)pyrimidine (37)

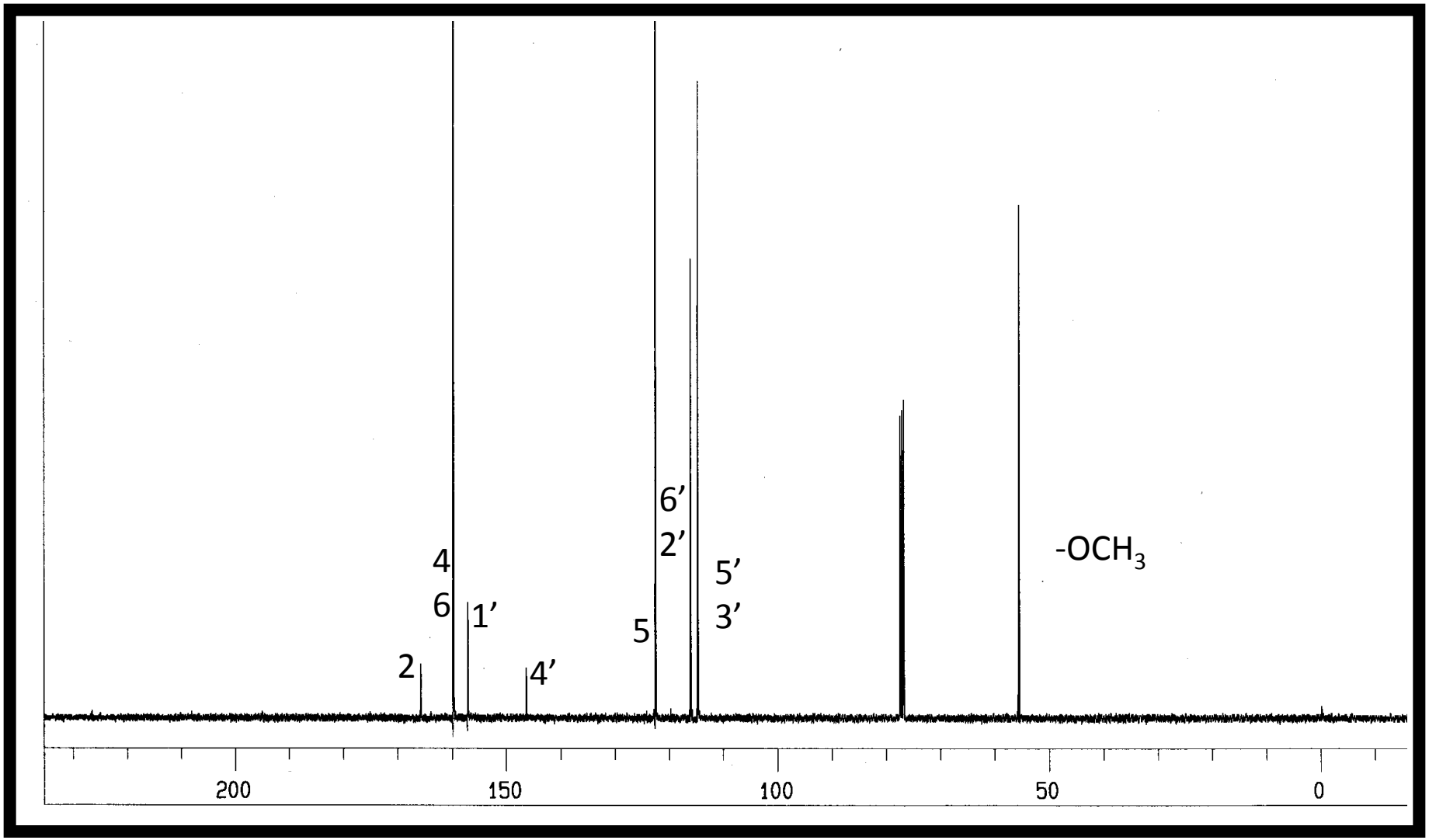


GCMS of 2-(2-methoxyphenoxy)pyrimidine (37)

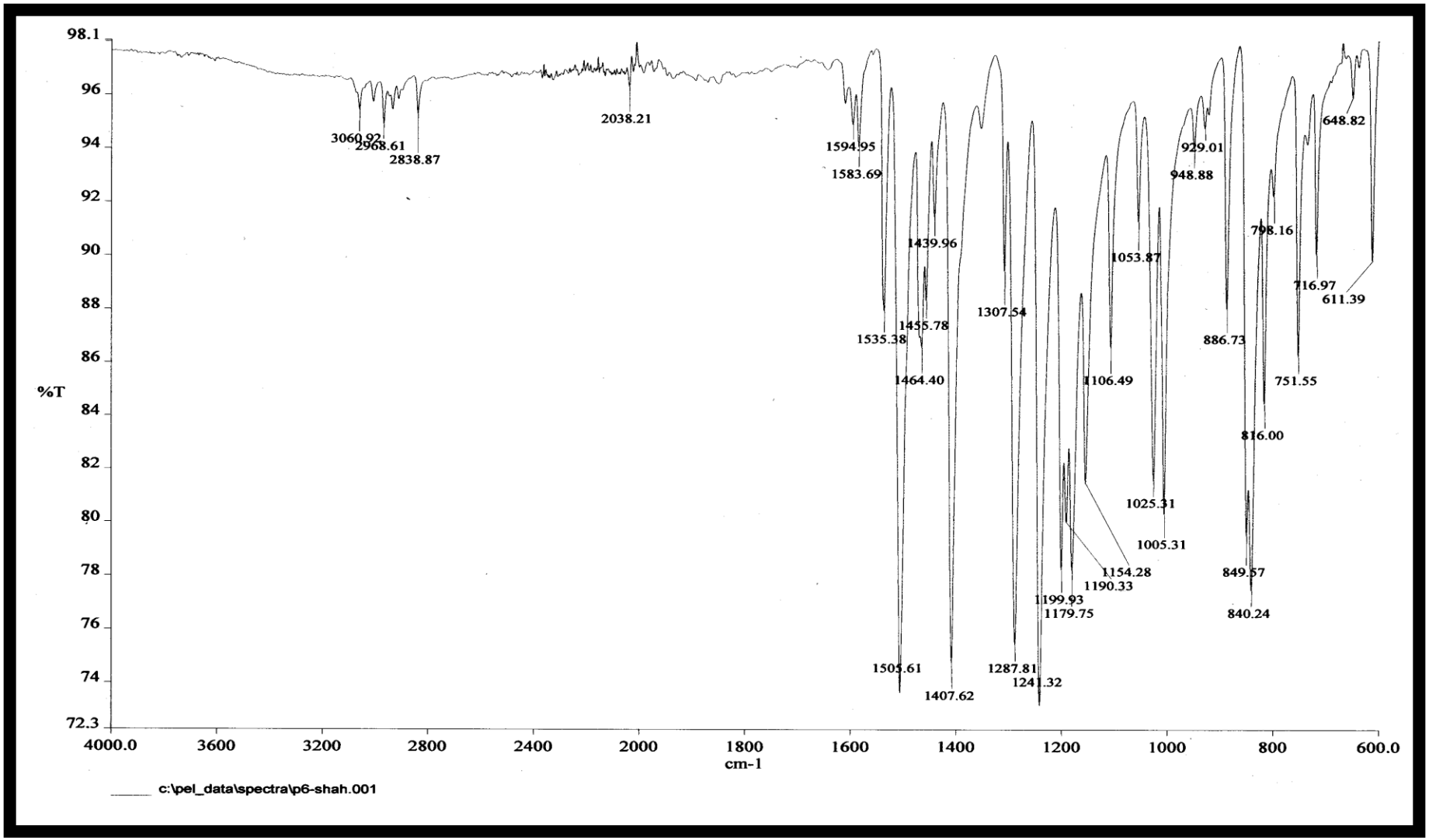
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



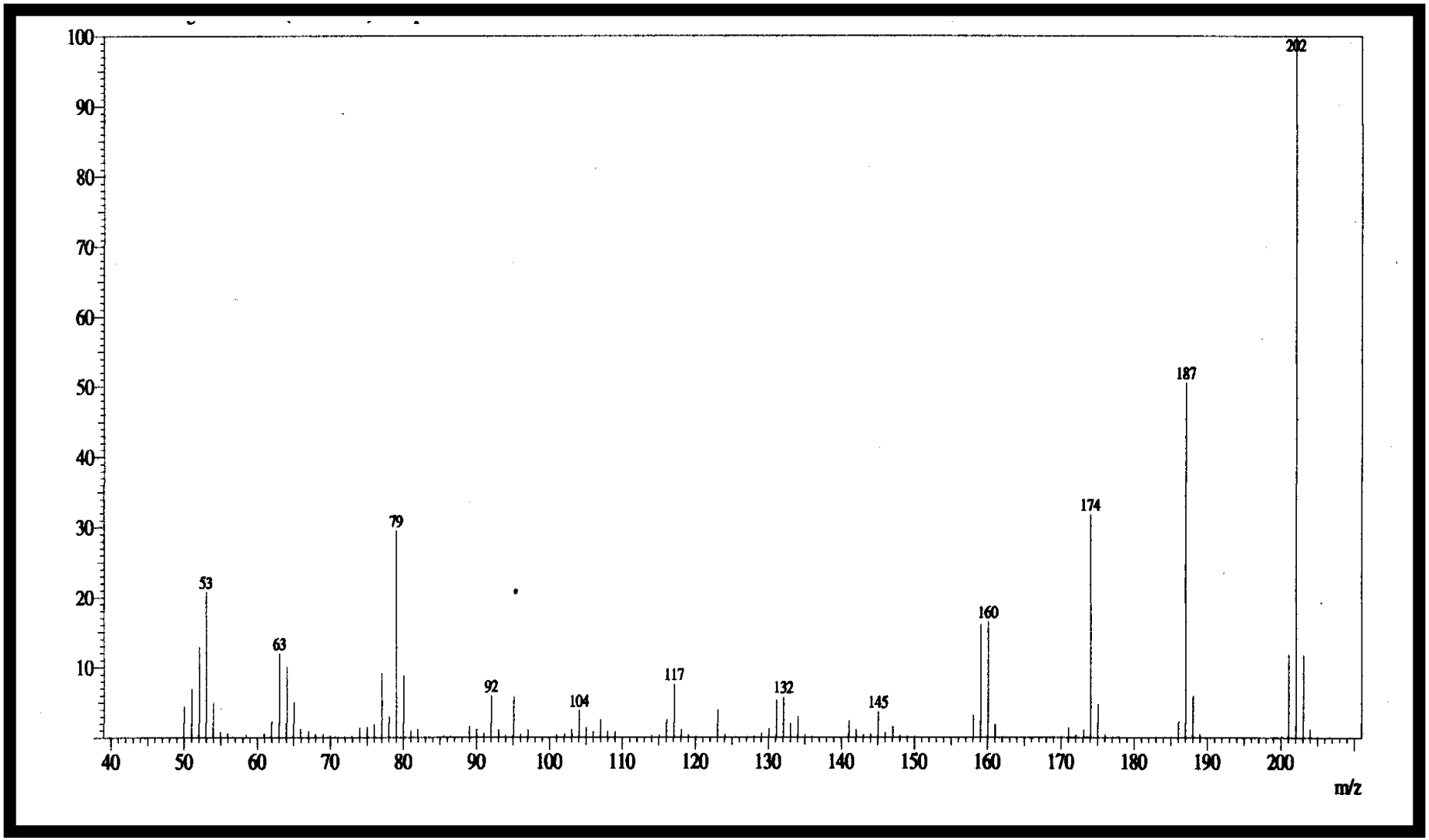
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-(4-methoxyphenoxy)pyrimidine (39)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-(4-methoxyphenoxy)pyrimidine (39)

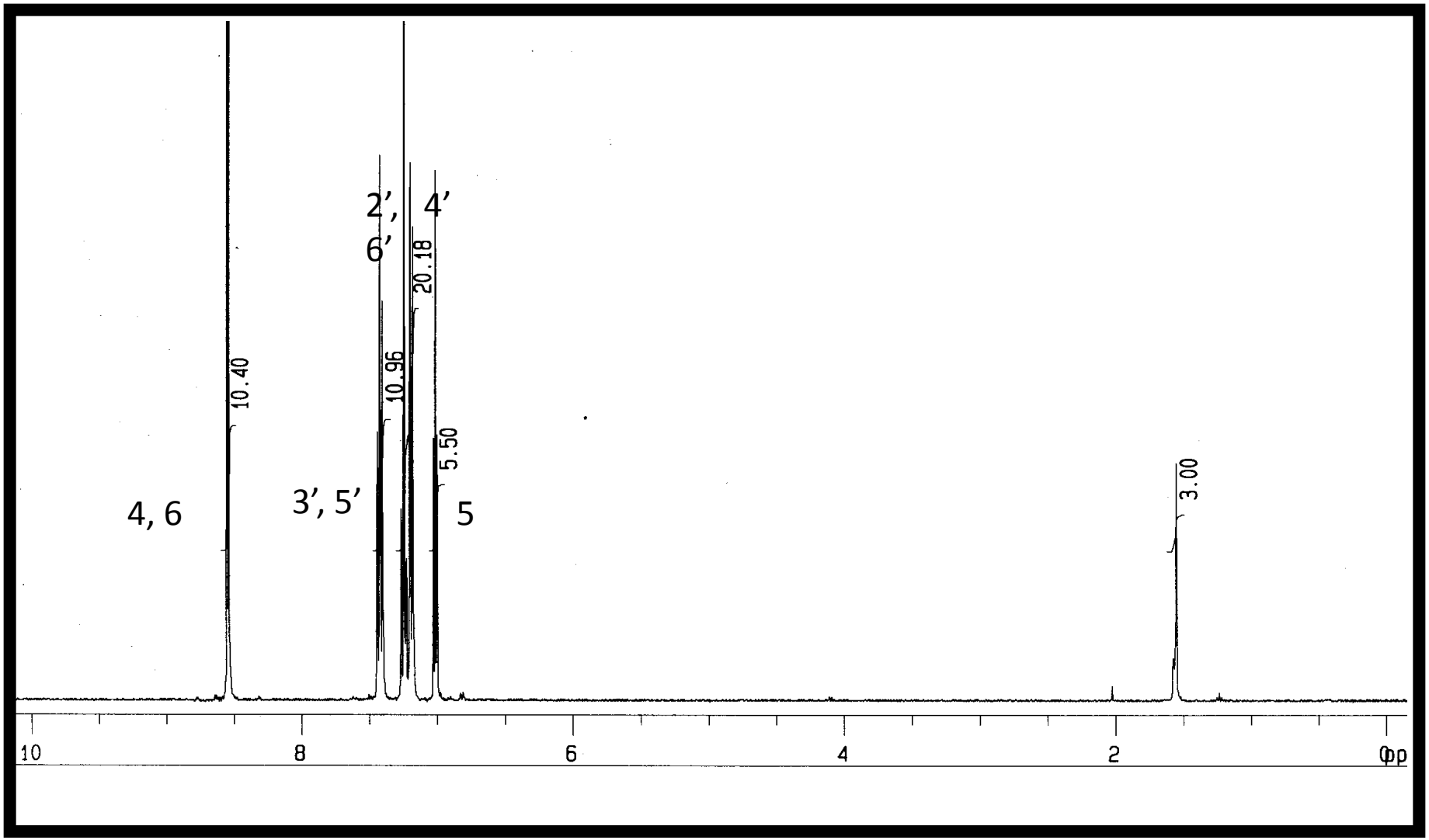


IR Spectrum of 2-(4-methoxyphenoxy)pyrimidine (39)

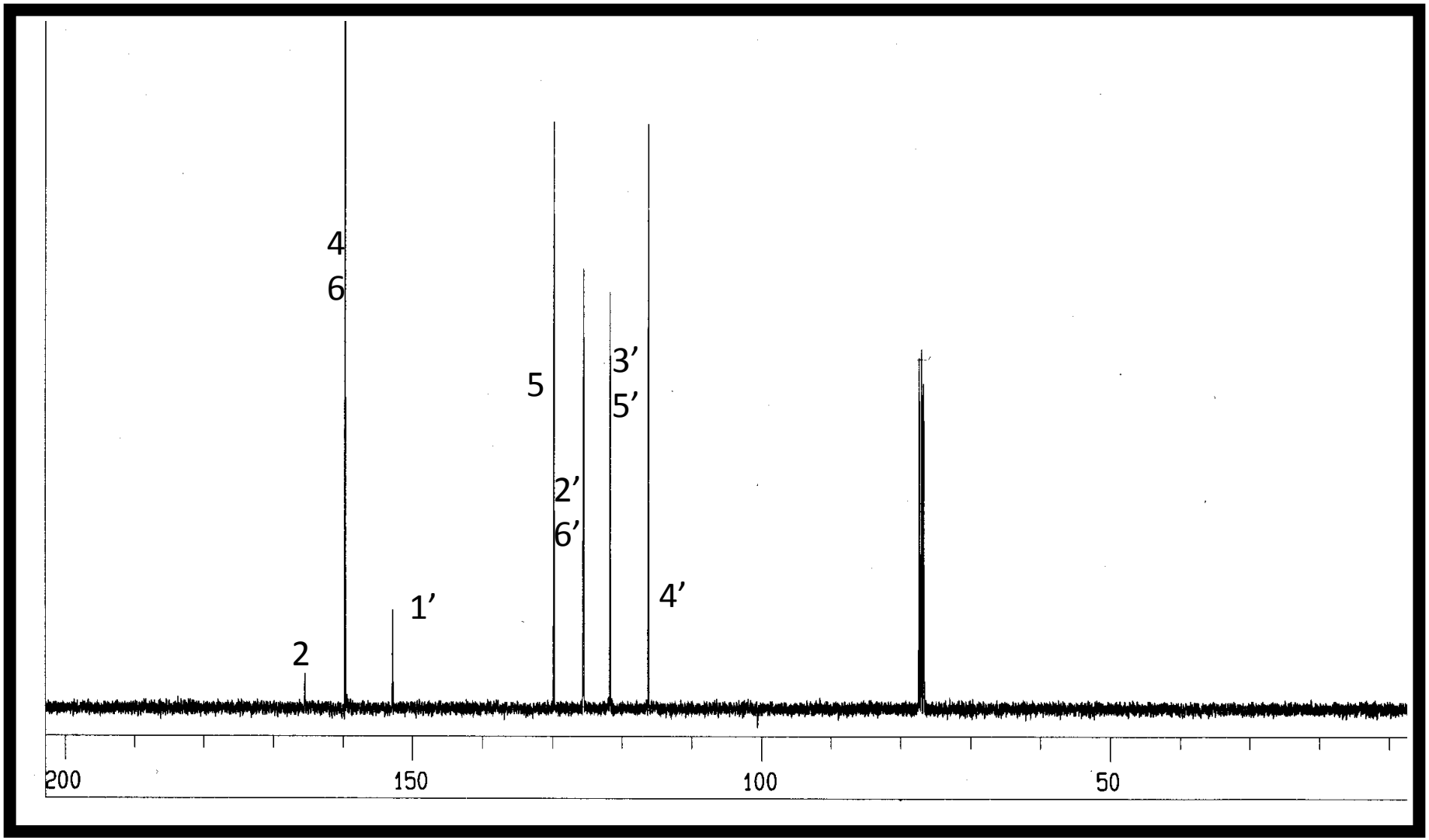


GCMS of 2-(4-methoxyphenoxy)pyrimidine (39)

