**An-Najah National University**

**Faculty of Graduate Studies**

# Preparation of aromatic esters of 2-phenoxyethanol and exploring some of their biological activities

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# Dedication

To my husband Waleed for his support, love, and encouragement.

To my daughters Loreen and Dania for their patience for being far from me, as I was busy all the time.

To my parents for helping, taking care and praying for me.

To my sister Haneen who supported me and shared my worries.

To my husband's family whom supported me and helped me by taking care of my daughters.

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To my friends for their continuous support.

To all who prayed for me.

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## الإقرار

أنا الموقع أدناه، مقدم الرسالة التي تحمل العنوان:

# Preparation of aromatic esters of 2-phenoxyethanol and exploring some of their biological activities

أقر بأن ما شملت عليه هذه الرسالة إنما هو نتاج جهدي الخاص، باستثناء ما تمّت الإشارة إليه حيثما ورد، وأنّ هذه الرسالة ككل، أو أيّ جزء منها لم يقدّم من قبل لنيل أيّ درجة أو لقب علميّ لدى أيّ مؤسسة تعليمية أو بحثية أخرى.

## Declaration

The work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

**Student's Name:** Nadine Mohammed Kamel Qatatweh **اسم الطالب:**

**Signature:** **التوقيع:**

**Date:** 29/9/2015 **التاريخ:**

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# List of Abbreviations

| Symbol | abbreviation |
|---|---|
| **RNS** | Reactive nitrogen species |
| **ROS** | reactive oxygen species |
| **BERC** | Biodiversity & Environmental Research Center |
| **NARC** | National Agriculture Research *Center* |
| **DPPH** | 1,1-Diphenyl-2-picryl-hydrazyl |
| **PABA** | p-aminobenzoic acid |
| **DCFC** | Dry column flash chromatography |

**Preparation of aromatic esters of 2-phenoxyethanol and exploring some of their biological activities.**

**By**
**Nadine Mohammed Kamel Qalalweh**
**Supervisors**
**Dr. Waheed J. Jondi**
**Dr. Orwa Housheya**

# Abstract

2-Phenoxyethanol was reacted with twelve different benzoic acids to give the corresponding substituted benzoate esters (I – XII). The structures of these esters were established by Fourier Transform Infrared (FT-IR), Gas Chromatography Mass Spectrometry (GC-MS), and Proton Nuclear Magnetic Resonance ($^1$H-NMR).

The benzoate esters were tested for their anti-fungal, anti-oxidant, and anti-bacterial activity.

The fungus *M. canis* was 100% (completely inhibited) when treated with V, VI, VII, X, XI (1500 µg/ml); III (750 µg/ml); and XII (375 µg/ml).

Fungus T. rubrum was 100% inhibition when treated with IX (1500 µg/m); and V, X, XII (750 µg/ml).

The last fungus *E. flaccosum* was 100% inhibition when treated with V, IX, X, XII (1500 µg/ml). The anti-oxidant test show very good results with compound XII which has $IC_{50}$=22 compared to ascorbic acid $IC_{50}$=95.

The anti-bacterial test show negative results compared with gentamicin. Biological activity of the esters has shown promising results.

# Chapter One

# Introduction

## 1.1 Esterification

Esters are organic compounds derived from the reaction of an acid (organic or inorganic) and an alcohol catalyzed by small amount of concentrated sulfuric acid or hydrogen chloride through a condensation reaction known as Fischer esterification as illustrated in **Fig 1.1**. [1]

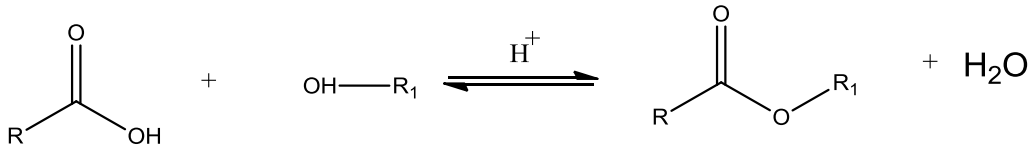



**Figure 1.1:** general equation of Fischer esterification

Fischer esterification is reversible with an equilibrium shifted forward in simple alcohols and simple carboxylic acids, but backward when one or both of the alcohol and the carboxylic acid are bulky. The hydrolysis is, also preferred in aqueous solutions [1, 2, 3].

A none reversible method for the preparation of none hindered esters is the reaction of alcohols with acid chloride [1, 4] or acid anhydrides, but the yield for the bulky esters still low [1]. Equations for classical methods of the formation and hydrolysis of esters are shown in **Fig. 1.2**

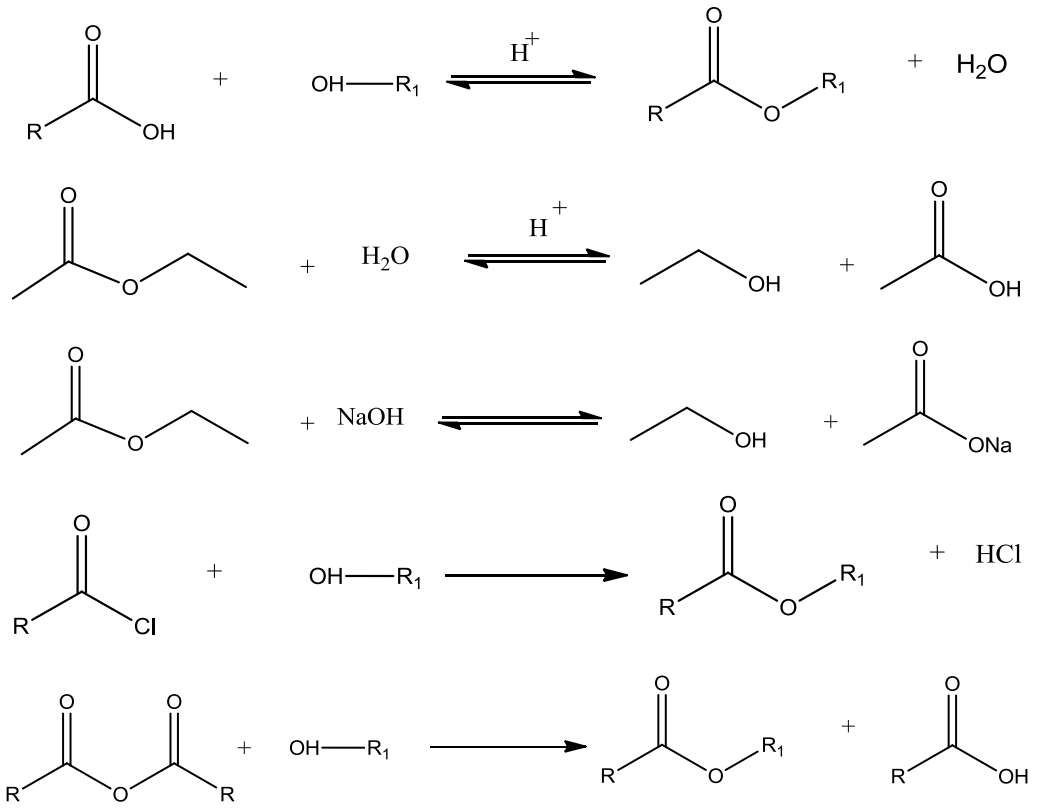



**Figure 1.2: Equations** for classical methods of the formation and hydrolysis of esters

## 1.2 Natural esters

Natural esters are found in many fruits, flowers and vegetables, and responsible for the pleasant smell, taste and aroma. These esters are fairly volatile, as a result of their low molecular weights [5]. Aroma or fragrance is a chemical compound that has a scent or perfume. Aroma of oranges. For example, contains 30 different esters along with 10 carboxylic acids, 34 aldehydes, 34 alcohols, ketones, and 36 hydrocarbons [6]. Examples of natural esters are shown in **Fig.1.3**.