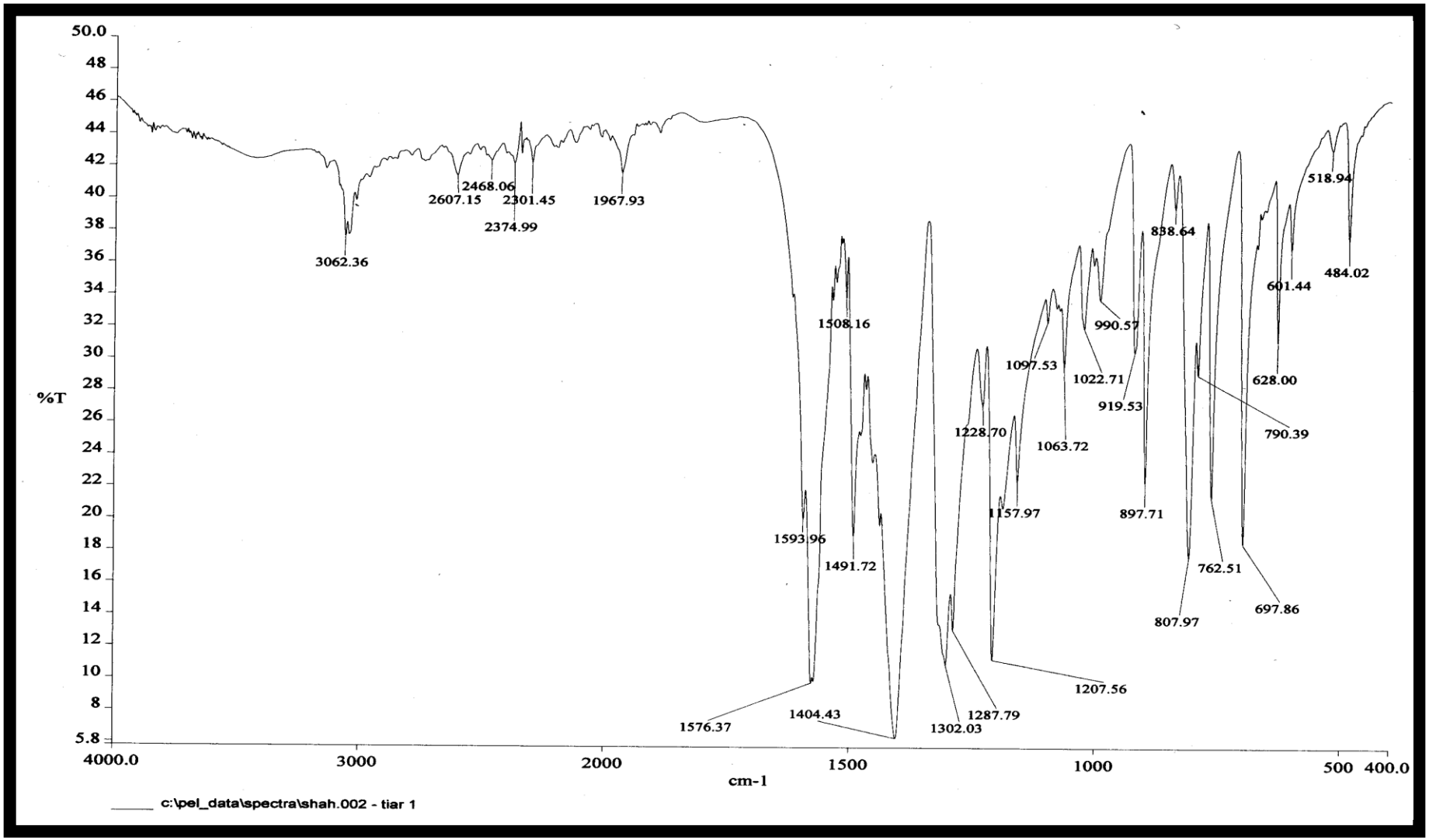
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



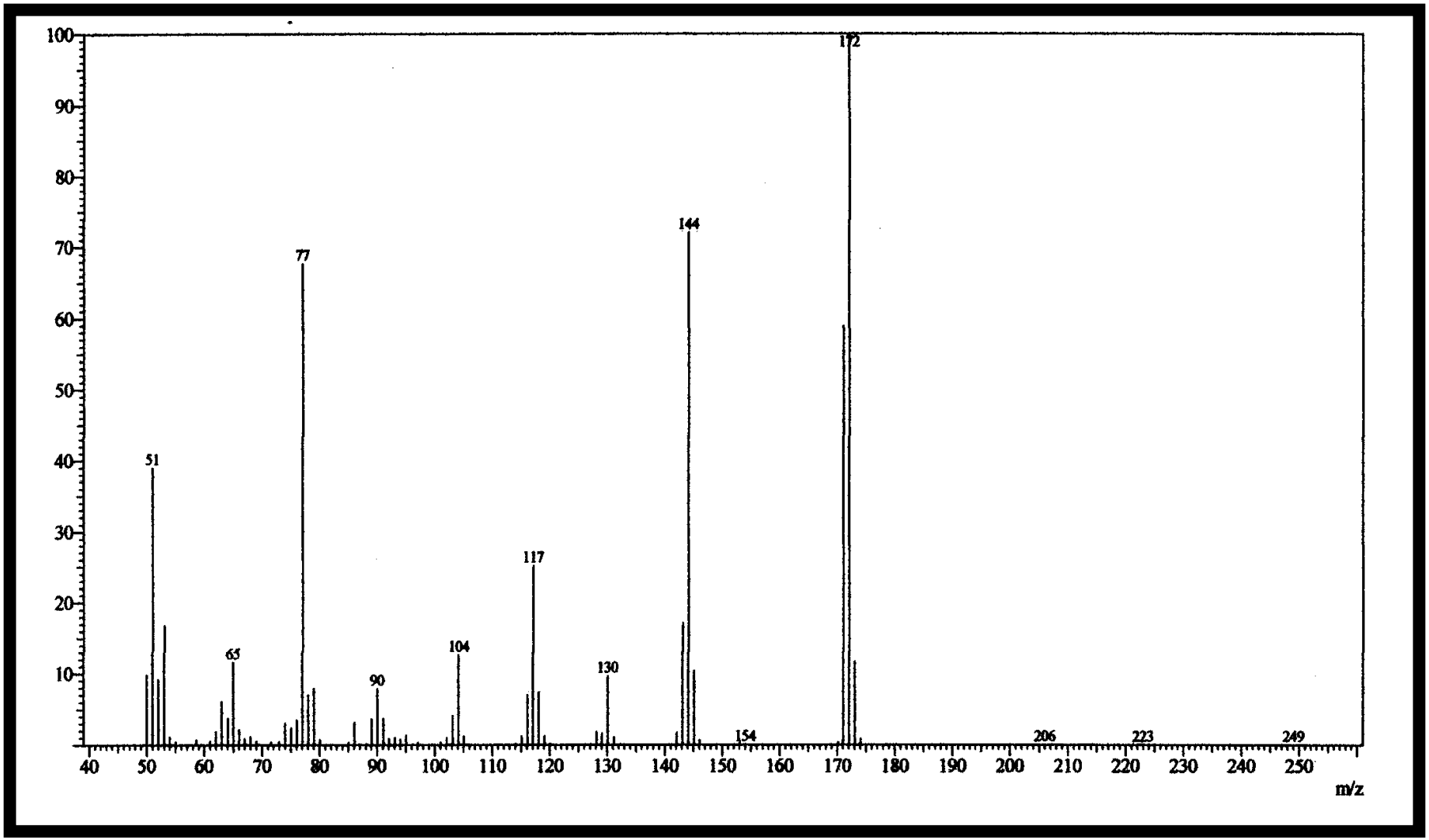
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-phenoxypyrimidine (41)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-phenoxypyrimidine (41)

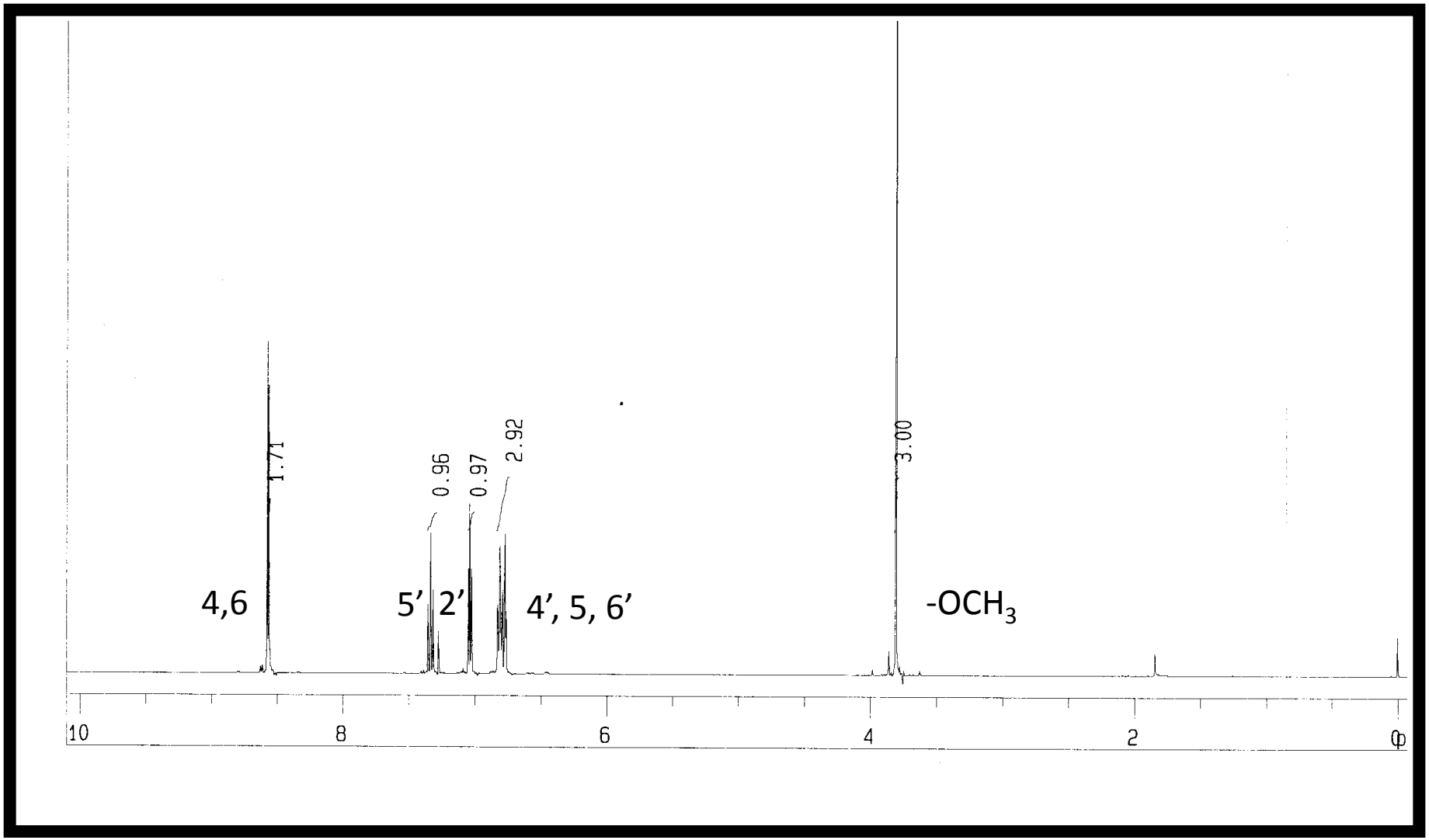


IR Spectrum of 2-phenoxypyrimidine (41)

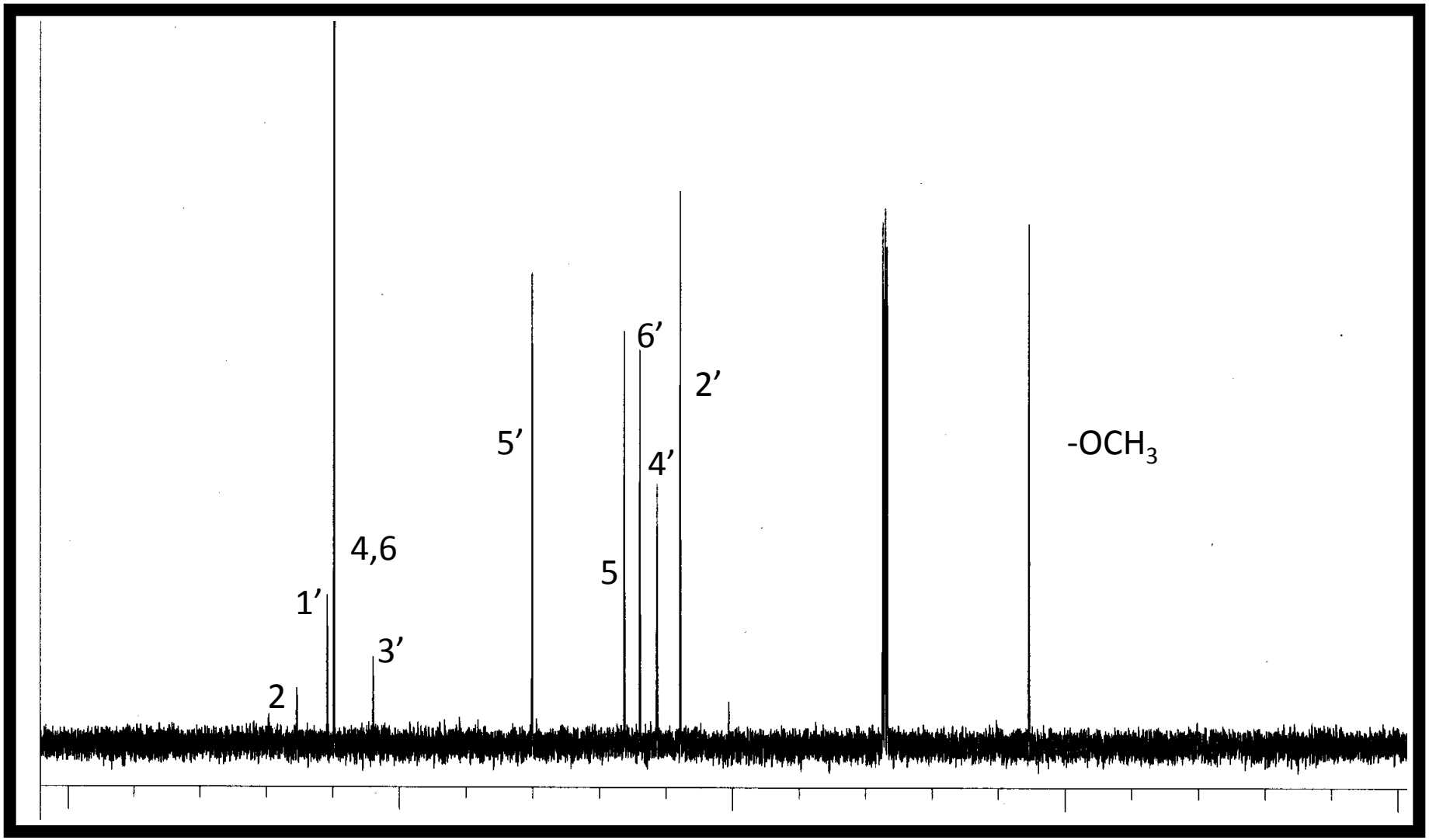


GCMS of 2-phenoxypyrimidine (41)

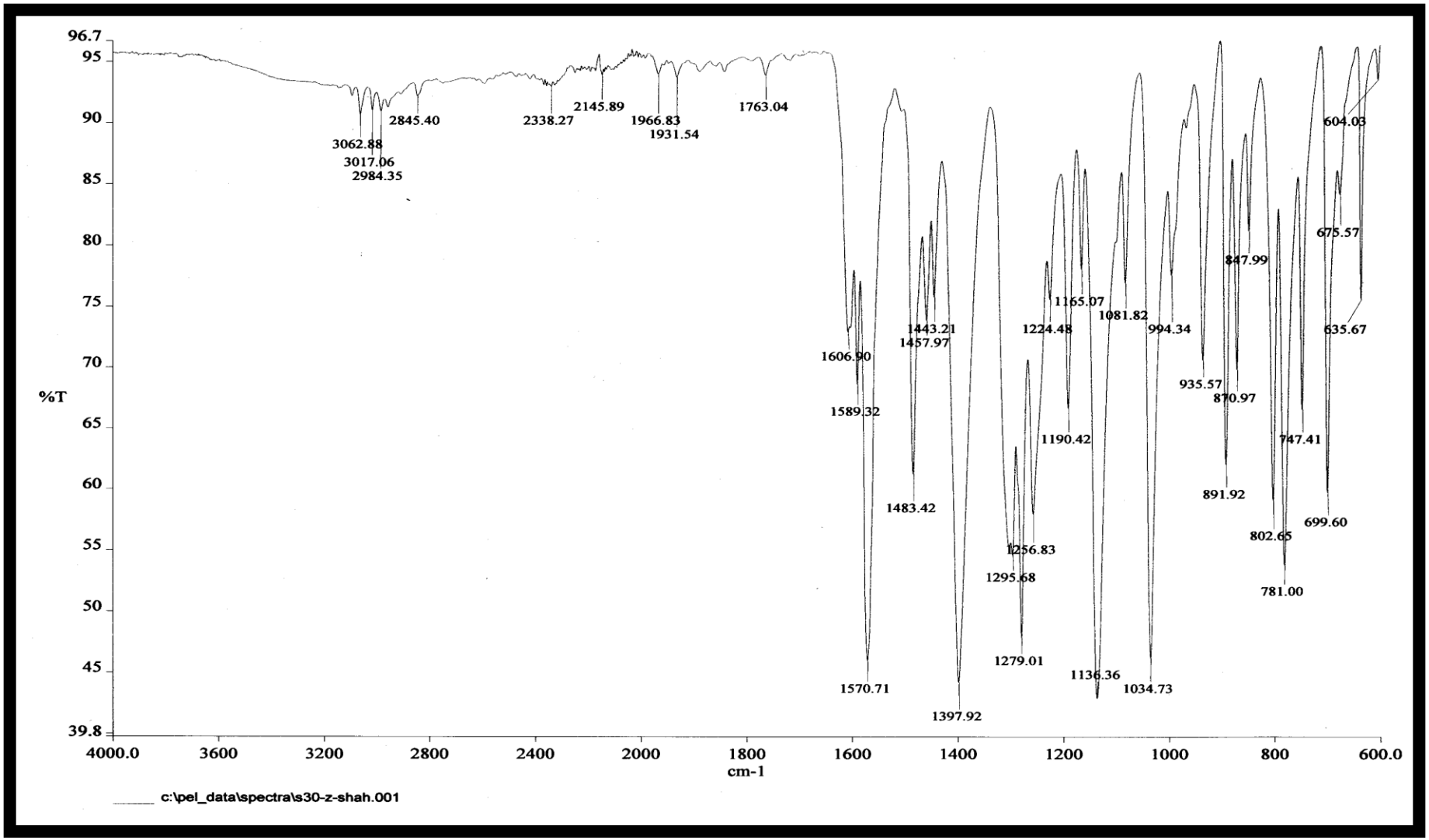
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