## 1.3 Esters as antioxidants

Esters can be used as food additives, preservative and flavoring agents. Easters containing phenolic functional groups may exhibit antioxidant activity. These antioxidants not only have a wide range of uses as food preservative, but also are used in cosmetics, pharmaceuticals and industrial products. Examples of such antioxidants are Octyl, Dodecyl, Tetradecyl, Hexadecyl, and Octadecyl gallates [7, 8].The antioxidant activity of phenolic acids alkyl esters also shows high levels of potency [9].

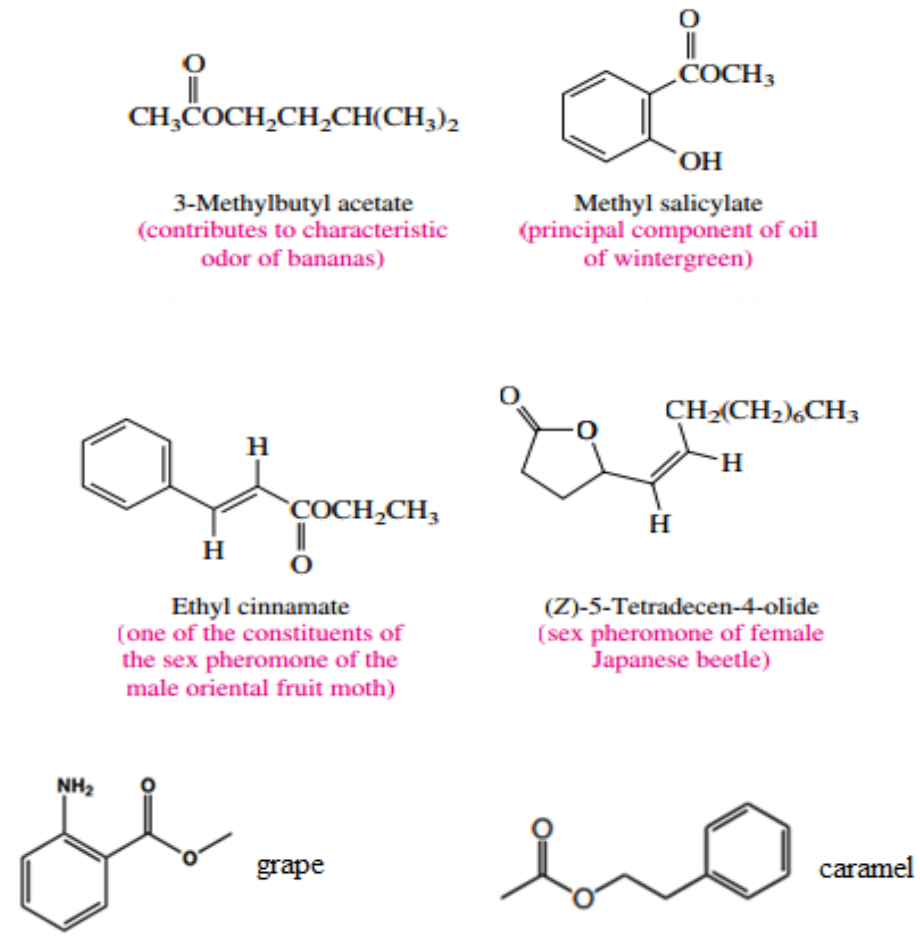



**Figure 1.3**: Examples on natural esters [6].

## 1.4 Phenoxyethanol

Phenoxyethanol**Fig.1.4** is a colorless liquid. It is used as a chemical preservative. Phenoxyethanol is an excellent and manageable alternative form of preservatives to the standard formaldehyde/phenol-based embalming fluids [10].

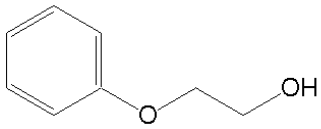



**Figure 1.4:** Phenoxyethanol

Other uses of phenoxyethanol include, skin disinfection during the first seven days of life in premature newborns [11].Phenoxyethanol is used in cosmetic products as a preservative and fixative. Literature suggests that dermal exposure to phenoxyethanol does not have severe toxic effects. Many human irritation patch tests have shown that skin irritation is rare, but some case reports have associated phenoxyethanol with skin dermatitis [12].

Several plants contain ingredients that have antibacterial, antifungal, and anticancer activities and Urticapilulifera is one of them. Traditional medicine uses plants due to their biological activity, such as antioxidant properties. Many herbs and spices have medicinal properties that alleviate symptoms or prevent disease. [13, 14].

Phenoxyethanol was extracted from Urticapilulifera, called (nettle) in Roman and (qurraus) in Palestine. It is known in many countries around the

world as a traditional medicine for curing sore joints which can be done by mixing plant juice with oil. It also has a good antioxidant activity [15, 14].

## 1.5 Carboxylic acids and carboxylic acid derivatives

The carboxylic acid functional group can be an important constituent of a pharmacophore [16]. Carboxylic acid derivatives have varied applications. Formic acid, for example, is the simplest carboxylic acid and has an effective role in the treatment against warts under the trade name Vårtfri (="Wart free") [17]. Aspirin is the ester of salicylic acid. Omega-3 carboxylic acids (Epanova) [OM3-CA] is an adjunct in diets to lower triglyceride levels in patients [18].

PABA is ashort name of p-aminobenzoic acid. Its potassium salt is used as a drug against fibrotic skin disorders, as for example Peyronie's disease. The trade name of this drug is Potaba. PABA is found in the folic acid vitamin and in several foods including grains, milk, eggs, and meat. [19].p-Methoxybenzoic acid was found to possess significant antihepatotoxic activity [20].

## 1.6 Other benzoate esters

**Table 1.1Similar benzoate esters and its biological activity**

| compounds | biological activity [15] |
|---|---|
| 2-phenoxyethyl benzoate | anti-bacterial [15] |
| 2-phenoxyethyl 4-hydroxybenzoate | anti-fungal and anti-cancer [15] |
| 2-phenoxyethyl 3-hydroxybenzoate | anti-bacterial [15] |
| 2-phenoxyethyl 2-hydroxybenzoate | anti-cancer [15] |

## 1.7 Chromatography

Chromatography was employed by the scientist Mikhail Tsvet in 1906, when he tried to separate pigments of a colored leaf such as chlorophyll, carotenes, and xanthophylls. The different colors of these compound gave the techniques its name [15][21].