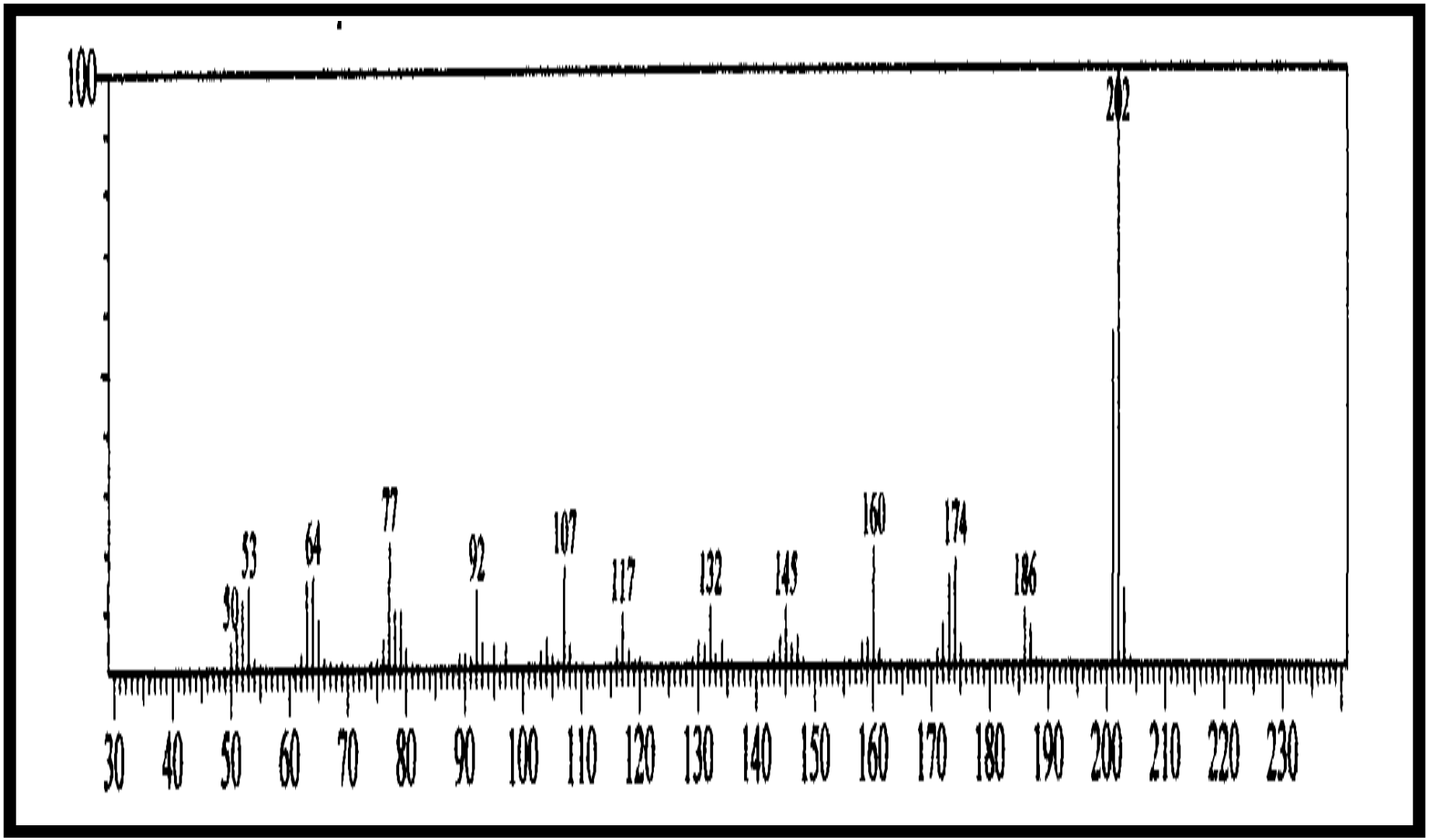
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-(3-methoxyphenoxy)pyrimidine (43)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-(3-methoxyphenoxy)pyrimidine (43)

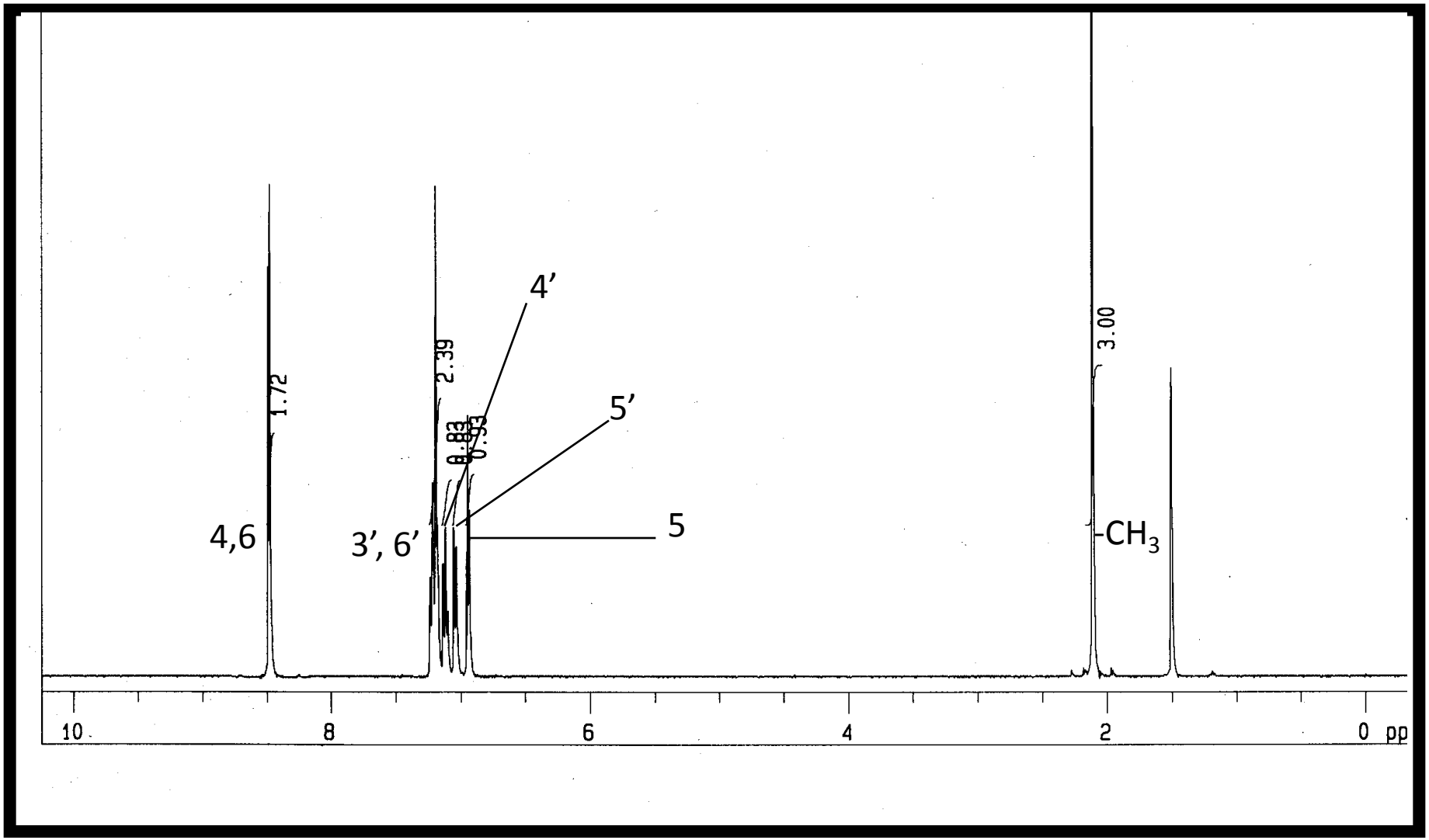


IR Spectrum of 2-(3-methoxyphenoxy)pyrimidine (43)

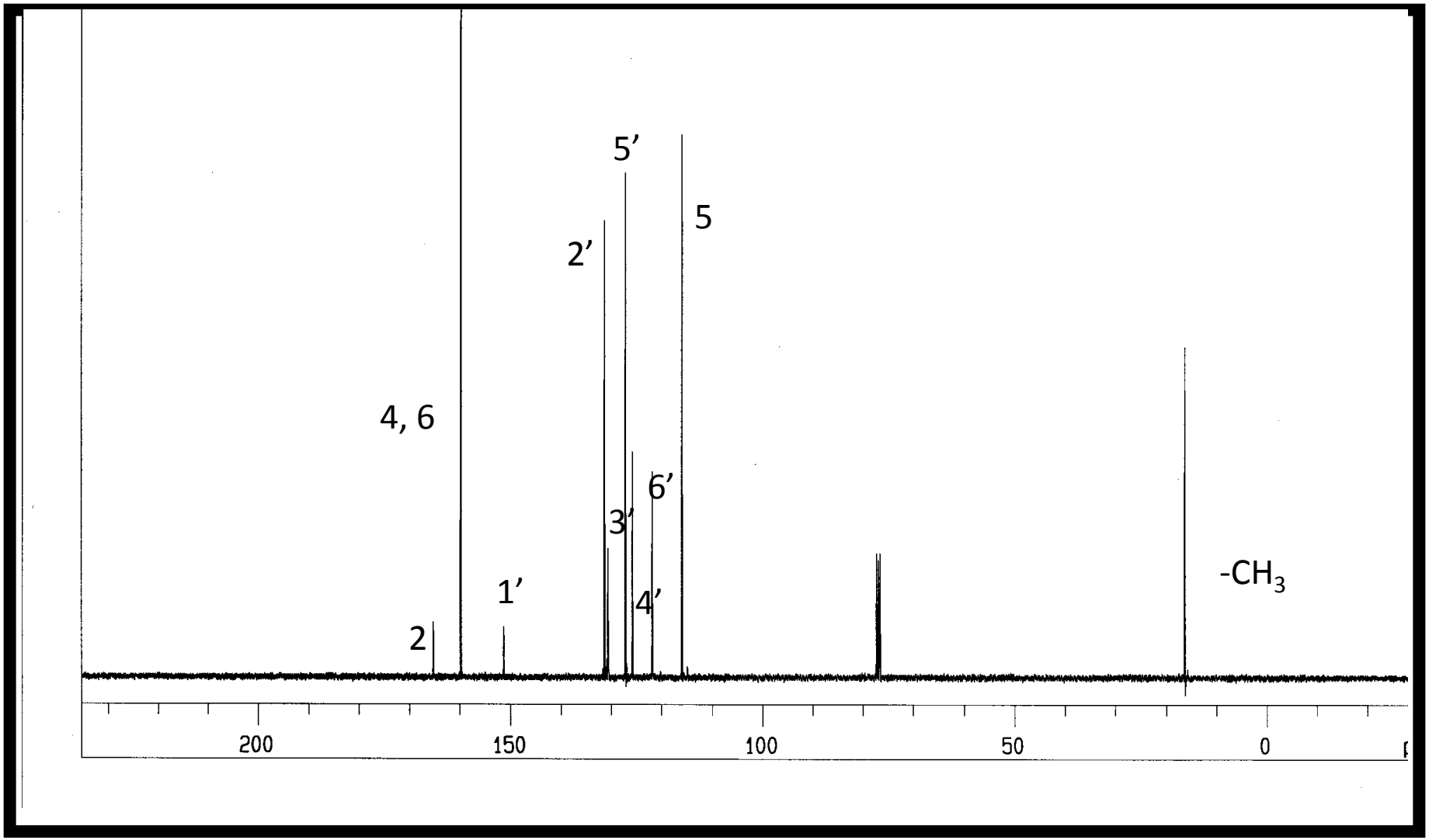


GCMS of 2-(3-methoxyphenoxy)pyrimidine (43)

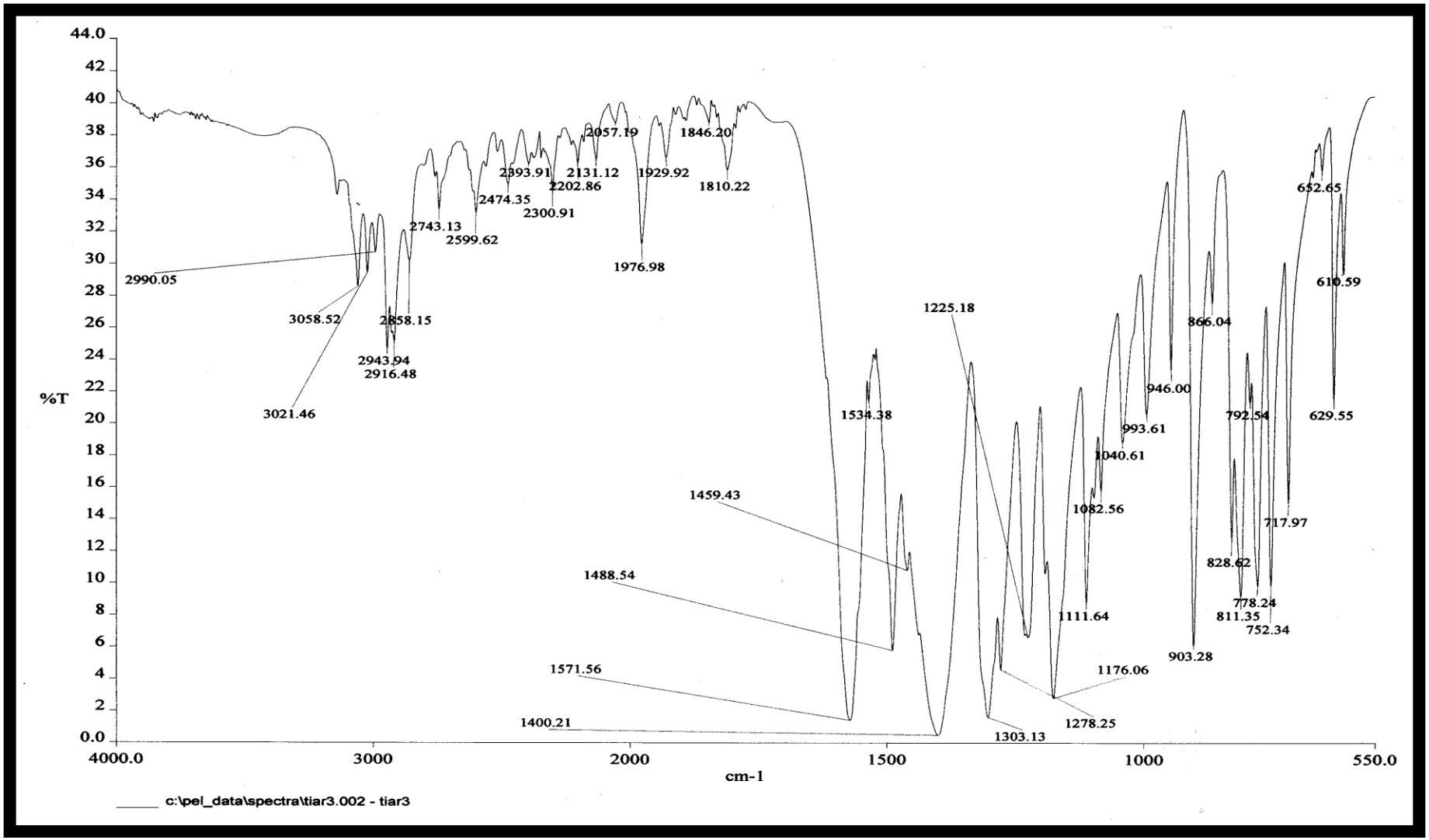
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



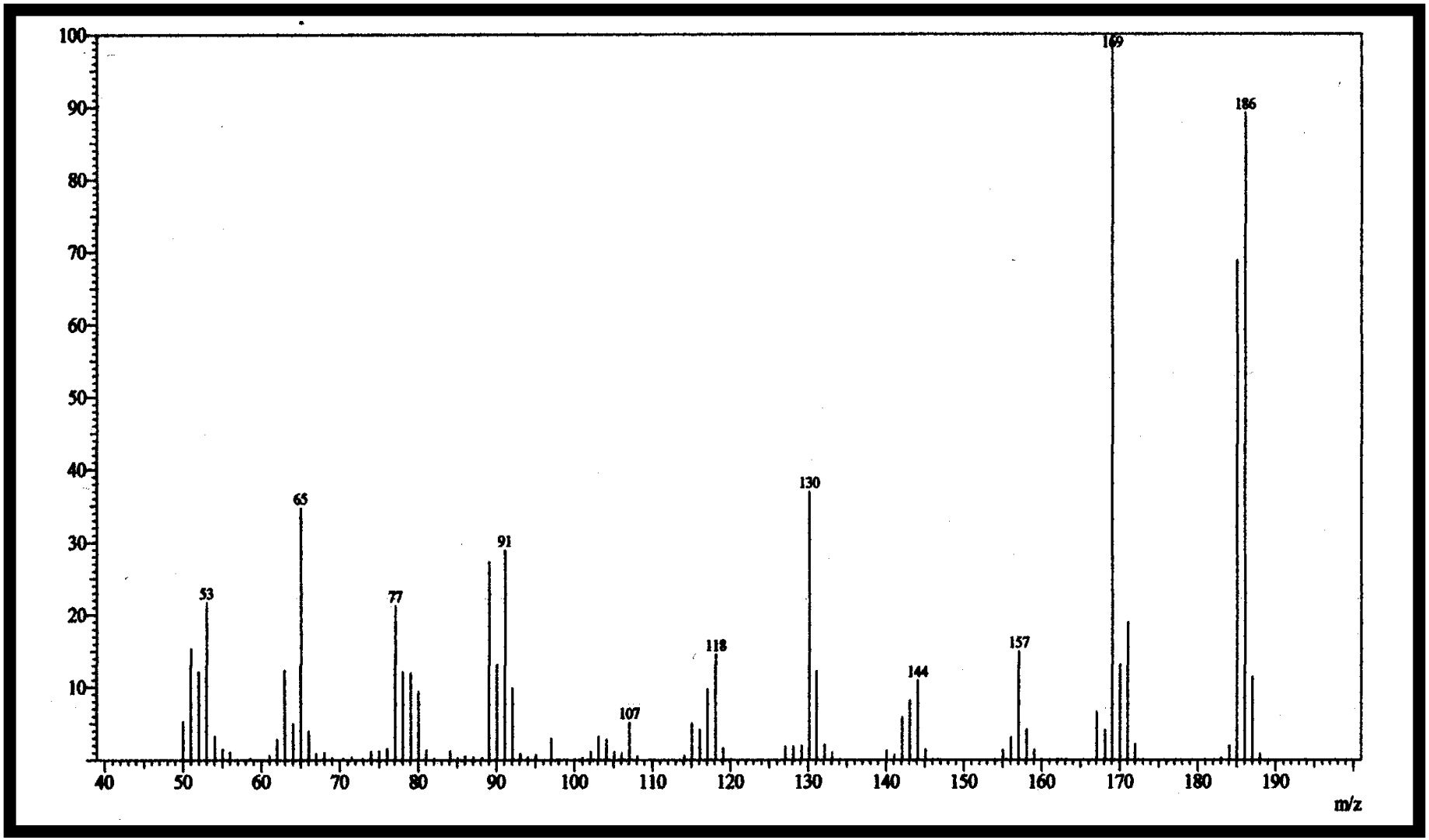
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-(*o*-tolyloxy)pyrimidine (45)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-(*o*-tolyloxy)pyrimidine (45)