**1.7.1 Thin layer chromatography:** TLC is used for non-volatile mixtures. The stationary phase is a solid of silica gel, aluminum oxide, or cellulose. The mobile phase is liquid.

**1.7.2 Column chromatography:** CC is used for large amounts of samples; and the separation depends on the partition, i.e., solute distribution between the mobile phase and stationary phase.

**1.7.3 Dry column flash chromatography:** DCFC is a safe, powerful, and easily applied preparative chromatography technique. Similar to the column chromatography, the dry-column flash chromatography includes packing the column with TLC adsorbent grade, loading the sample, and

eluting the column with suction **Fig 1.5 .**This will give the advantage of TLC in separation, and the advantage of column chromatography in quantities. it is similar to vacuum filtration that uses the same glassware. The column is a sintered glass funnel contain a “dry” bed of silica gel, and the elution occurs through suction. The column is then drained dry after each fraction, which makes it much easier to pack the column, and the person will not be worried about their columns going “dry” [22].

**Figure 1.5**: Dry column flash chromatography setup

## 1.8 Biological activity of some modified compound

Biological activity refers to substances having or producing an effect on the living tissue or its ability to effect a change in a biological process. The relation between the molecular entity and the biological activity can be tested by answering the following questions: (1) what is it? (2) What does it do? And (3) how much of it is present? These questions can express the activity of the compound. The importance of biological processes refers to the description of functional relationships between biological activities and the chemical substances that express them [23].

### 1.8.1 Anti-oxidants

Anti-oxidant “free radical scavengers” are substances that may prevent or delay some types of cell damage by reacting with and blocking the activity of free radicals and preventing them from causing the damage of scavengers so as to prevent/delay different diseased states. These free radicals are considered as highly reactive species that have an odd number of electrons, which gives them high potentials to cause damage to cells called cellular pathologies. Some of these damages may lead to cancer. In the biological system, oxygen gives rise to a large number of free radicals and other reactive species collectively known as ‘reactive oxygen species’ (ROS).‘Reactive nitrogen species’ (RNS) are another group of reactive species that play a dual role as both deleterious and beneficial species.[24,25, 26].

Antioxidants are very important organic compounds especially in designing new novel drugs. Two types of free radicals exist. The first type is synthesized naturally by the body. The second type is introduced to our bodies through external sources. Sources of radicals are tobacco smoke, exposure to the sun, and other pollution forms of the body. This makes endogenous antioxidants, which are used to neutralize free radicals. However, the body also needs external sources of antioxidants called (exogenous) sources or dietary antioxidants like fruits and vegetables [15, 27].

The high potential of free radicals gives them the high reactivity which harms the cells. They are created when an atom or a molecule either gains or loses an electron (a small negatively charged particle found in atoms) **Fig 1.6.** [28].

As the concentrations of free radicals increase, their hazard on the body increases and causes the damage to all major components of cells, including proteins, DNA, and cell membranes. Many of these mutagens and carcinogens may act through the generation of oxygen radicals, as a result of the damage of DNA. Such conditions are suitable environments for the establishment and progression of cancer [29, 30].

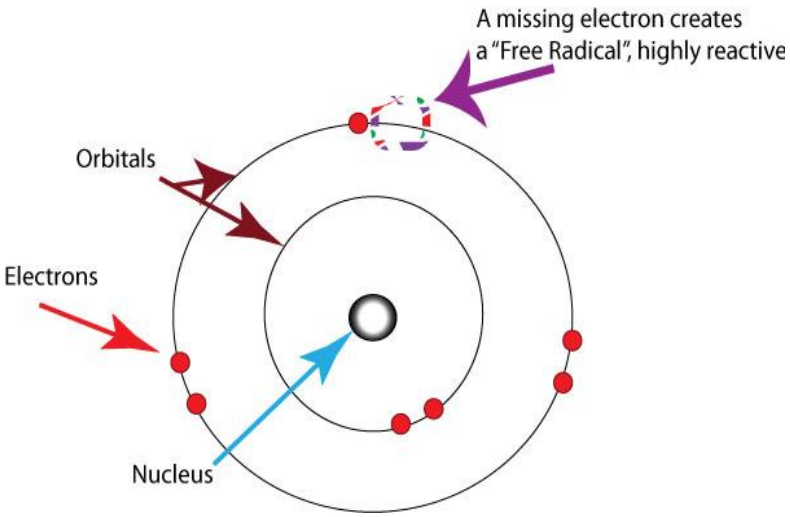



**Figure 1.6:** Configuration of free radical

Plants convert the solar energy into chemical energy so there's a hazard due to the excess energy and due to fear of oxidative damage of the plant cell. Nonetheless, the presence of antioxidant in plants will prevent the oxidative damage. Many of such compounds that protect plant cells are also found in human and protect human cells [31].

### 1.8.2 Anti-microbial (antibacterial)

Microbes are tiny organisms seen by a microscope. These microbes are found in air, soil, rock, plants, bodies and water. Microbes are known to replicate and spread rapidly. Microbial organisms include bacteria, viruses, fungi, and protozoa. Some microbes cause disease and are called parasites. However, many others exist in the body as normal flora without causing harm and may be beneficial [32].

Antimicrobial drugs are synthesized to inhibit the microbe without any side effects on the patients. [33].Antibiotics are one of the most important weapons we have in the fight against bacterial infections, and the manufacture of these antibiotics has a strong relationship with the nature of life associated with human health. But recently, these health benefits have become limitation because, and as a result of natural selection, bacterial resistance to these drugs is a major issue. In this respect, the development of medicines derived from natural sources play an important role in the prevention and treatment of human diseases [34].

### 1.8.3 Anti-microbial (antifungal activities)

An antifungal medicine is a drug that works selectively to eliminate fungal pathogens from a host with minimal toxicity to the host [26].Unlike bacterial disease, fungal diseases are more difficult to treat. Topical and oral treatments are long term and partially successful in controlling the fungus. Many of these infections will be chronic and if you are fortunate

enough to rid the infection from your body, there is always the possibility of recurrence of the disease [15].

Fungal infections of the skin are the most abundant and widespread group of all mycoses. Skin mycoses affect more than 20–25% of the world's population, which makes them one of the most frequent forms of infections. [35].

The presentations of tinea infections range and its causative species are shown in the **Table 1.2**[36].

## 1.9 Aim of the study

The main objectives of this study are the following:

1- To prepare a series of substituted benzoates of 2-phenoxyethanol
2- To explore some of the biological activity of these esters
3- To enrich the literature with the physical data of these esters.

**Table 1.2Tinea infections range and its causative species.**

| **Tineainfections- type** | **Commmon causative species** |
|---|---|
| Tineacapitis (scalp) | *Trichophytontonsurans* |
| | *Microsporumandouinii* |
| Tineacorporis (arms,legs and trunk) | *Microsporumcanis* |
| | *Microsporumcanis*<br>*Trichophytonrubrum* |
| | *M. Canis* |
| Tineacruris (gorin) | *T. tonsurans* |
| | *T. verrucosum* |
| | *T. verrucosum*<br>*T. rubrum* |
| | *Epidermophytonfloccosum* |
| Tineapedis (feet) | *Epidermophytonfloccosum*<br>*T. rubrum* |
| | *Trichophytonmentagrophytes* |
| Tineamanuum(hand) | var *interdigitale* |
| | *E. floccosum* |
| | *E. floccosum*<br>*T. rubrum* |
| Tineaunguium (finger,nails,and toe nails) | *T. rubrum* |
| Tineaunguium (finger,nails,and toe nails) | *Trichophytonmentagrophytes* |
| | var *mentagrophyte* |
| | |

# Chapter Two
# Materials and Methods

## 2.1 Chemicals

The following chemicals were used: 2-nitrobenzoic acid, 3-nitrobenzoic acid, 4-nitrobenzoic acid, 2-bromobenzoic acid, 3-bromobenzoic acid, 4-bromobenzoic acid, 4-tertbutylbenzoic acid, 2-methoxy benzoic acid, 3-methoxy benzoic acid, 4-methoxybenzoic acid, 3-aminobenzoic acid, 4-aminobenzoic acid, agar, ethanol, Muller–Hinton agar, gentamicin, and econazole were purchased in purist form from Sigma-Aldrich. 2-phenoxyethanol, diethyl ether, cyclohexane, ethyl acetate were purchased from FRUTAROM. All chemicals and reagents were of analytical grade and used without further purification.

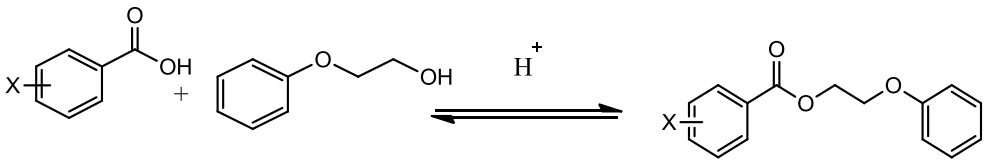
As for the microorganisms under microscope, all tested microorganisms in this work were obtained from Biodiversity & Environmental Research Center (BERC)Til Village-Nablus. The included bacteria were *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), *Klebsiellapneumoniae* (ATCC 13883), *Proteus vulgaris* (ATCC 13315), *Pseudomonas aeruginosa* (ATCC 27853) and *Escherichia coli* (JM109). On the other hand, the fungi included in this study were *Microsporum can is* CBS 132. 88, *Trichophytonrubrum* CBS 392 .58 and *Epidermophytonfloccosum* CBS 358.93, the isolates have been maintained on SDA (sabrose dextrose agar) Experimental cultures were kept on SDA media and subcultured on a monthly basis.

## 2.2Physical Measurements:

Melting point of each product was measured by stuart meting point apparatus, R00102618, $^{1}H$ –NMR was determined in Hashemite University/ Jordan (Bruker 500 MHz-Avance III). MS was done in the National Agriculture Research Center(NARC) by Thermofinnigan DSQ mass spectrometer. IR was performed through Fourier transform infrared spectrophotometer (Necolet Is5 - Id3).

## 2.3 General procedure for the synthesis of 2-phenoxyethyl benzoates:

The esters were prepared by the Fischer method according to the following equation:




**Scheme 2.1:** General equation for synthesis of 2-phenoxyethyl benzoates

Where X functional chemical group can be any of the following twelve entities:

I ( X = 2-$NO_2$, 2-phenoxyethyl 2-nitrobenzoate)

II (X = 3-$NO_2$, 2-phenoxyethyl 3-nitrobenzoate)

III (X =4-$NO_2$, 2-phenoxyethyl 4-nitrobenzoate)

IV (X = 2-Br, 2-phenoxyethyl 2-bromobenzoate)

V (X = 3-Br, 2-phenoxyethyl 3-bromobenzoate).

VI (X = 4-Br, 2-phenoxyethyl 4-bromobenzoate).

VII (X= 2-$OCH_3$, 2-phenoxyethyl 2-methoxybenzoate).

VIII (X= 3-$OCH_3$, 2-phenoxyethyl 3-methoxybenzoate).

IX(X= 4-$OCH_3$, 2-phenoxyethyl 4-methoxybenzoate).

X(X= 3-$NH_2$, 2-phenoxyethyl 3-aminobenzoate).

XI (X= 4-$NH_2$, 2-phenoxyethyl 4-aminobenzoate).

XII (X= 4-*tert*-butyl, 2-phenoxyethyl 4-*tert*-butylbenzoate).

The proper amount of the corresponding substituted benzoic acid was mixed with a slight excess of 2-phenoxyethanol and one ml sulfuric acid, and refluxed for three hours in ultra-dry apparatus. The system was cooled to room temperature and allowed to stand overnight, then the solid product was collected and purified by Dry Column Flash Chromatography (DCFC) and by recrystallization.

### 2.3.1 Preparation of 2-phenoxyethyl 2-nitrobenzoate (I)

The condensation of 2-nitrobenzoic acid (13.3 g, 0.080 mol) and2-phenoxyethanol (11 ml, 12.1g, 0.090mol) produced (I). (87.8%) (m.p.= 147-149 $^oC$, lit. not found).

**IR**:3030; 2800; 2927; 1734; 1602; 1536; 1354; 1281; 1236;1086; 1038; 734; 689 $cm^{-1}$.

**Mass:** m/z =287 ; 257 ; 195; 194; 150; 167; 165; 150;148; 104; 120; 122; 93; 77.

**$^1$H NMR:** δ = 8.08(1H, d, *J* =7.5 Hz); 7.85, (3H, m); 7.3 (2H, t, *J* =8.01Hz); 6.97 (2H, d, *J* =8.01 Hz); 6.95 (1H, t, *J* = 8.01 Hz); 4.62 (2H, t, *J* = 4.37 Hz); 4.28(2H, t, *J* =4.37 Hz) ppm.

### 2.3.2 Preparation of 2-phenoxyethyl 3-nitrobenzoate (II)

The condensation of 3-nitrobenzoic acid (13.3 g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, 0.090 mol) produced (II).(70.2%). (m.p.= 142-146 ºC, lit. not found).

**IR**: 3050; 2831; 2974; 1718; 1686; 1580; 1486; 1275; 1242; 1098; 1040; 933; 749; 679; 544 $cm^{1}$.

**Mass:** m/z =287 ; 257 ; 195; 194; 150; 167; 165; 150; 148; 104; 120; 122; 93; 77.

**$^1$H NMR ppm:** δ = 8.62 (1H, s); 8.5 (1H, d, *J* =8.01 Hz); 8.36(1H, d, *J* =8.01 Hz); 7.84 (1H, t, *J* =8.01 Hz); 7.3 (2H, t, *J* =7.57 Hz); 7(t, 2H,, *J* = 7.57 Hz); 6.95(1H, t, *J* =7.57Hz); 4.69(2H, t, *J* = 4.50 Hz); 4.38 (2H, t, *J* = 4.50 Hz) ppm.