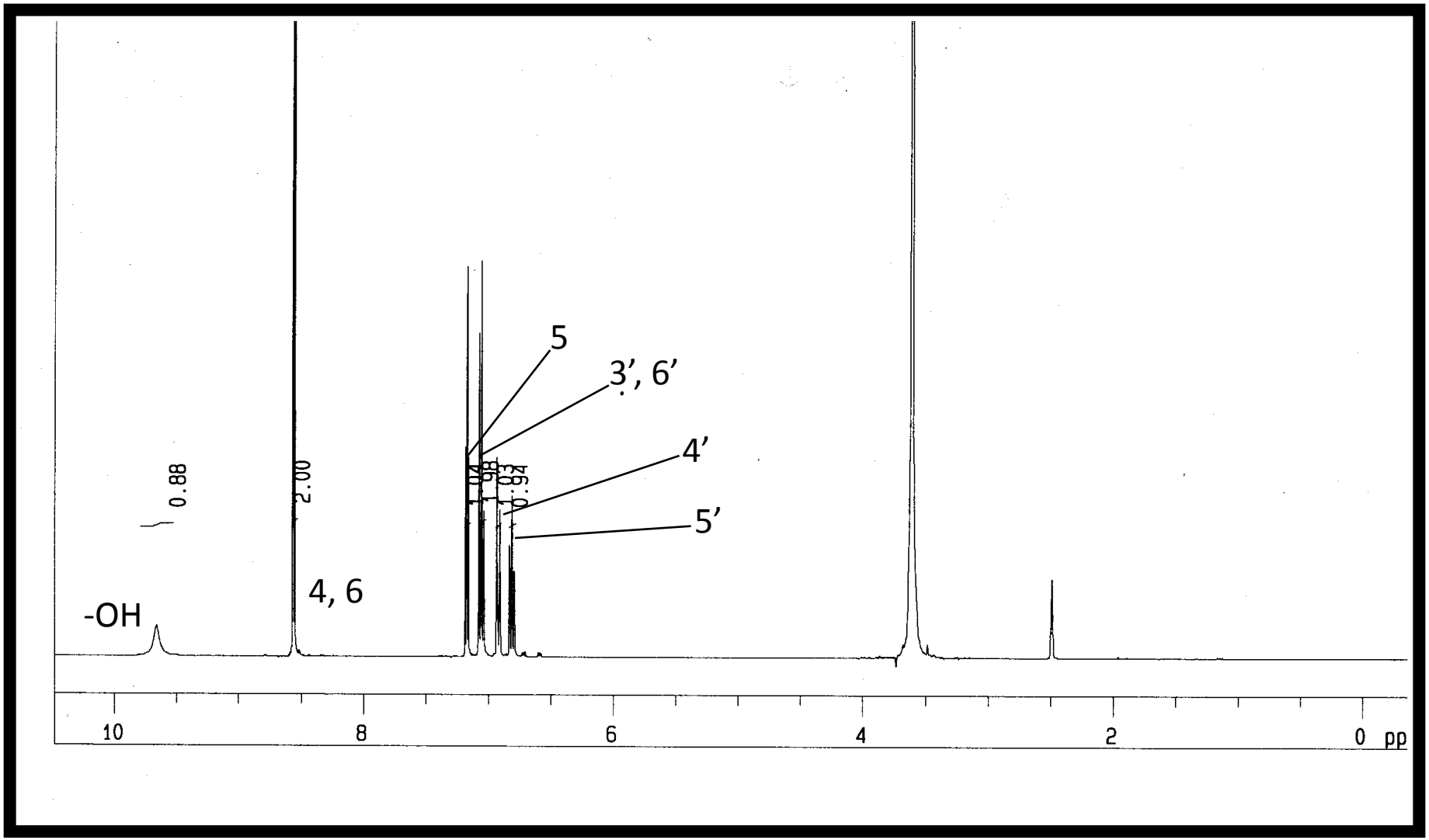


IR Spectrum of 2-(*o*-tolyloxy)pyrimidine (45)

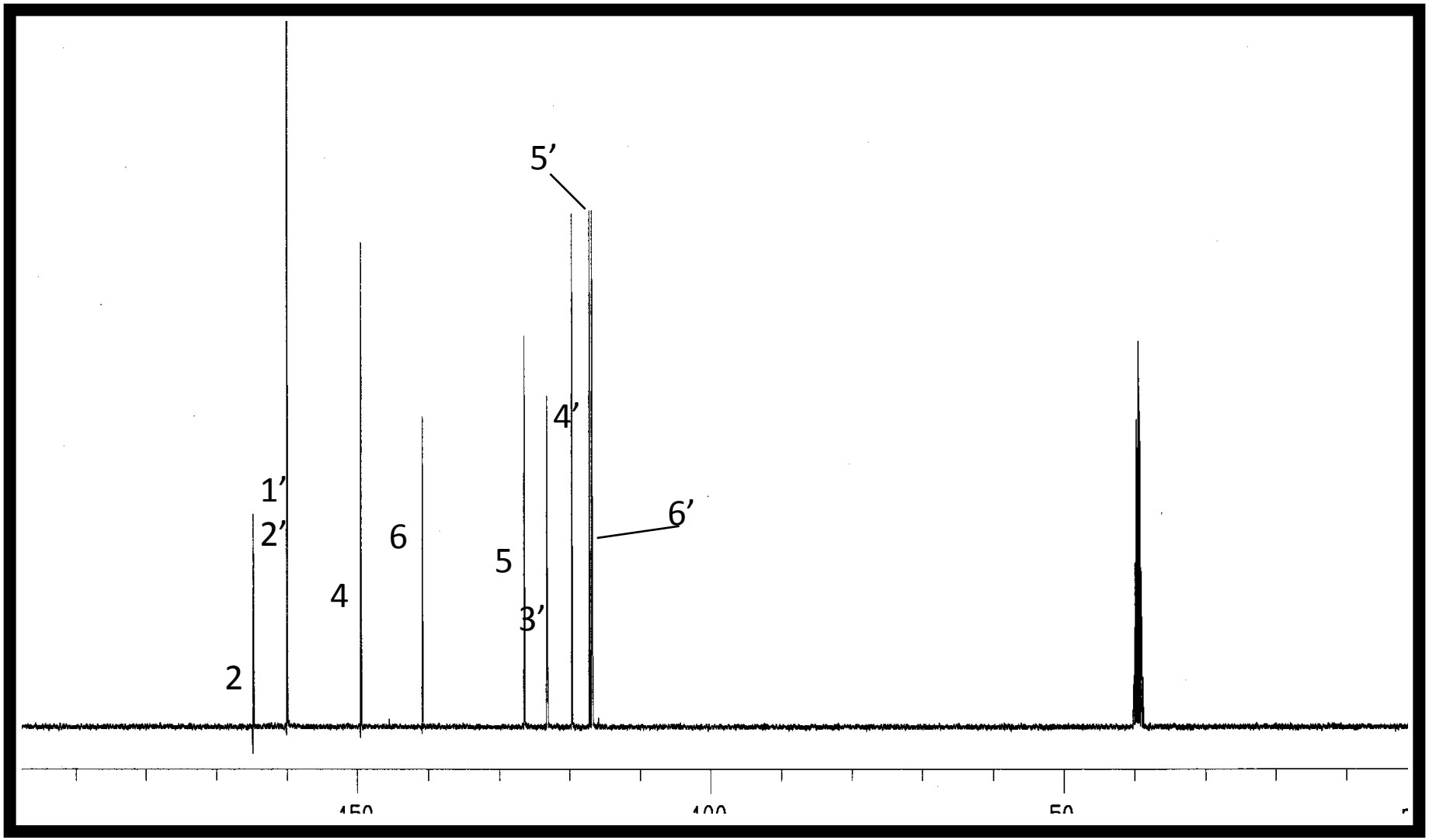


GCMS of 2-(*o*-tolyloxy)pyrimidine (45)

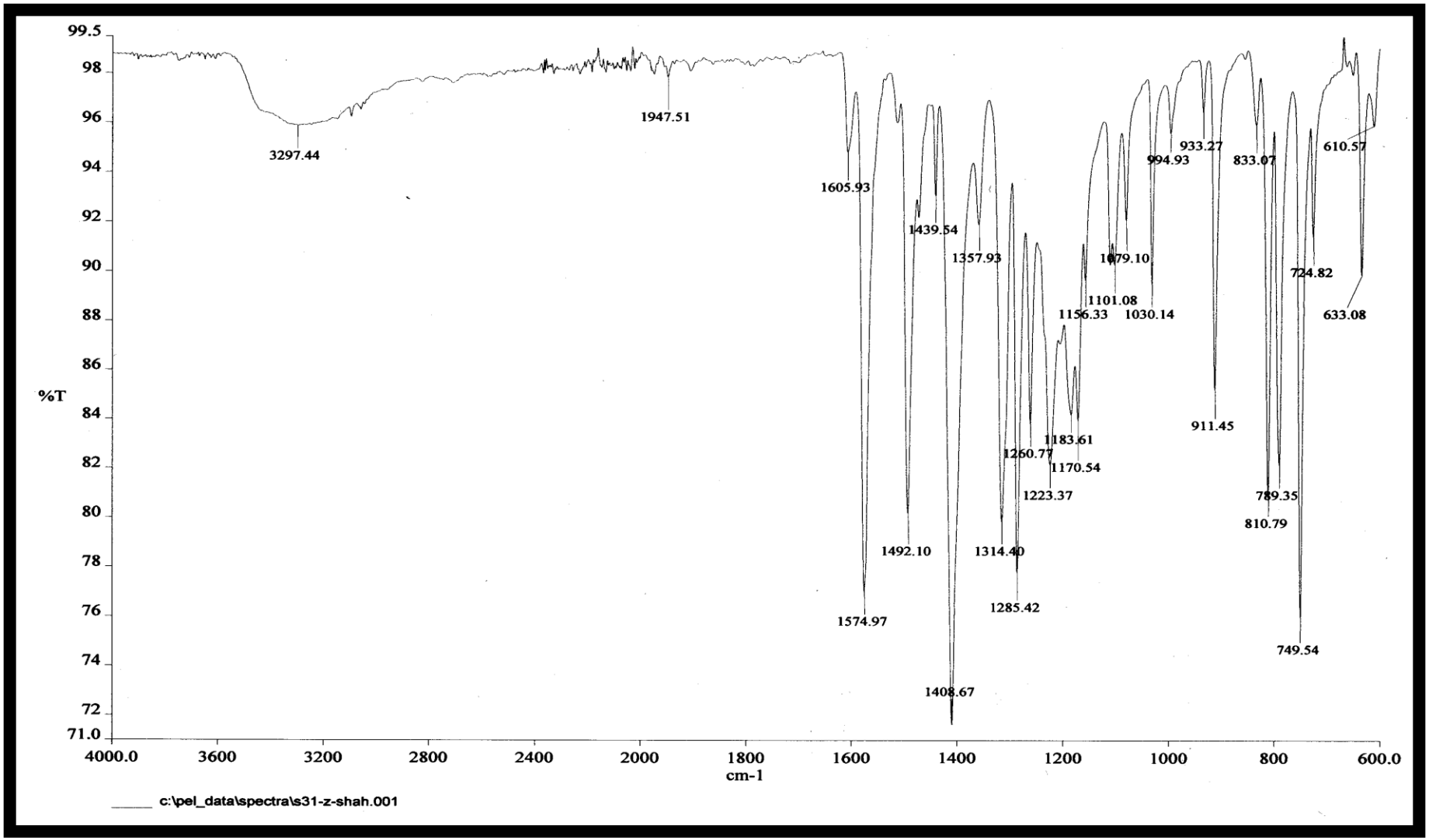
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



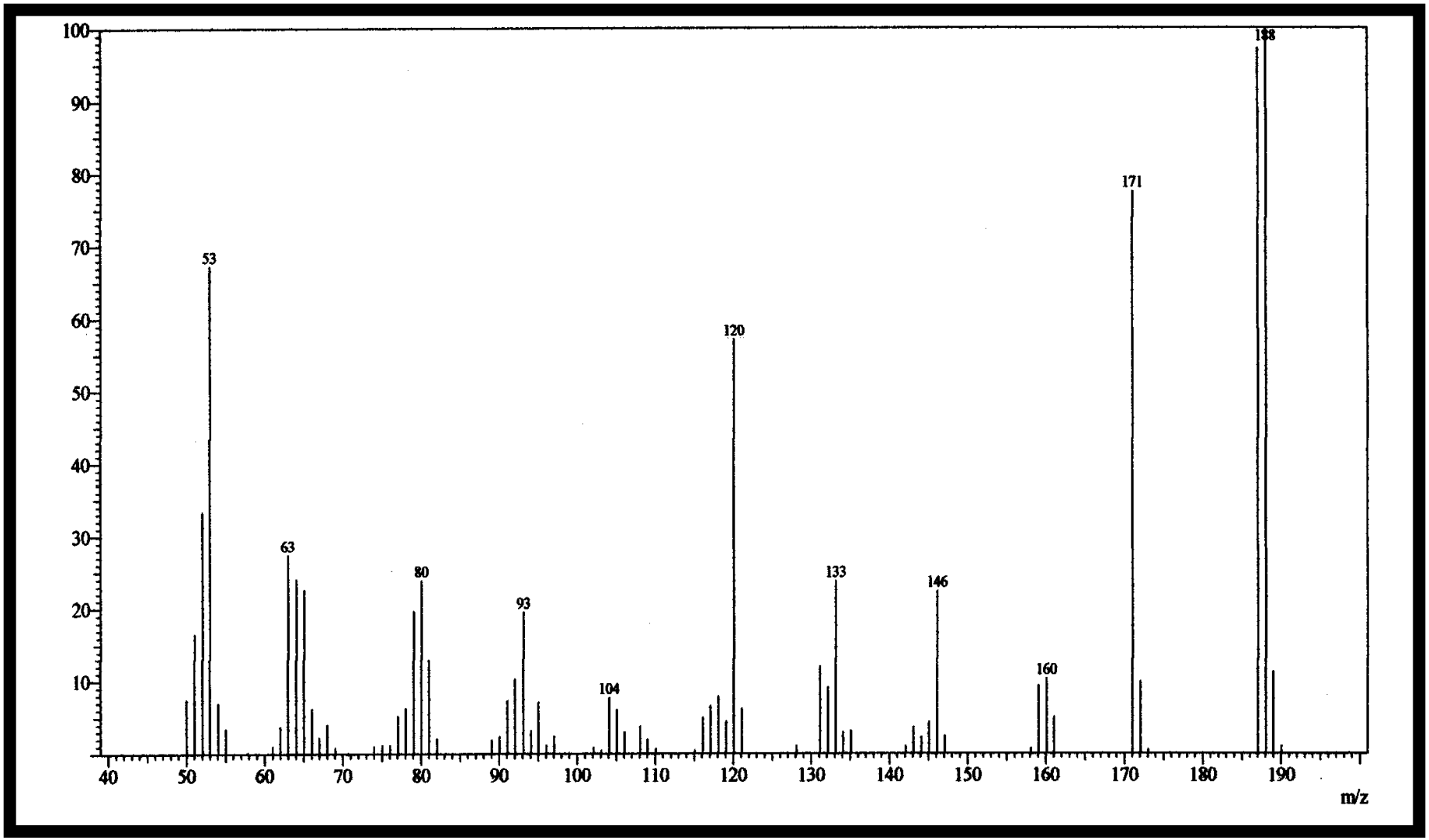
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-(pyrimidin-2-yloxy)phenol (47)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-(pyrimidin-2-yloxy)phenol (47)

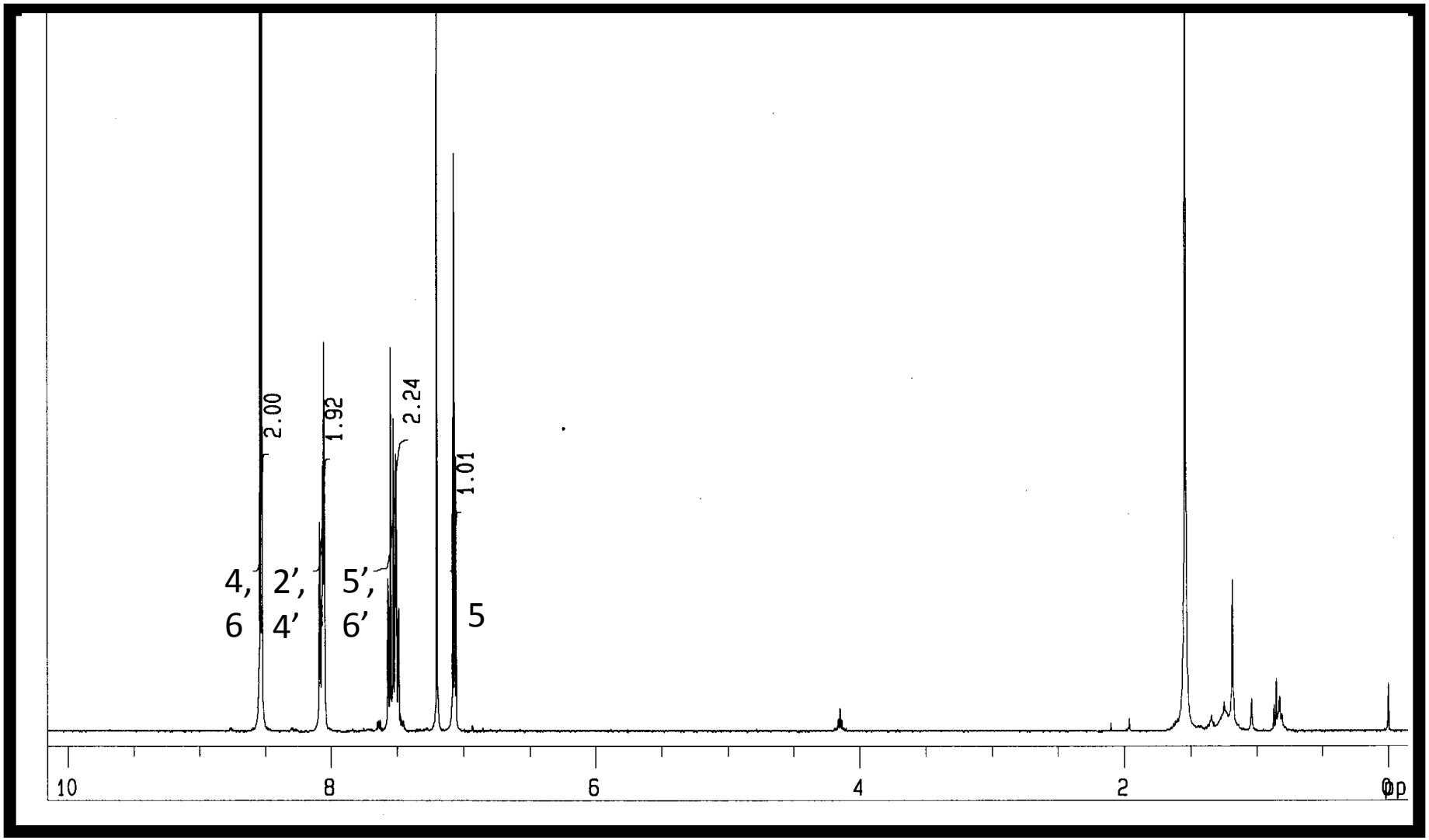


IR Spectrum of 2-(pyrimidin-2-yloxy)phenol (47)