### 2.3.3 Preparation of 2-phenoxyethyl 4-nitrobenzoate (III)

The condensation of 4-nitrobenzoic acid (13.3 g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, 0.090 mol) produced (III).(76.5%). (m.p.= 136-139ºC, lit. not found).

**IR**:3053; 2970; 2890; 1719; 1599; 1522; 1498; 1344; 1439; 1274; 1085; 1063; 890; 754; 715; 508 $cm^{-1}$.

**Mass:** m/z = 287 ; 257 ; 195; 194; 150; 167; 165; 150; 148; 104; 120; 122; 93; 77.

**$^1$H NMR:** δ = 8.35(2H, d, *J* =8.83 Hz); 8.19(2H, d, *J* =8.83 Hz); 7.31(2H, t, *J* =7.56 Hz); 6.99(2H, d, *J* =7.56 Hz); 6.96 (1H, t, *J* = 7.56 Hz); 4.67 (2H, t, *J* = 4.4 Hz); 4.37(2H, t, *J* = 4.4 Hz ) ppm.

### 2.3.4 Preparation of 2-phenoxyethyl 2-bromobenzoate (IV)

The condensation of 2-bromobenzoic acid (16 g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, 0.090 mol) produced (IV). (77.3%). (m.p.= 155-158 ºC, lit. not found).

**IR**: 3010;2962; 2944; 1728; 1584; 1288; 1233; 1101; 1081; 1019; 928; 885; 743; 688; 641$cm^{-1}$.

**Mass:** m/z =322; 320; 229; 227; 185; 183; 165; 157; 155; 121; 104; 93; 77.

**$^1$H NMR:** δ = 7.76(2H); 7.5(2H); 7.3(2H, t, *J* =7.66 Hz); 6.98 (2H, d, *J* =7.66 Hz); 6.97(1H,t); 4.62 (2H); 4.33(2H) ppm.

### 2.3.5 Preparation of 2-phenoxyethyl 3-bromobenzoate(V)

The condensation of 3-bromobenzoic acid (16 g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, 0.090mol) produced (V).(70.3%). (m.p.= 160-163 ºC, lit. not found).

**IR**:3055; 2949; 2854; 1715; 1589; 1565; 1489; 1453; 997; 893; 807; 792; 932; 760; 740; 722; 688; 669; 513 $cm^{-1}$.

**Mass:** m/z =321; 320; 229; 227; 185; 183; 165; 157; 155; 121; 104; 93; 77.

**$^1$H NMR:** δ = 8.05 (1H,s); 7.96 (1H, d, *J* =8.06 Hz);7.89 (1H, d, *J* =8.06 Hz); 7.76(2H); 7.51 (1H, t, *J* =8.06 Hz); 7.31 (2H, t, *J* =7.98 Hz);7(2H, d, *J* = 7.9 Hz);6.96 (1H, t, *J* =7.33 Hz); 4.62 (2H, t, *J* = 4.5 Hz); 4.36 (2H, t, *J* = 4.5 Hz) ppm.

### 2.3.6 Preparation of 2-phenoxyethyl 4-bromobenzoate(VI)

The condensation of 4-bromobenzoic acid (16 g, 0.080 mol) and 2-phenoxyethanol(11 ml, 12.1g, 0.090 mol) produced (VI).(65.6%). (m.p.= 165-167 ºC, lit. not found).

**IR**:3047; 2954; 2881; 1715; 1589; 1566; 1489; 1453; 1294; 1244; 1084; 1130; 822; 807; 792; 760; 740; 688; 670 $cm^{-1}$.

**Mass:** m/z =321; 320; 229; 227; 185; 183; 165; 157; 155; 121; 104; 93; 77.

**$^1$H NMR:** δ = 7.88 (2H, d, *J* = 7.58Hz); 7.75(2H, d, *J* =7.58Hz); 7.3 (2H); 6.99 (3H); 4.61(2H, t); 4.34 (2H, t) ppm.

### 2.3.7 Preparation of 2-phenoxyethyl 2-methoxybenzoate (VII)

The condensation of 2-methoxybenzoic acid (12.1g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, and 0.090 mol) produced (VII). (84.7%). (m.p.= 134-137 ºC, lit. not found).

**IR**: 3060; 2953; 2810; 1722; 1597; 1490; 1459; 1285; 1247; 1138; 1078; 1061; 760; 552 $cm^{-1}$.

**Mass:** m/z =227; 179; 165; 152; 135; 122; 107; 93; 77.

**$^1$H NMR:** δ = 7.64(1H, d, *J* =7.67 Hz); 7.54(1H, t, *J* =7.67 Hz); 7.3(2H, t, *J* =**7.**84 Hz); 7.14(1H, d, *J* =7.67 Hz); 7.02(1H, t, *J* =7.67 Hz); 6.99(2H, d, *J*= 7.84 Hz); 6.95(1H, t, *J* =7.84 Hz);4.55(2H, t, *J* = 4.3 Hz ); 4.29(2H, t, *J* = 4.3 Hz); 3.8(3H,s) ppm.

### 2.3.8 Preparation of 2-phenoxyethyl 3-methoxybenzoate (VIII)

The condensation of 3-methoxybenzoic acid (12.1g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, 0.090 mol) produced (VIII)(88.9%). (m.p.= 127-130 ºC, lit. not found).

**IR**: 3050; 2942; 2831; 1718; 1686; 1581; 1486; 1428; 1306; 1243; 1098; 1041; 933; 749; 679; 544 $cm^{-1}$.

**Mass:** m/z = 227; 179; 165; 152; 135; 122; 107; 93; 77.

**$^1$H NMR:** δ =7.55 (1H, t, *J* =7.7 Hz); 7.44 (2H, m); 7.3 (1H, t, *J* =7.55 Hz); 7.23 (1H, dd, $J_1$ =1.88 Hz, $J_2$ =7.7 Hz); 7.19 (1H, dd, $J_1$=1.9 Hz, $J_2$ =7.7 Hz); 7 (2H, d, *J* =7.55 Hz); 6.96(1H, t, *J* =7.55 Hz); 4.61 (2H, t, *J* = 4.5 Hz); 4.34 (2H, t, *J* = 4.5 Hz ); 3.81 (3H, s) ppm.

### 2.3.9 Preparation of 2-phenoxyethyl 4-methoxybenzoate (IX)

The condensation of 4-methoxybenzoic acid (12.1g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, 0.090 mol) produced (IX) (82.9%). (m.p.= 123-126 ºC, lit. not found).

**IR**:3040; 2927; 2842; 1708; 1604; 1497; 1456; 1279; 1249; 1167; 1084; 1029; 927; 844; 750; 689; 598; 567 $cm^{-1}$.

**Mass:** m/z= 227; 179; 165; 152; 135; 122; 107; 93; 77.

**$^1$H NMR:** δ = 7.92 (2H, d, *J* =8.85 Hz); 7.3 (2H, t, *J* =7.95 Hz); 7.05 (2H, d, *J* =8.85 Hz); 6.99 (2H, d, *J* =8 Hz); 6.96 (1H, t, *J* =7.33 Hz*);* 4.57 (2H, t, *J* = 4.5 Hz); 4.33 (2H, t, *J = 4.5 Hz*); 3.84(3H, s) ppm.

### 2.3.10 Preparation of 2-phenoxyethyl 3-aminobenzoate(X)

The condensation of 3-aminobenzoic acid (10.9g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, 0.090 mol) produced (X) (65.9%). (m.p.= 180-182 ºC, lit. not found).

**IR:**3371; 3450;3050; 2924; 2875; 1702; 1598; 1454; 1289; 1240; 1082; 1043; 748; 688 $cm^{-1}$.

**Mass:** m/z= 321; 257; 207; 165; 164; 137; 122; 120; 93; 92; 77.

**$^1$H NMR:** δ = 7.31(2H, t, *J* =8.03Hz); 7.2 (1H, s); 7.15(1H, d, *J* = 7.5Hz*);* 7.11 (1H, t, *J* =7.5Hz); 6.99 (2H, d, *J* =8.03 Hz); 6.94 (1H, t, *J* = 8.03 Hz*);* 6.8 (1H, d, J =7.5 Hz); 5.38 (2H, s); 4.55 (2H, t, *J* = 4.2 Hz); 4.3 (2H, t, *J* = 4.2Hz) ppm.

### 2.3.11 Preparation of 2-phenoxy ethyl 4-amino benzoate (XI)

The condensation of 4-aminobenzoic acid (10.9g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, 0.090 mol) produced (XI) (81.4%). (m.p.= 107-110 ºC), not found.

**IR**: 3349; 3214; 3035;3000; 2980; 1700; 1618; 1599; 1496; 1311; 1271; 1174;1153; 1053; 1027; 995; 880; 747; ;688; 526 $cm^{-1}$.

**Mass:** m/z = 321; 257; 207; 165; 164; 137; 122; 120; 93; 92; 77

**$^1$H NMR:** not measured.

### 2.3.12 Preparation of 2-phenoxy ethyl 4-tertbutyl benzoate (XII)

The condensation of 4-tertbutylbenzoic acid (14.2g, 0.080 mol) and 2-phenoxyethanol (11 ml, 12.1g, 0.090 mol) produced (XII) (85.2%). (m.p.= 151-154 ºC, lit. not found).

**IR**: 2961; 2850; 1703; 1597; 1495; 1461; 1279; 1240; 1188; 1110; 1082; 1060; 1013; 924; 860 ; 751; 688; 605; 549 $cm^{-1}$.

**Mass:** m/z =298; 283; 205; 205; 191; 178; 165; 161; 146; 133; 120; 93; 77.

**$^1$H NMR:** δ = 7.9 (2H, d, *J* =8.45 Hz); 7.54 (2H, d, *J* =8.45 Hz); 7.3 (2H, t, *J* =7.57Hz); 6.99 (2H, d, *J* =7.54 Hz); 6.96 (1H, t, *J* = 7.33 Hz*);* 4.6 (2H, t, *J* = 4.5 Hz); 4.33(2H, t, *J* = 4.5 Hz); 1.3 (9H, s) ppm.

## 2.4 General procedure of anti-fungal test for benzoate compounds

### 2.4.1 Preparation of samples for testing

Eachcompound (100 mg) was dissolved in 10 mL of mixed solution (7 ml ethanol and 3 ml ethyl acetate), and the solution was sterilized using membrane filtration (0.45 μm millipore filters) for all of the following tests.

### 2.4.2 Antifungal testing

All benzoate compounds were tested at different concentrations **Table 2.1.** for their antifungal activities against the test pathogens by a modified "poisoned food" technique [37]. Different amounts of each compound were

incorporated in pre-sterilized SDA medium to prepare a series of concentrations of the compound (375, 750, 1500µg/ml). A mycelial agar disk of 5 mm diameter was cut out of 12 days old culture of the test fungus and inoculated on to the freshly prepared agar plates. In controls, sterile distilled water was used in place of the tested sample. Four replicate plates were used for each treatment (concentration).The inoculated plates were incubated in the dark at 24˚C and the observations were recorded after 10 days. Percentage of mycelial inhibition was calculated using the following formula:

% mycelial inhibition = $(\frac{dc-ds}{dc})$ x100%

where,

**dc:** colony diameter of the control

**ds:** colony diameter of the sample

As already introduced in the previous section, the twelve samples are listed in **Table** 2.1. The three mentioned fungi underwent the twelve different tests for the efficiency of benzoate treatment, namely Trychophyton rubrum **Table 2.2**,*Microsporum canis* **Table 2.3**,and Epidermophyton floccosum **Table 2.4.**

**Table 2.1 Benzoate antifungal compounds**

| Sample number | Name of compound |
|---|---|
| I | 2-phenoxyethyl 2-nitrobenzoate |
| II | 2-phenoxyethyl 3-nitrobenzoate |
| III | 2-phenoxyethyl 4-nitrobenzoate |
| IV | 2-phenoxyethyl 2-bromobenzoate |
| V | 2-phenoxyethyl 3-bromobenzoate |
| VI | 2-phenoxyethyl 4-bromobenzoate |
| VII | 2-phenoxyethyl 2-methoxy benzoate |
| VIII | 2-phenoxyethyl 3-methoxy benzoate |
| IX | 2-phenoxyethyl 4-methoxy benzoate |
| X | 2-phenoxyethyl 3-aminobenzoate |
| XI | 2-phenoxyethyl 4-aminobenzoate |
| XII | 2-phenoxyethyl 4-tertbutyl benzoate |

**Table 2.2 Diameter zone (mm) of *Trychophyton rubrum* CBS 392.58 Netherland against three different concentration ($c_1$,$c_2$ and $c_3$)**

| Control | Diameter zone (mm) =22,21,23,22,23,23 | | | | | |
|---|---|---|---|---|---|---|
| Compound | C1=1500ug/ml | Mean | C2=750ug/ml | Mean | C3=375ug/ml | Mean |
| I | 11,12,10,11 | 11 | 13,15,14,14 | 14 | 17,18,19,18 | 18 |
| II | 10,9,10,11 | 10 | 14,15,13,14 | 14 | 17,18,19,17 | 17.75 |
| III | 9,8,8,7 | 8 | 13,12,11,11 | 11.75 | 16,18,17,18 | 17.25 |
| IV | 13,12,14,13 | 13 | 16,17,16,18 | 16.75 | 21,20,22,21 | 21 |
| V | no growth | no growth | no growth | no growth | 12,11,13,12 | 12 |
| VI | 12,13,11,11 | 11.75 | 17,16,18,17 | 17 | 20,21,19,20 | 20 |
| VII | 11,10,9,10 | 10 | 17,18,15,16 | 16.5 | 17,18,20,19 | 18.5 |
| VIII | 10,9,11,10 | 10 | 12,13,14,13 | 13 | 17,18,19,18 | 18 |
| IX | no growth | no growth | 13,12,14,12 | 12.75 | 16,14,15,17 | 15.5 |
| X | no growth | no growth | no growth | no growth | 7,7,8,7 | 7.25 |
| XI | 7,8,8,7 | 7.5 | 13,14,12,13 | 13 | 15,16,17,17 | 16.25 |
| XII | no growth | no growth | no growth | no growth | 14,15,16,16 | 15.25 |