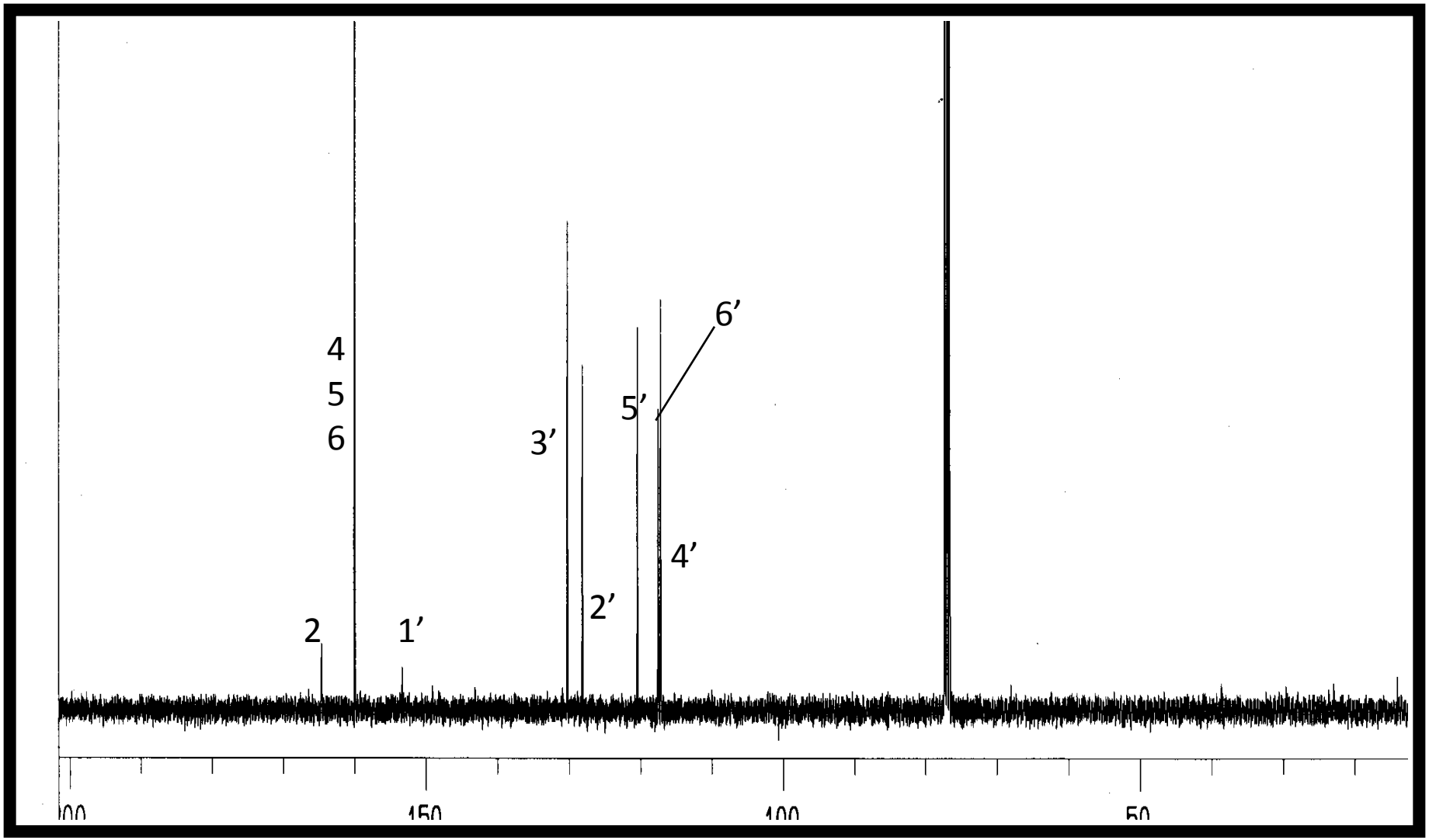


GCMS of 2-(pyrimidin-2-yloxy)phenol (47)

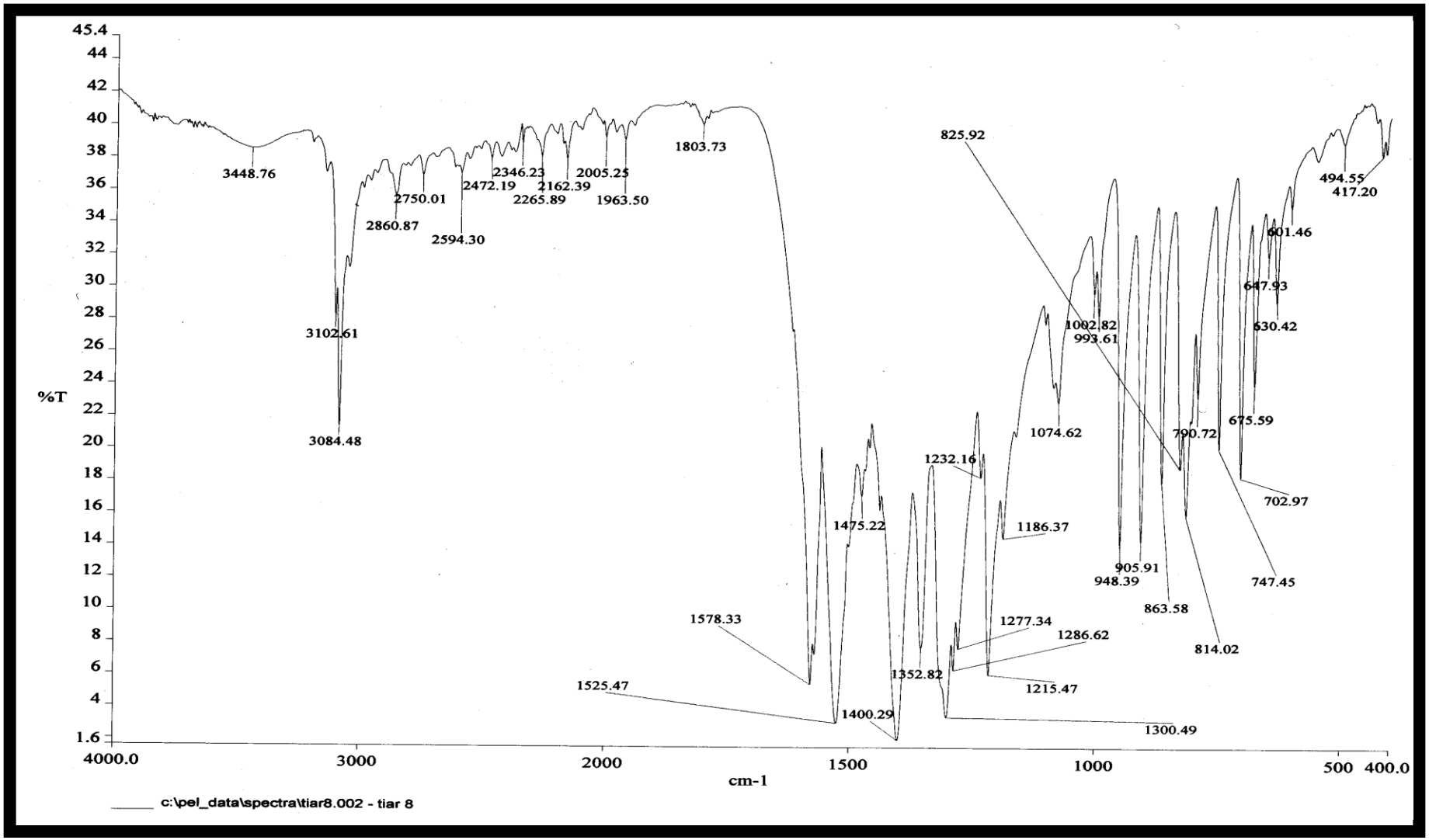
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



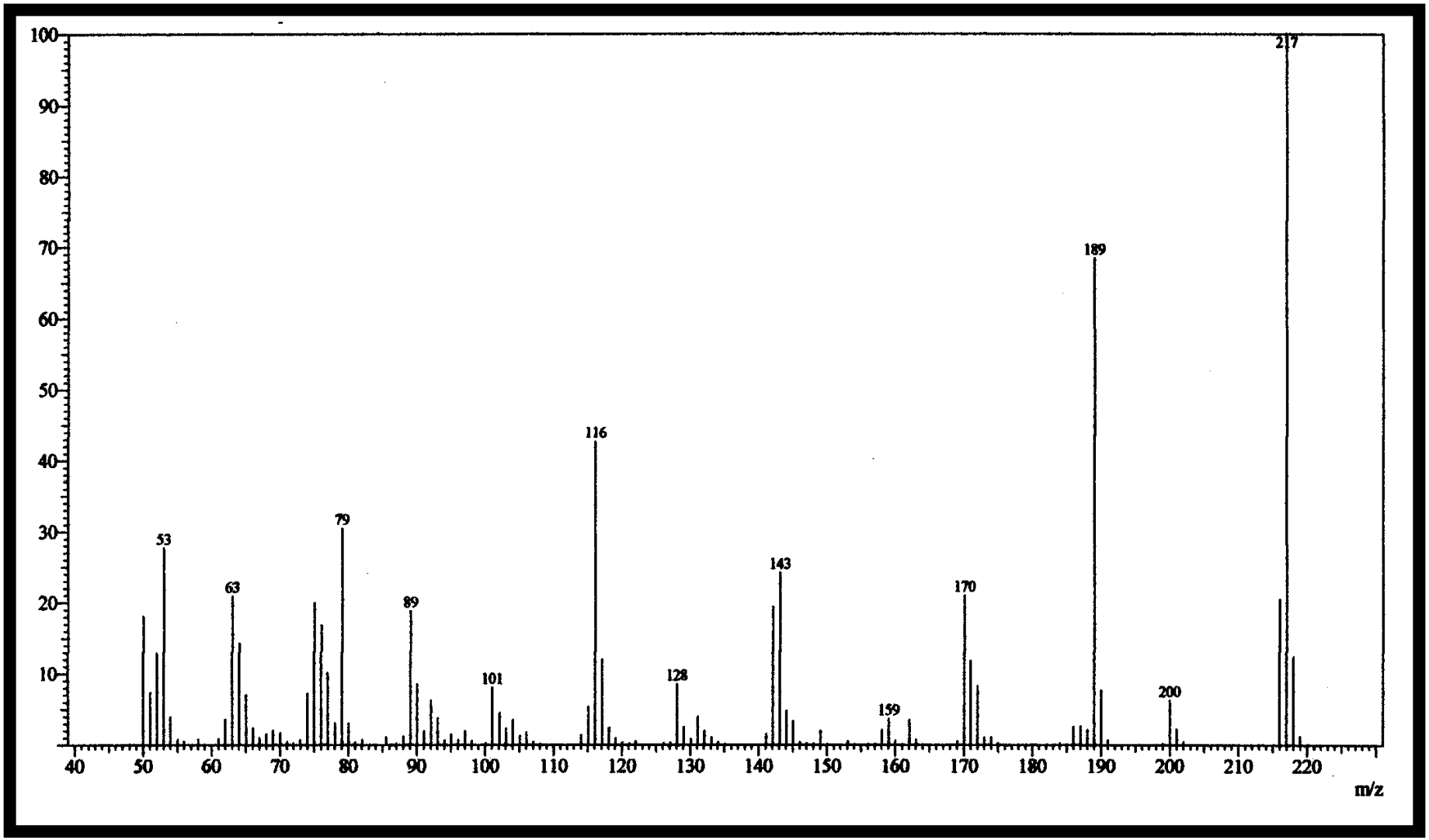
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-(3-nitrophenoxy)pyrimidine (49)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-(3-nitrophenoxy)pyrimidine (49)

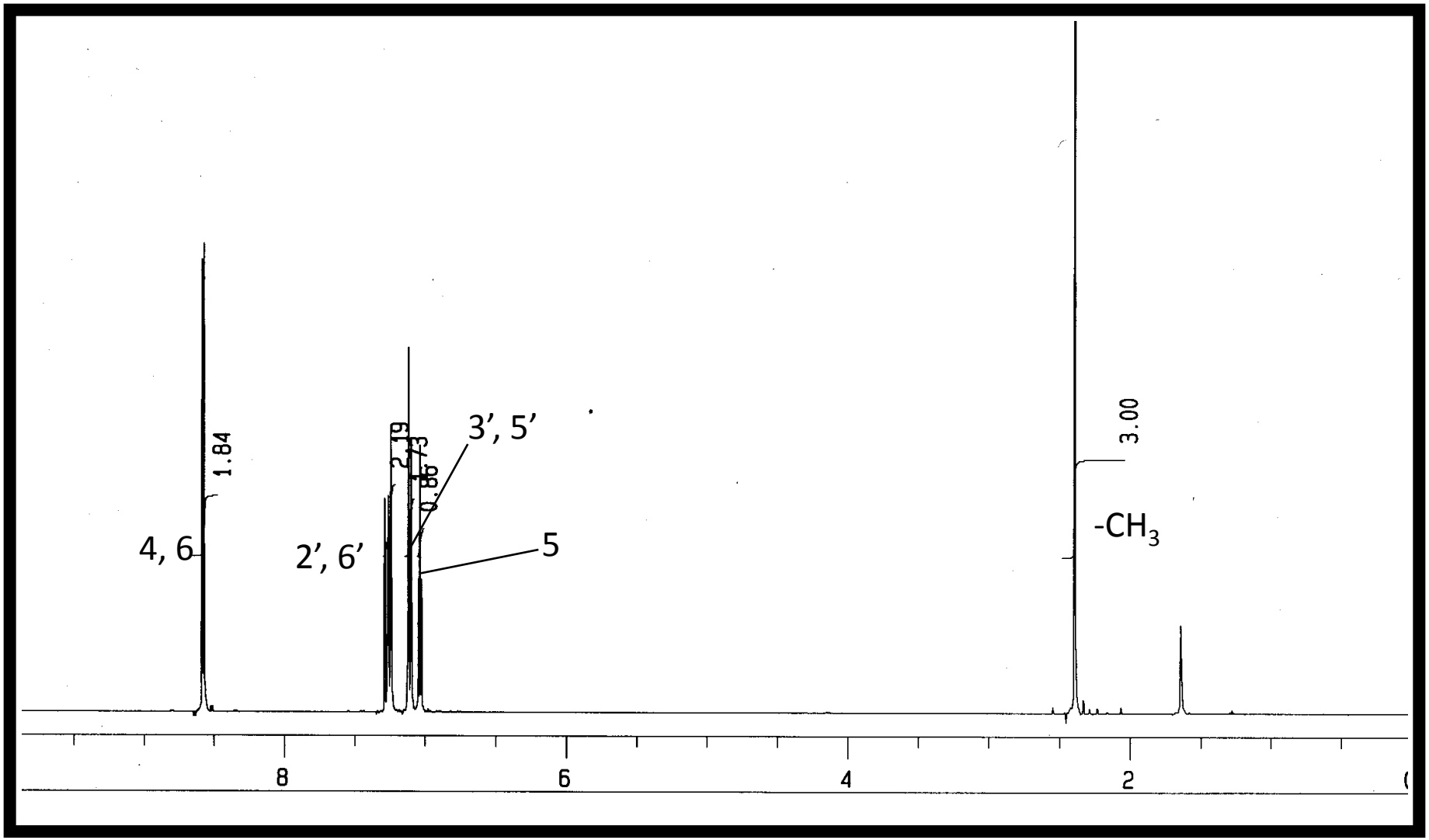


IR Spectrum of 2-(3-nitrophenoxy)pyrimidine (49)