**Table 2.3 Diameter zone (mm) of *Microsporumcanis* CBS 132.88 against three different concentration ($c_1$,$c_2$ and $c_3$) 2- Microsporumcanis CBS 132.88**

| Control | Diameter zone (mm) =32,31,31,32,32,30 mean =31.3 | | | | | |
|---|---|---|---|---|---|---|
| Compound | C1=1500ug/ml | mean | C2=750ug/ml | mean | C3=375ug/ml | mean |
| I | 15,14,16,14 | 14.75 | 20,21,20,20 | 20.25 | 23,22,22,21 | 22 |
| II | 11,12,10,11 | 11 | 21,22,23,21 | 21.75 | 32,31,26,28 | 29.25 |
| III | 0 | 0 | 0 | 0 | 10,12,11.13 | 11.5 |
| IV | 17,16,18,17 | 17 | 23,24,25,25 | 24.25 | 30,29,31,29 | 29.75 |
| V | 0 | 0 | 10,9,11,9 | 9.75 | 12,10,12,14 | 12 |
| VI | 0 | 0 | 21,20,21,19 | 20.25 | 32,31,30,31 | 31 |
| XII | 0 | 0 | 10,12,10,9 | 10.25 | 18,17,33,32 | 25 |
| VIII | 10.11.11.12 | 11 | 12,14,11,11 | 12 | 15,14,16,14 | 14.75 |
| IX | 15,14,13,13 | 13.75 | 20,21,20,22 | 20.75 | 31,31,32,31 | 31.25 |
| X | 0 | 0 | 9,10,10,8 | 9.25 | 12,10,11,9 | 10.5 |
| XI | 0 | 0 | 22,23,23,21 | 22.25 | 30,31,29,30 | 30 |
| XII | 0 | 0 | 0 | 0 | 0 | 0 |

**Table 2.4 Diameter zone (mm) of *Epidermophyton floccosum* against three different concentration ($c_1$,$c_2$ and $c_3$).**

| **Control** | **Diameter zone (mm) = 22,21,23,22,23** | | | | | |
|---|---|---|---|---|---|---|
| **Compound** | **C1=1500ug/ml** | **mean** | **C2=750ug/ml** | **mean** | **C3=375ug/ml** | **mean** |
| I | 11,12,10,11 | 11 | 13,15,14,14 | 14 | 17,18,19,18 | 18 |
| II | 10,9,10,11 | 10 | 14,15,13,14 | 14 | 17,18,19,17 | 17.75 |
| III | 9,8,8,7 | 8 | 13,12,11,11 | 11.75 | 16,18,17,18 | 17.25 |
| IV | 13,12,14,13 | 13 | 16,17,16,18 | 16.75 | 21,20,22,21 | 21 |
| V | no growth | no growth | no growth | no growth | 12,11,13,12 | 12 |
| VI | 12,13,11,11 | 11.75 | 17,16,18,17 | 17 | 20,21,19,20 | 20 |
| XII | 11,10,9,10 | 10 | 17,18,15,16 | 16.5 | 17,18,20,19 | 18.5 |
| VIII | 10,11,12,11 | 11 | 16,14,17,17 | 16 | 17,18,19,18 | 18 |
| IX | no growth | no growth | 13,14,14,12 | 13.25 | 16,14,15,17 | 15.5 |
| X | no growth | no growth | no growth | no growth | 7,7,8,7 | 7.25 |
| XI | 7,8,8,7 | 7.5 | 13,14,12,13 | 13 | 15,16,17,17 | 16.25 |
| XII | no growth | no growth | no growth | no growth | 14,15.16,16 | 15.25 |

## 2.5 General procedure of anti-oxidant test for benzoate compounds

The hydrogen atom or electron donation abilities of the corresponding compounds were measured from the bleaching of the purple-colored methanolic solution of DPPH (1,1-Diphenyl-2-picryl-hydrazyl). This spectrophotometric assay uses the stable radical DPPH as a reagent [15].

One mL of various concentrations of the compounds (25,50,100,200,400 ug/ml) in (ethyl acetate and ethanol) was added to 4 mL of 0.004% methanol solution of DPPH. After 30 minutes of an incubation period at room temperature, the absorbance was read against a blank at 517 nm. The percent Inhibition I (%) of free radical by DPPH was calculated as follows:

$$I(\%)=((A_{blank}-A_{sample})/A_{blank})x\ 100\%$$

where $A_{blank}$ is the absorbance of the control reaction (containing all reagents except the test compound), and $A_{sample}$ is the absorbance of the test compound. Compounds concentrations providing 50% inhibition ($IC_{50}$) were calculated from the plot of inhibition (%) against compound concentration. Tests were carried out in triplicates.The control is ascorbic acid.

**Table 2.5 Absorbance for blank at different concentrations**

| Concentrationug/ml | | Abs |
|---|---|---|
| C1 | 25 | 0.94 |
| C2 | 50 | 0.78 |
| C3 | 100 | 0.58 |
| C4 | 200 | 0.26 |
| C5 | 400 | 0.12 |

**Table 2.6 Absorbance for the samples at different concentrations after the addition of benzoates**

| Sample number | Sample name | Absorbance (Mean) | Concentration ug/ml |
|---|---|---|---|
| I | 2-phenoxyethyl 2-nitrobenzoate | 0.65 | 25 |
| | | 0.63 | 50 |
| | | 0.62 | 100 |
| | | 0.61 | 200 |
| | | 0.42 | 400 |
| | | | |
| II | 2-phenoxyethyl 3-nitrobenzoate | 0.66 | 25 |
| | | 0.62 | 50 |
| | | 0.61 | 100 |
| | | 0.48 | 200 |
| | | 0.45 | 400 |
| | | | |
| III | 2-phenoxyethyl4-nitrobenzoate | 0.67 | 25 |
| | | 0.62 | 50 |
| | | 0.61 | 100 |
| | | 0.6 | 200 |
| | | 0.44 | 400 |
| | | | |
| IX | 2-phenoxyethyl2-bromobenzoate | 0.65 | 25 |
| | | 0.64 | 50 |
| | | 0.61 | 100 |
| | | 0.48 | 200 |
| | | 0.46 | 400 |
| | | | |
| V | 2-phenoxyethyl 3-bromobenzoate | 0.65 | 25 |
| | | 0.64 | 50 |
| | | 0.26 | 100 |
| | | 0.52 | 200 |
| | | 0.46 | 400 |
| | | | |