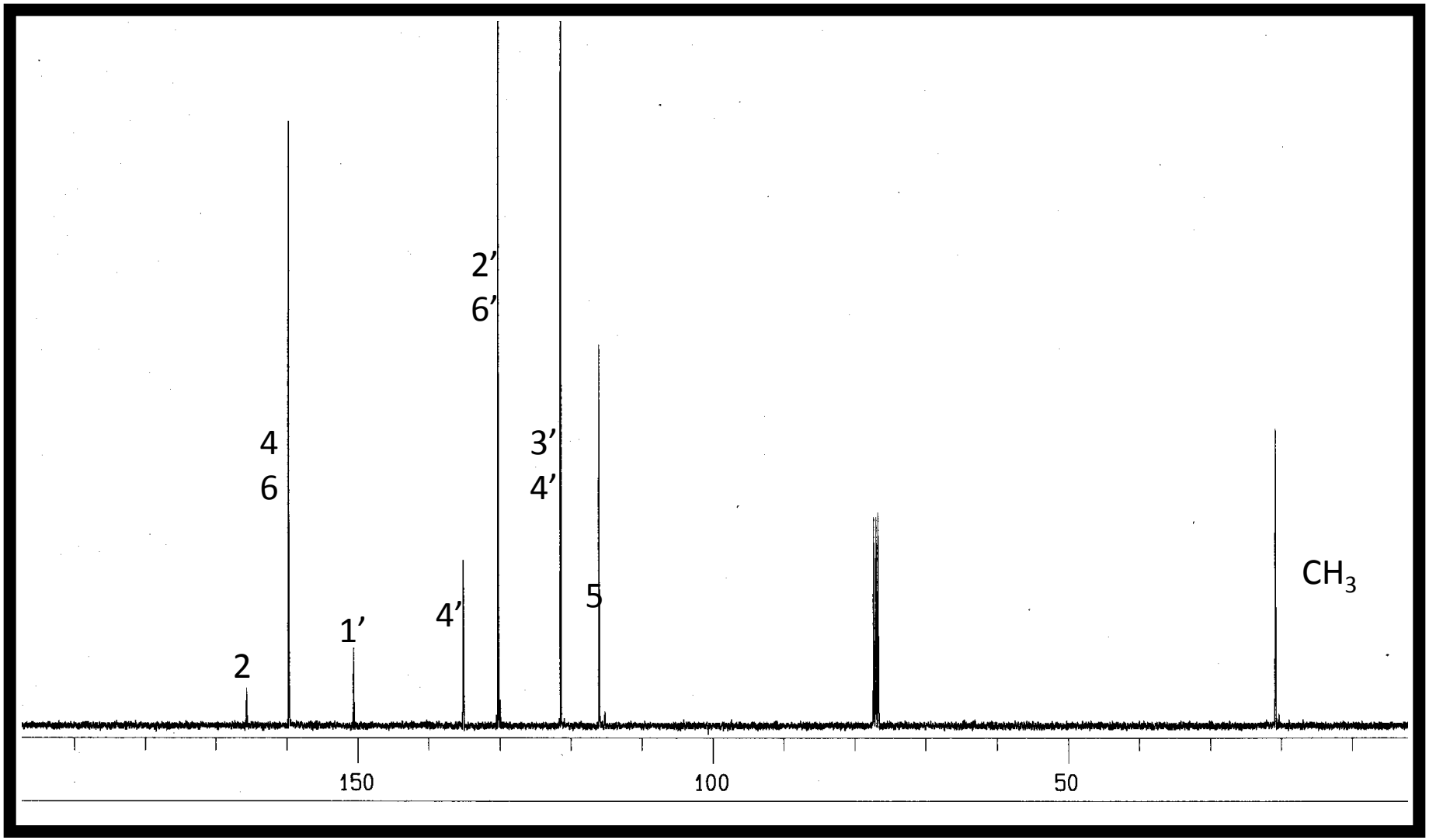


GCMS of 2-(3-nitrophenoxy)pyrimidine (49)

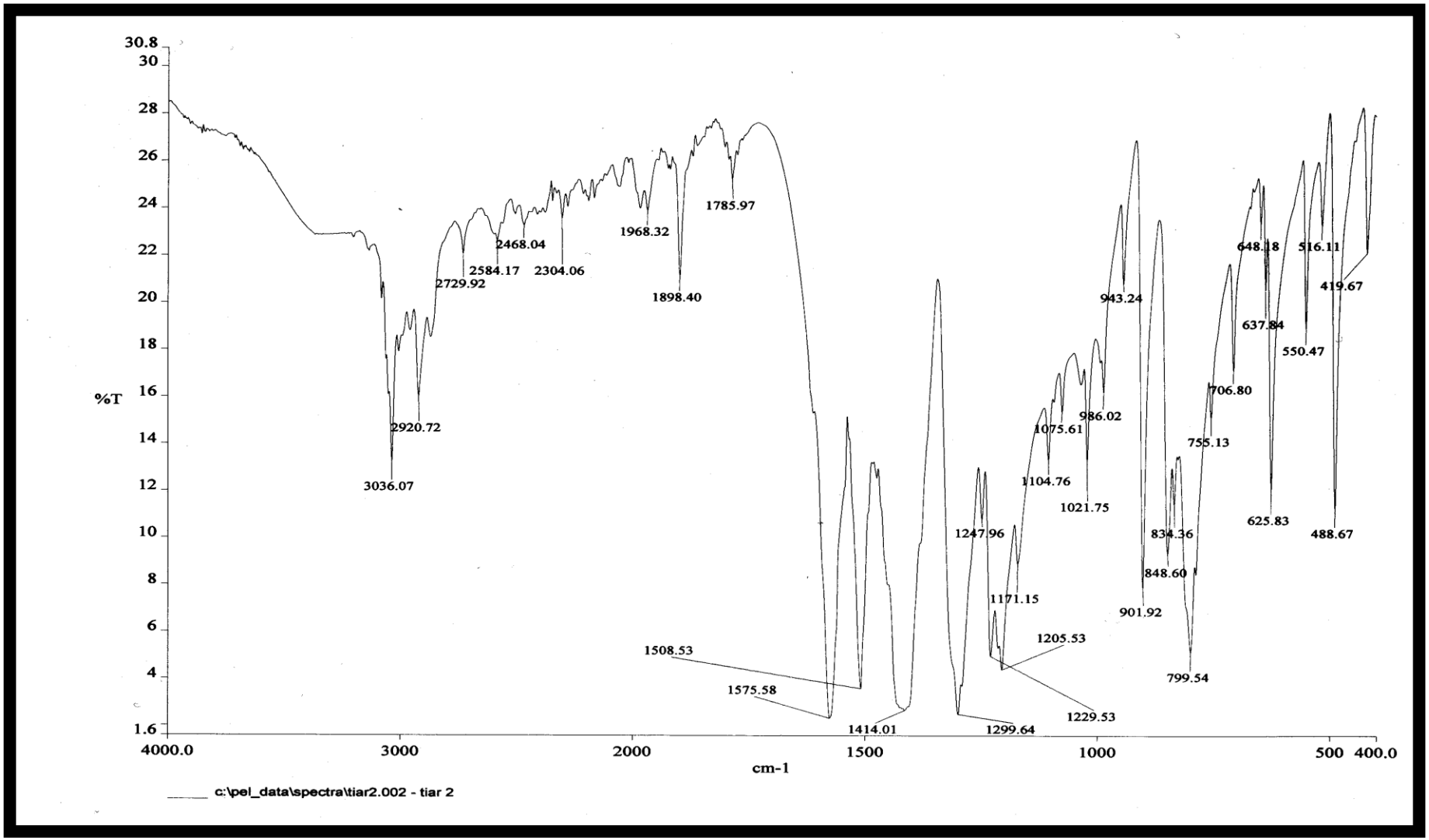
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



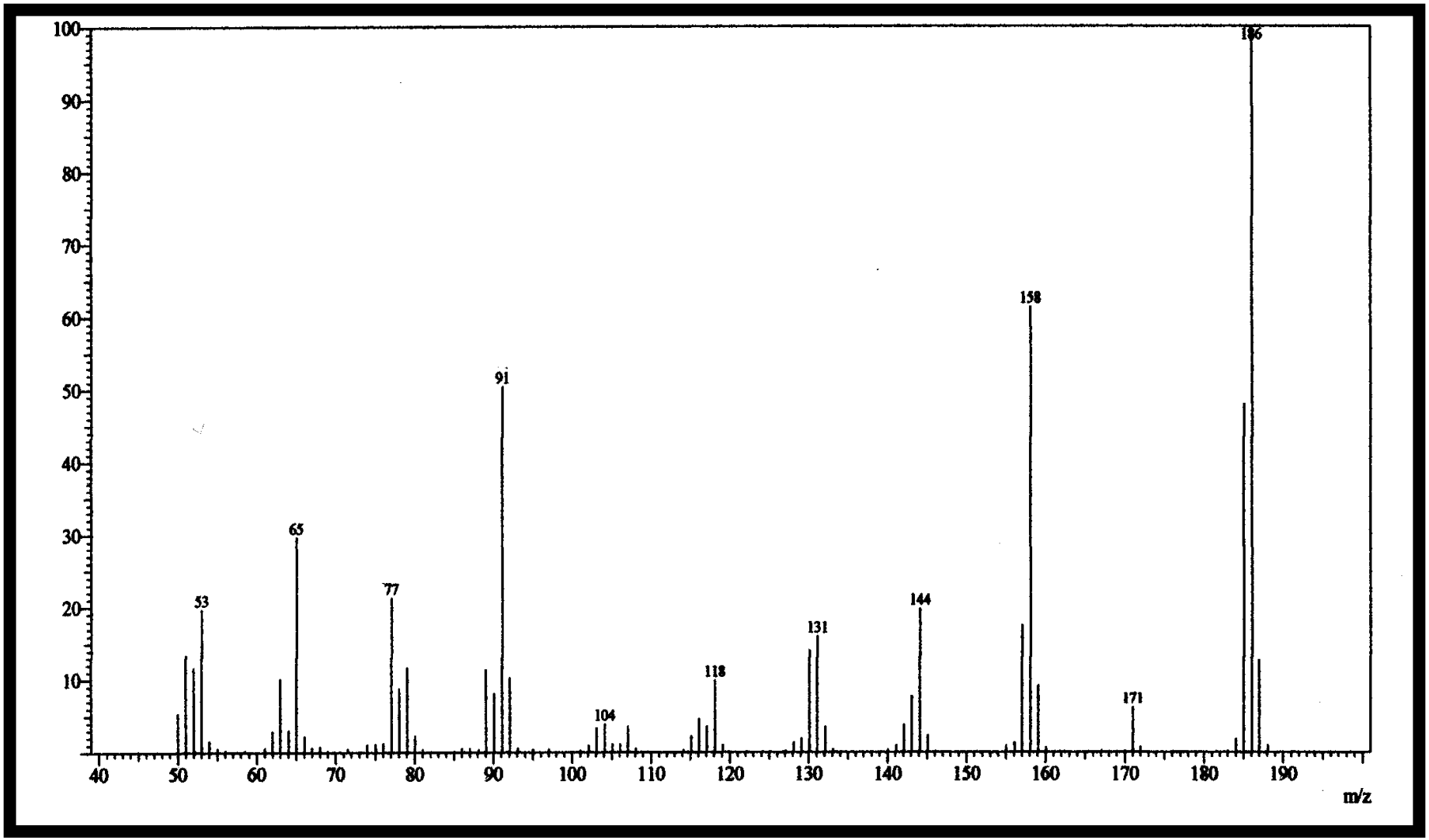
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-(*p*-tolyloxy)pyrimidine (51)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-(*p*-tolyloxy)pyrimidine (51)

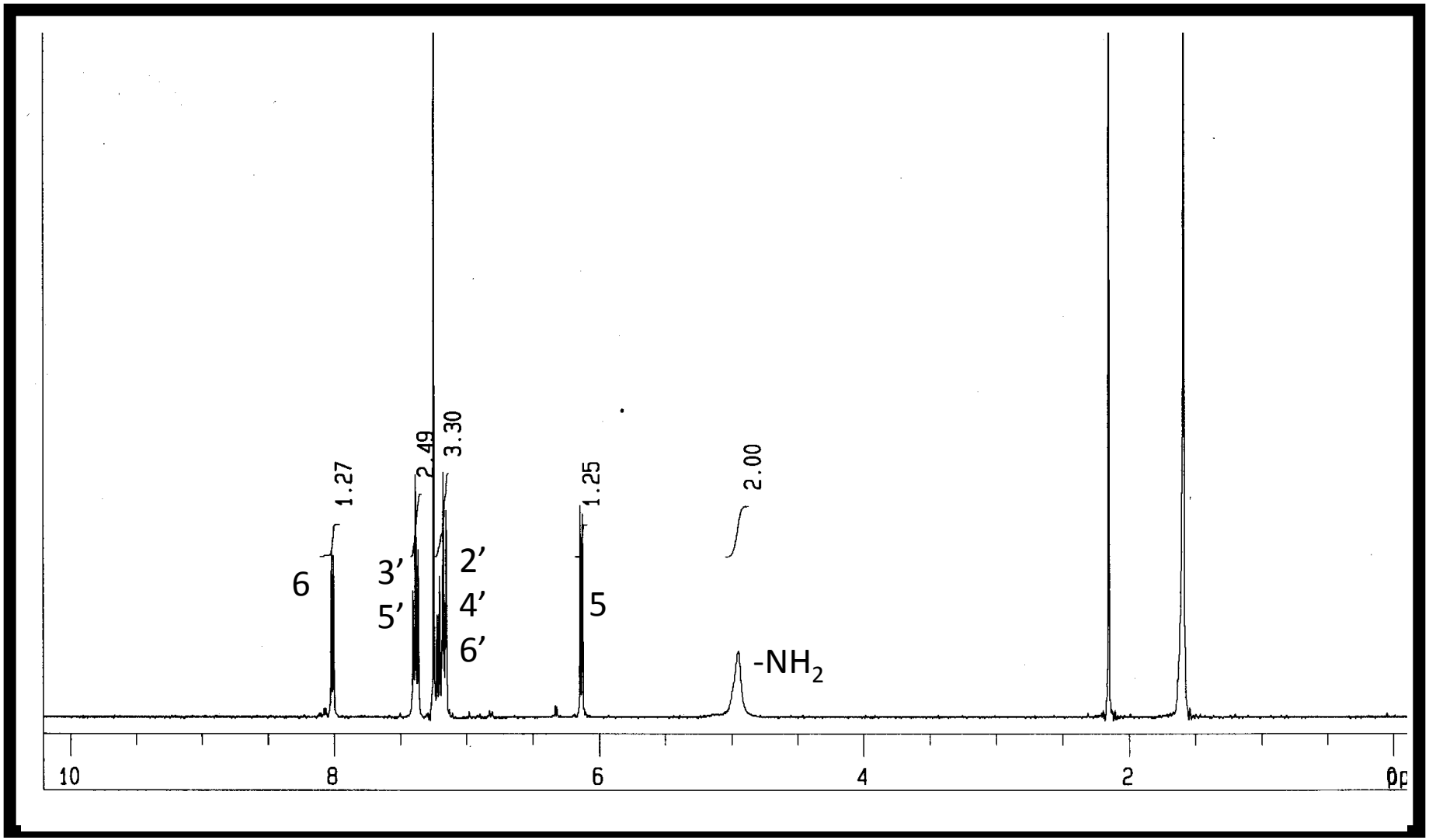


IR Spectrum of 2-(*p*-tolyloxy)pyrimidine (51)

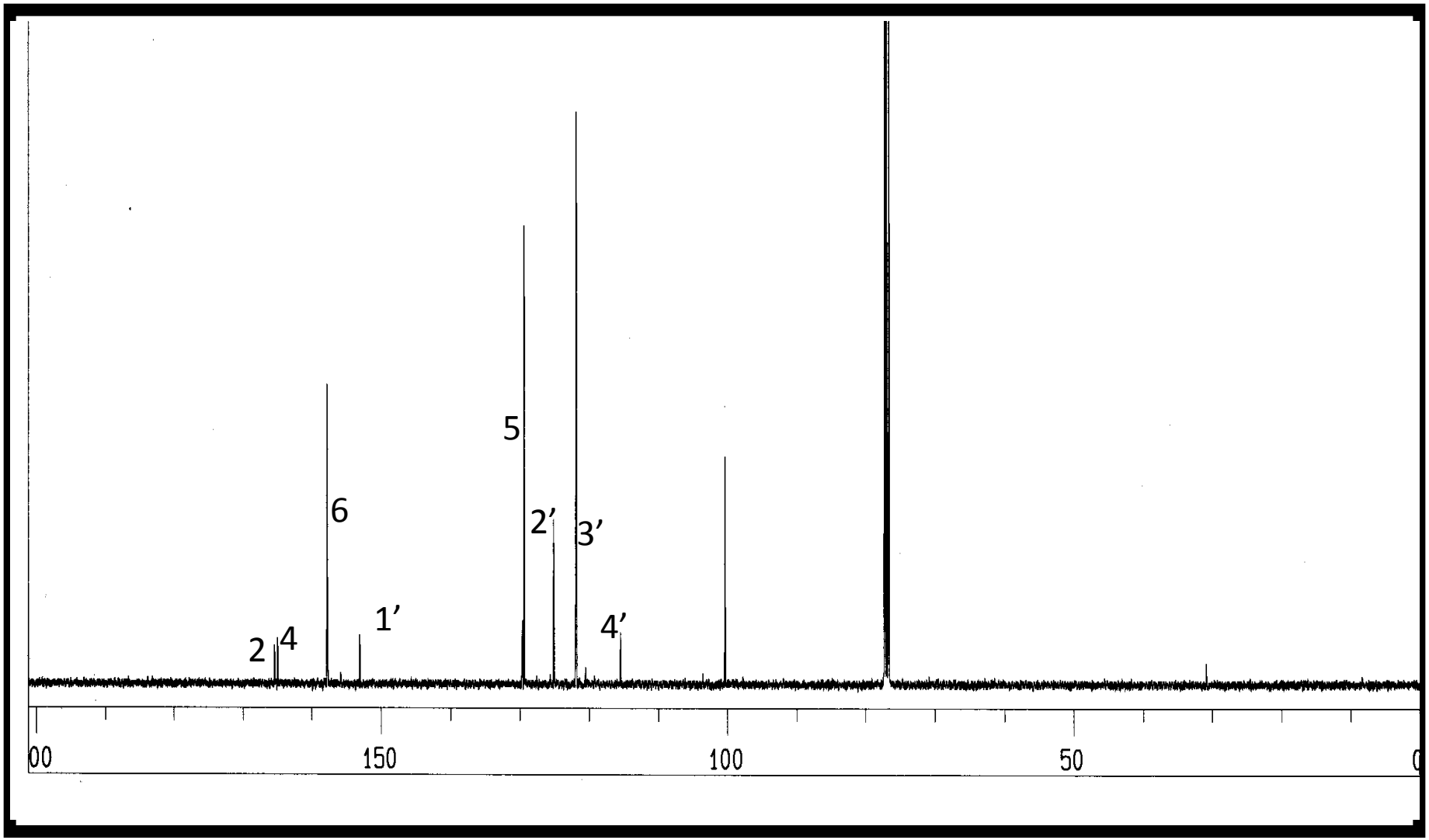


GCMS of 2-(*p*-tolyloxy)pyrimidine (51)

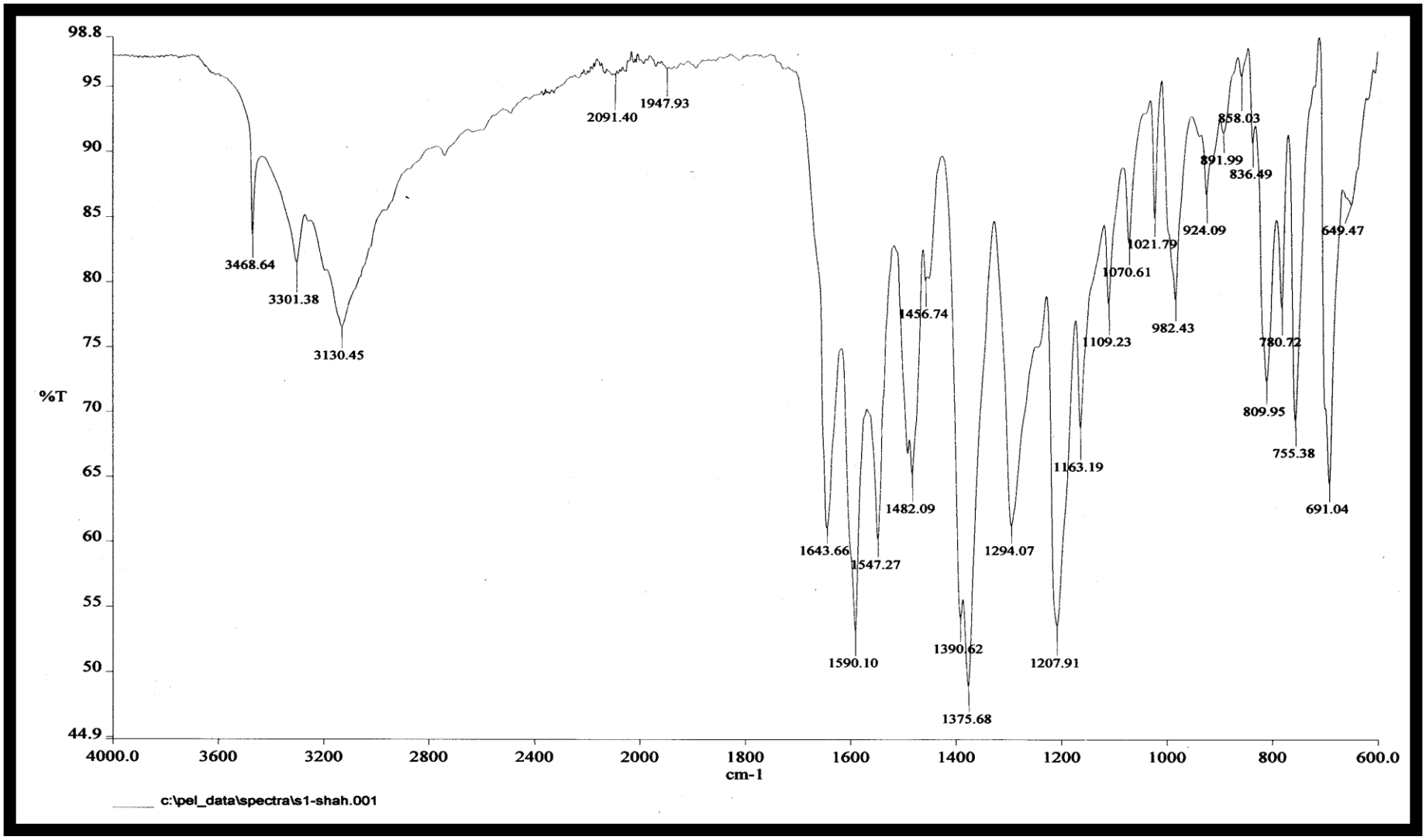
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



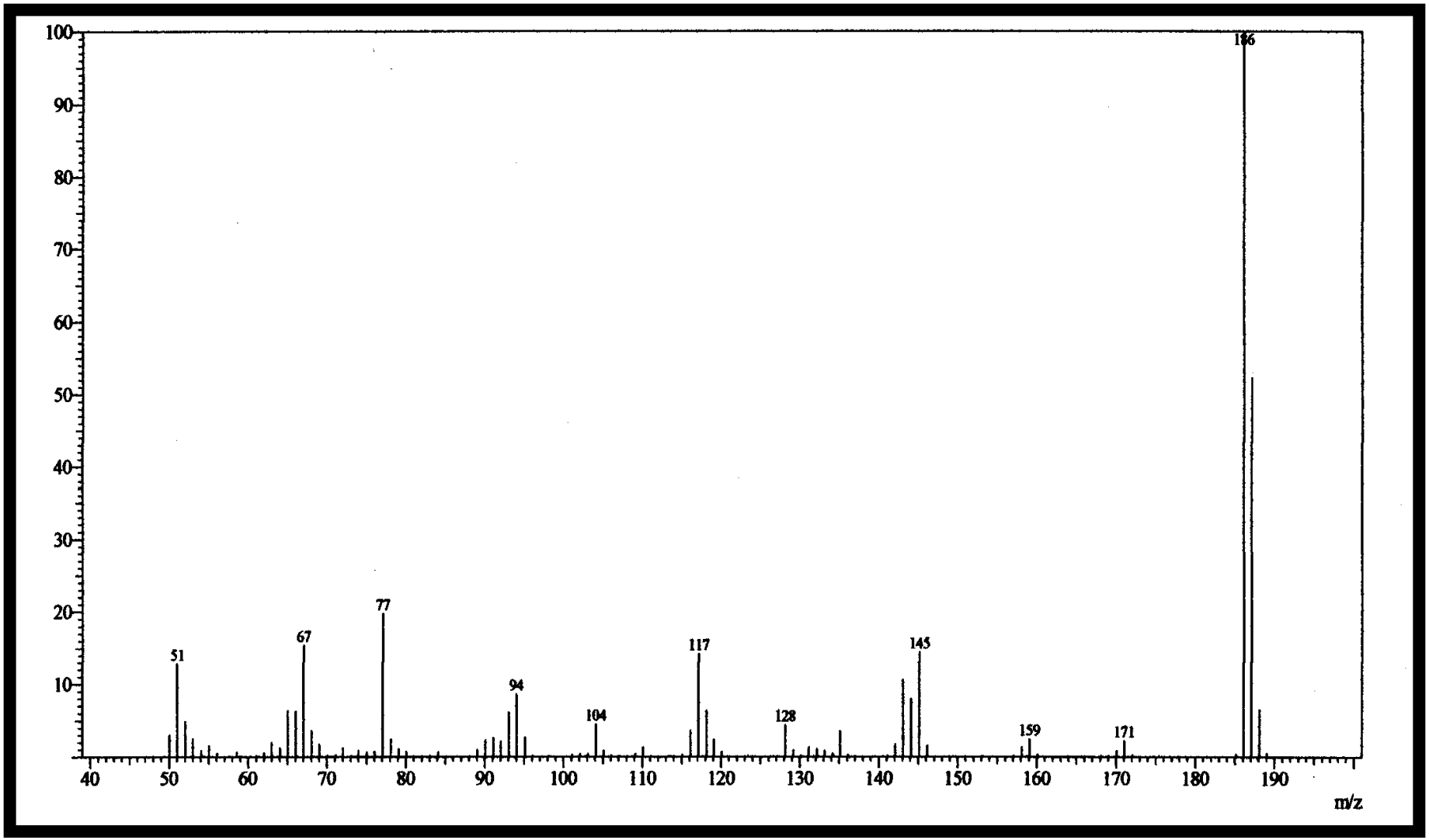
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-phenoxypyrimidin-4-amine (53)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-phenoxypyrimidin-4-amine (53)

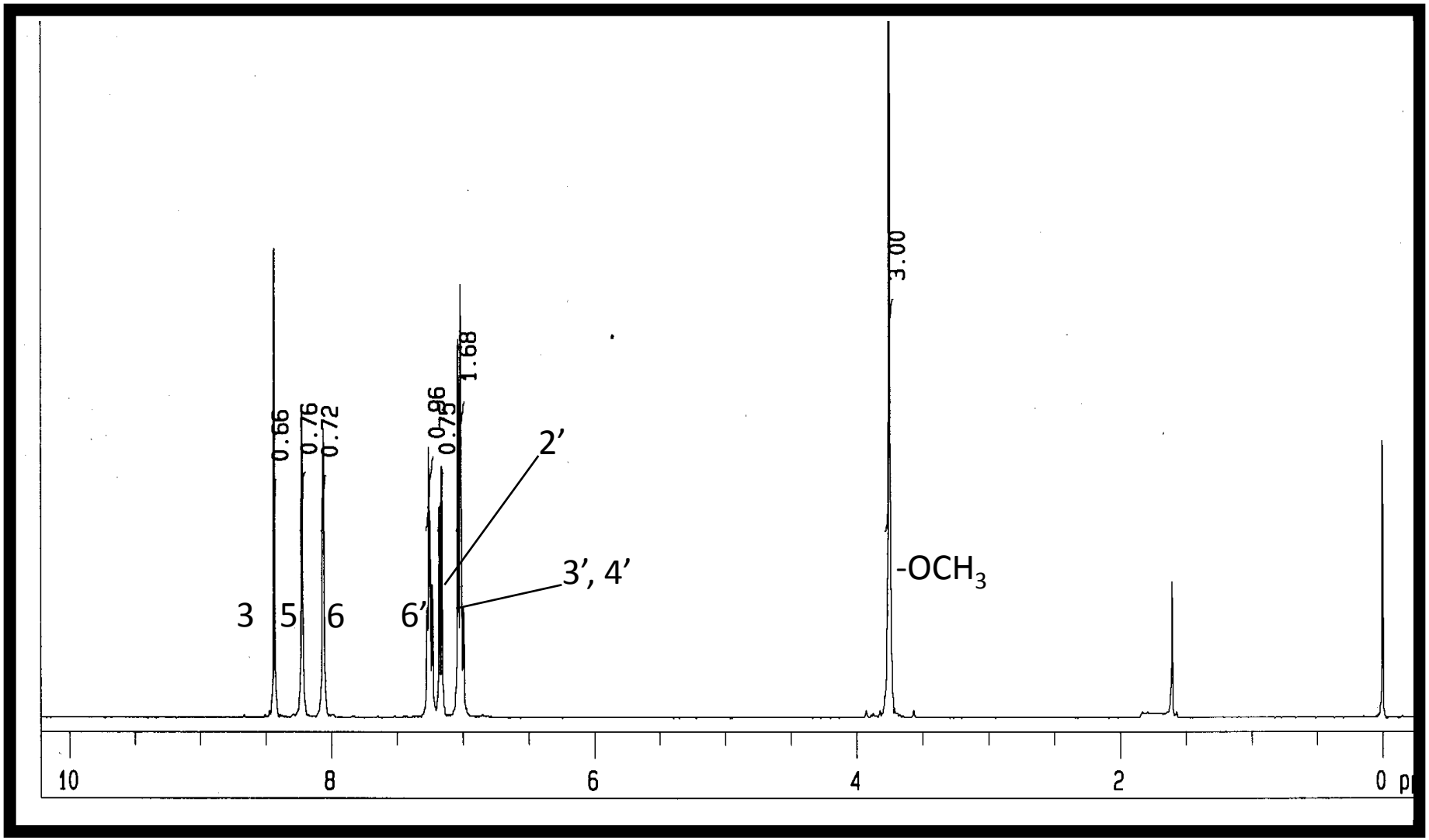


IR Spectrum of 2-phenoxypyrimidin-4-amine (53)

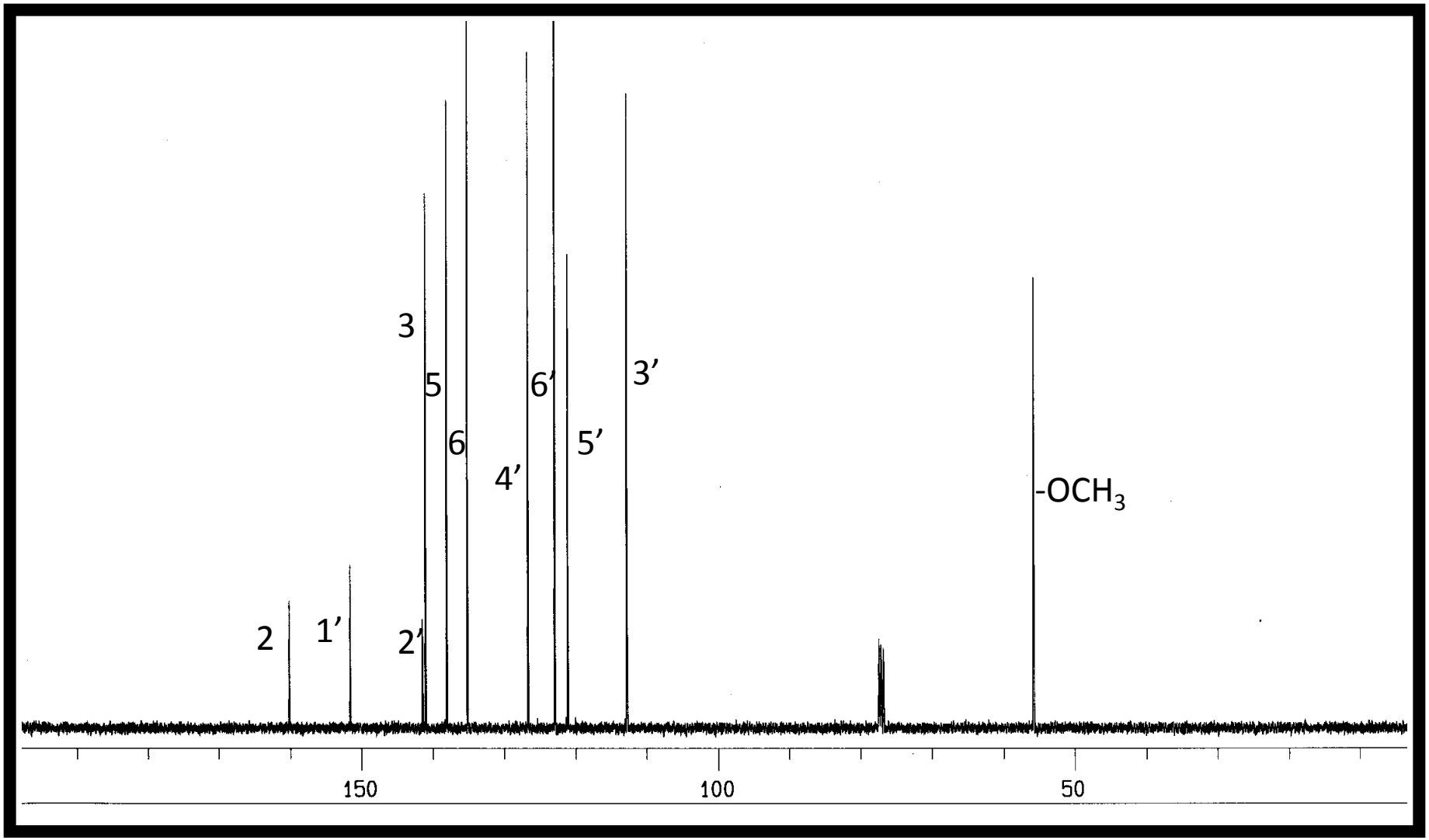


GCMS of 2-phenoxypyrimidin-4-amine (53)

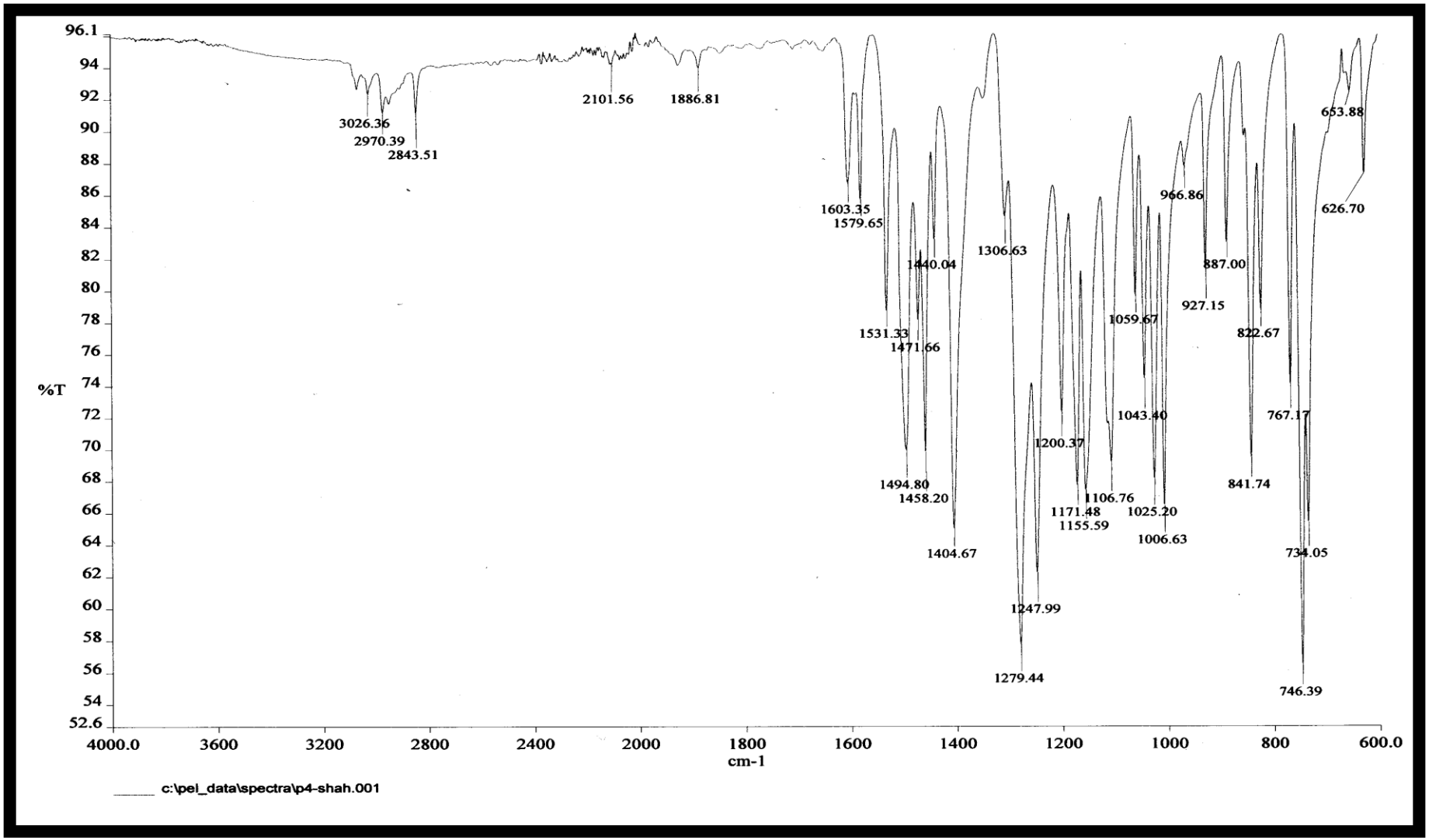
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



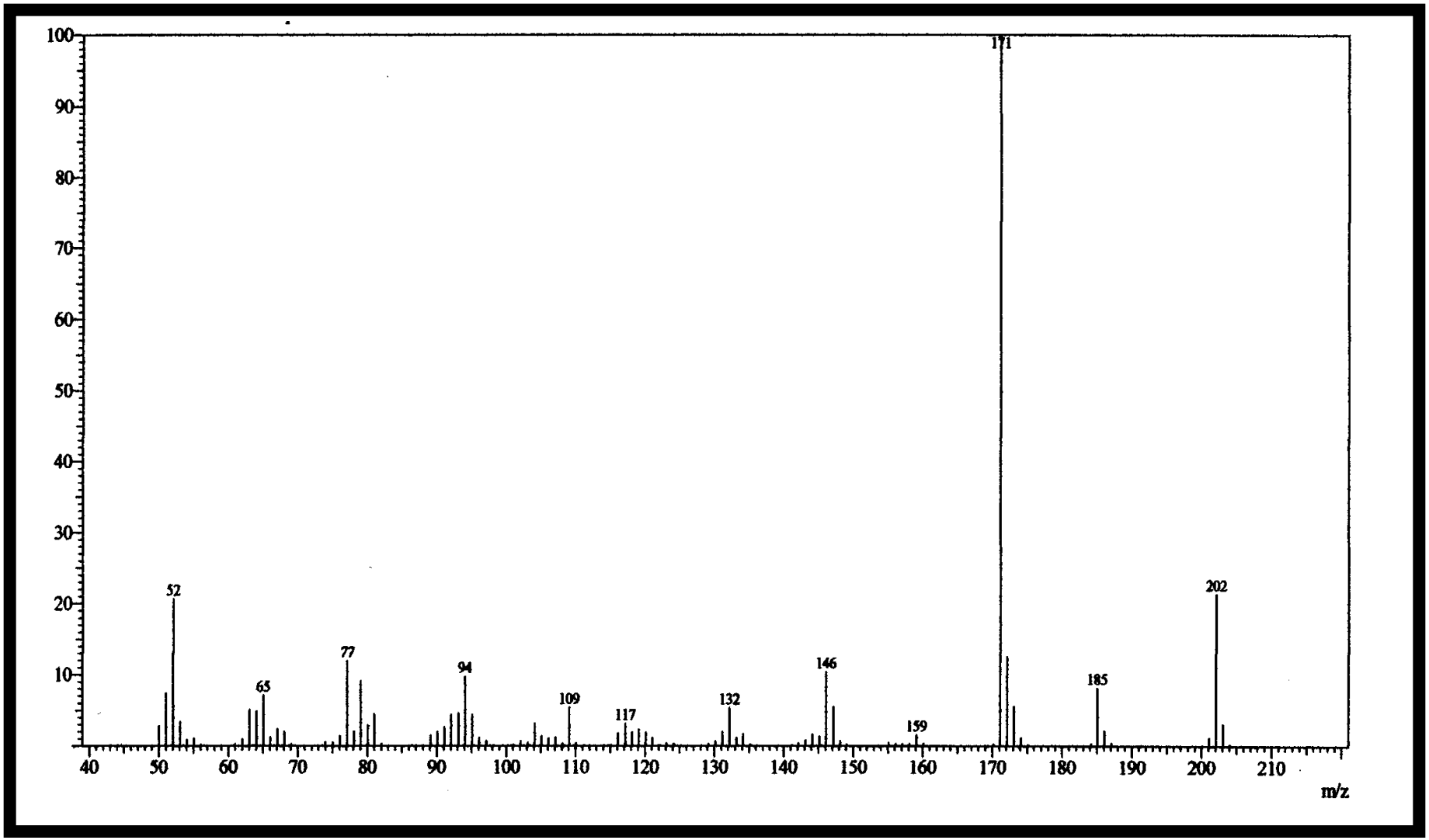
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-(2-methoxyphenoxy)pyrazine (55)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-(2-methoxyphenoxy)pyrazine (55)

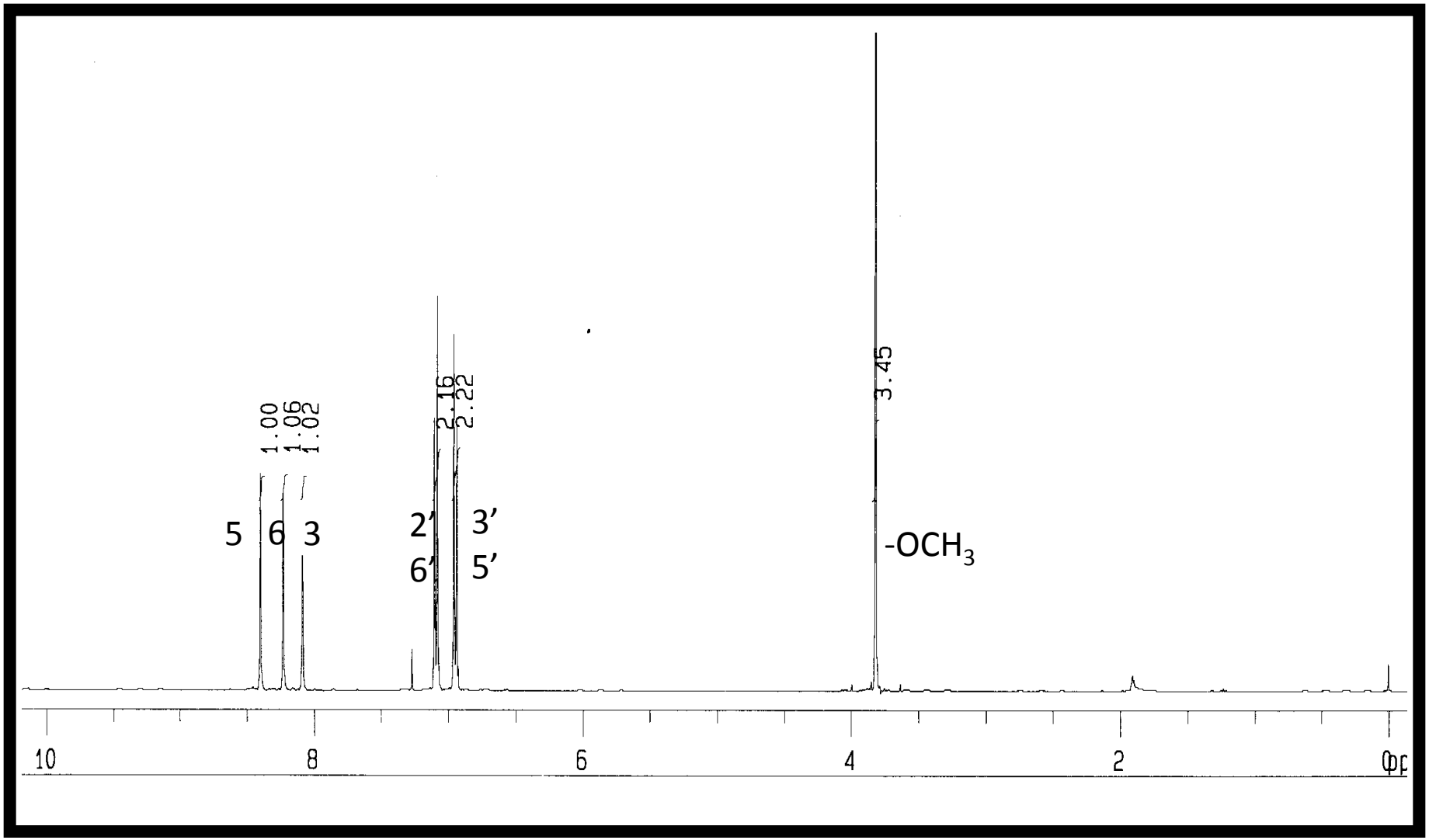


IR Spectrum of 2-(2-methoxyphenoxy)pyrazine (55)

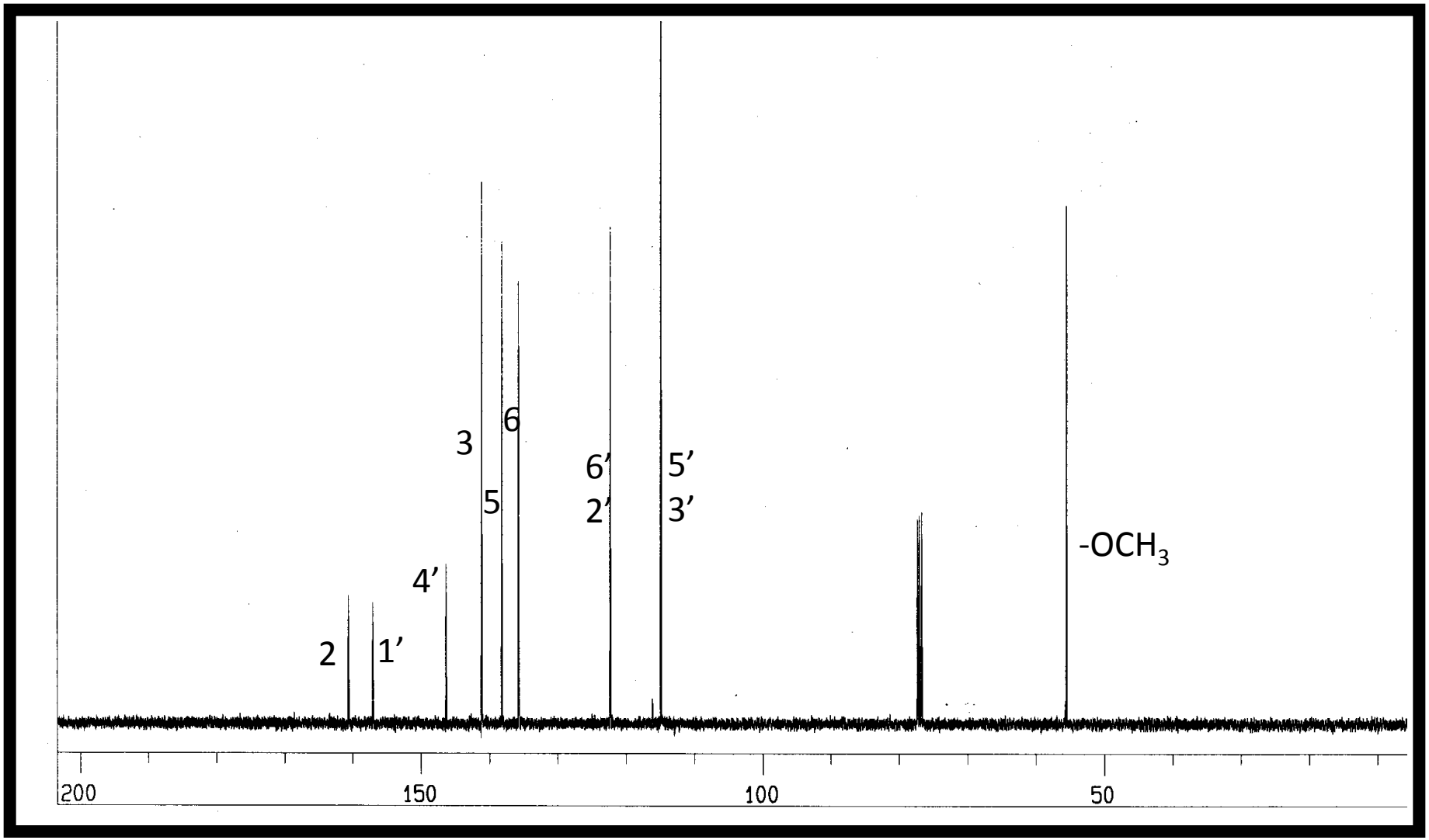


GCMS of 2-(2-methoxyphenoxy)pyrazine (55)

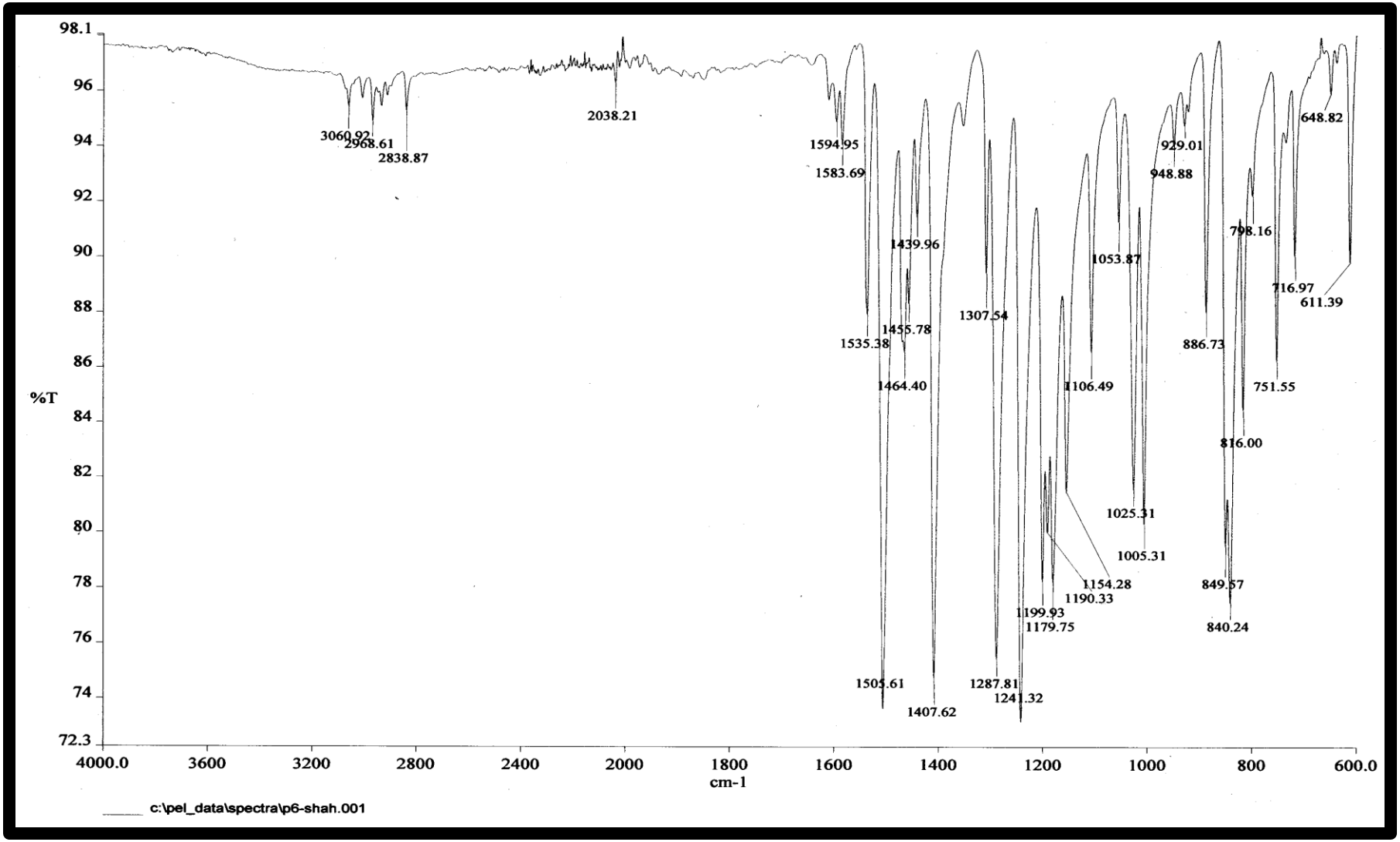
Appendix 1- ^{1}H NMR, ^{13}C NMR, IR and GCMS spectra



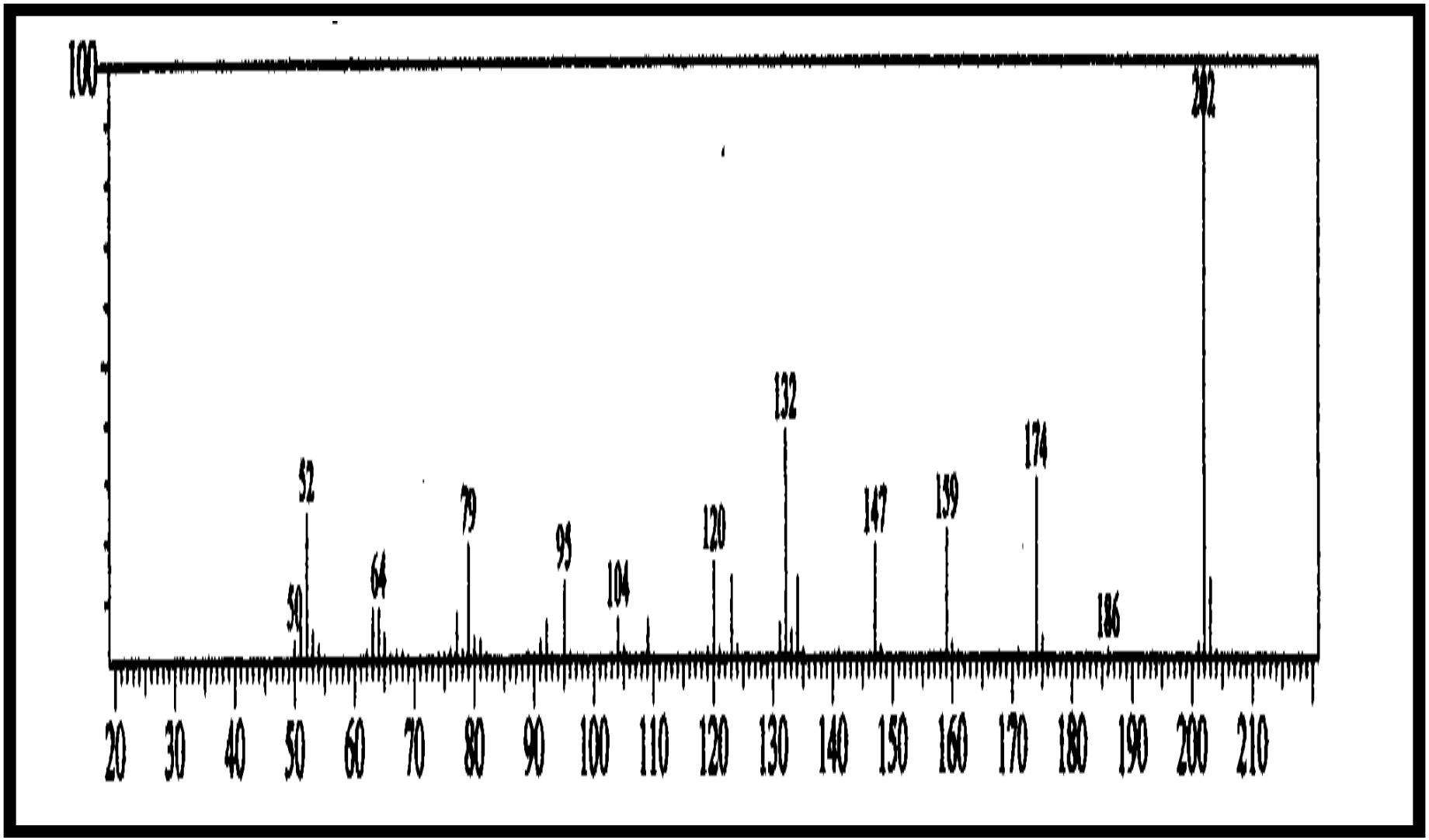
^{1}H NMR Spectra ($CDCl_3$, 400 MHz) of 2-(4-methoxyphenoxy)pyrazine (56)



^{13}C NMR Spectra ($CDCl_3$, 100 MHz) of 2-(4-methoxyphenoxy)pyrazine (56)



IR Spectrum of 2-(4-methoxyphenoxy)pyrazine (56)



GCMS of 2-(4-methoxyphenoxy)pyrazine (56)