| | | | |
|---|---|---|---|
| VI | 2-phenoxyethyl 4-bromobenzoate | 0.65 | 25 |
| | | 0.63 | 50 |
| | | 0.62 | 100 |
| | | 0.6 | 200 |
| | | 0.45 | 400 |
| | | | |
| VII | 2-phenoxyethyl 2-methoxybenzoate | 0.66 | 25 |
| | | 0.62 | 50 |
| | | 0.6 | 100 |
| | | 0.59 | 200 |
| | | 0.45 | 400 |
| | | | |
| VIII | 2-phenoxyethyl3-methoxybenzoate | 0.64 | 25 |
| | | 0.63 | 50 |
| | | 0.62 | 100 |
| | | 0.6 | 200 |
| | | 0.45 | 400 |
| | | | |
| IX | 2-phenoxyethyl4-methoxybenzoate | 0.64 | 25 |
| | | 0.62 | 50 |
| | | 0.61 | 100 |
| | | 0.6 | 200 |
| | | 0.42 | 400 |
| | | | |
| X | 2-phenoxyethyl3-aminobenzoate | 0.64 | 25 |
| | | 0.62 | 50 |
| | | 0.58 | 100 |
| | | 0.54 | 200 |
| | | 0.45 | 400 |
| | | | |
| XI | 2-phenoxyethyl-4-aminobenzoate | 0.65 | 25 |
| | | 0.62 | 50 |
| | | 0.61 | 100 |
| | | 0.59 | 200 |
| | | 0.46 | 400 |
| | | | |
| XII | 2-phenoxyethyl-4-tertbutyl benzoate | 0.54 | 25 |
| | | 0.47 | 50 |
| | | 0.41 | 100 |
| | | 0.4 | 200 |
| | | 0.33 | 400 |
| | | | |

## 2.6 General procedure of anti-bacterial test for benzoate compounds

Antibacterial tests were then carried out by the disc diffusion method [38].Using an inoculums containing $10^6$ bacterial cells/ml spread on Muller–Hinton agar plates (1 ml inoculums/plate). The discs (diameter= 6 mm) were impregnated with 2 ml of compounds(50 µg/disc) at a concentration of 10 mg/ml and placed on the inoculated agar and incubated at 37°C for 24 h. the control was gentamicin .

# Chapter Three

# Results and Dissections

## 3.1 Identification of 2-phenoxyethanol benzoates:

The structures of products were established by their Mass, Infra-red and Proton NMR spectral data.

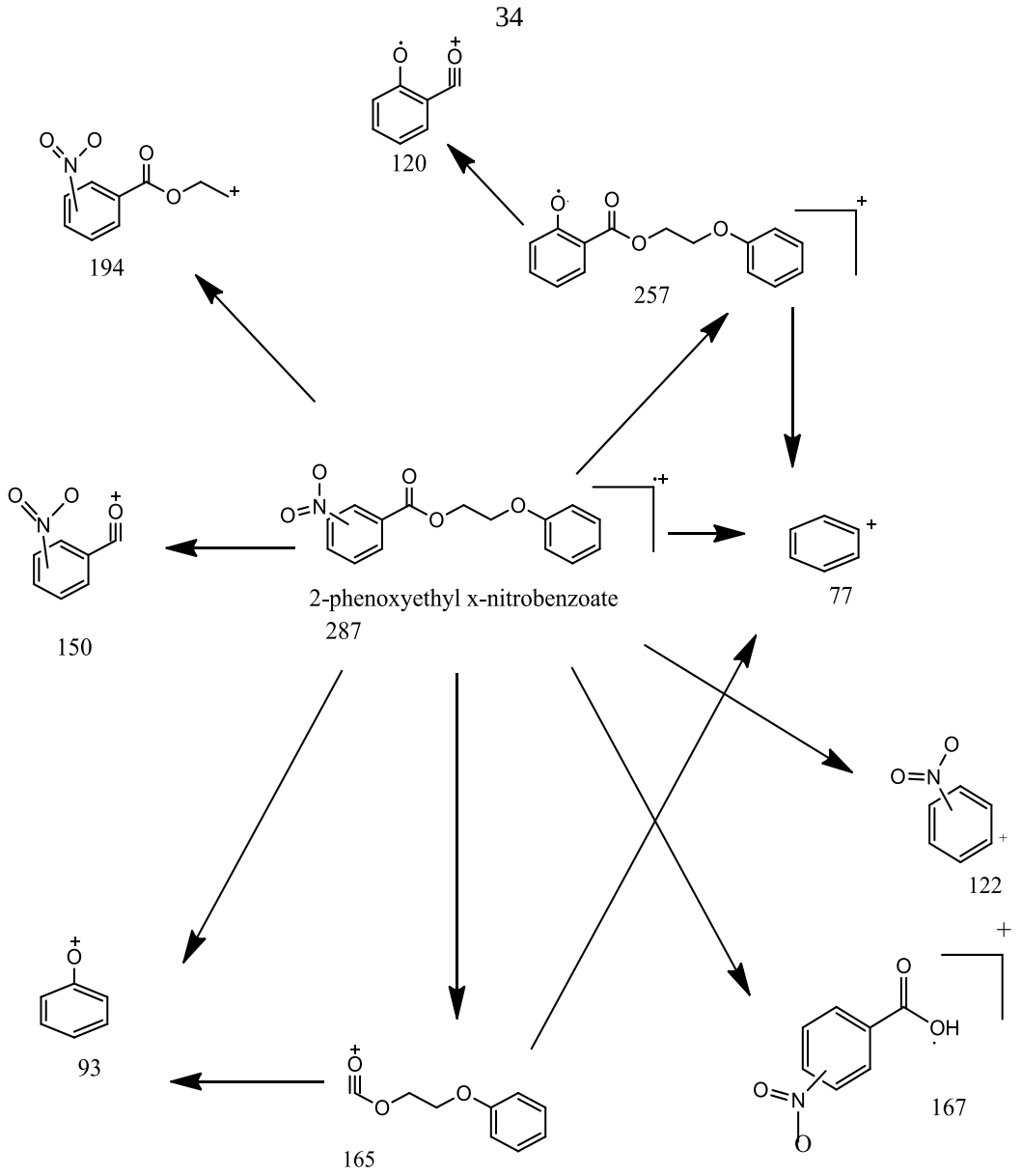
### 3.1.1 Mass Spectra:

All esters are for the same alcohol, 2-phenoxyethanol, with substituted benzoic acids, so, the mass patterns are expected to be similar, except those fragments related to the type of substituent on the benzoic acid part of the ester **Table3.1, Schemes (3.1, 3.2, 3.3, 3.4, and 3.5), Appendix I**.

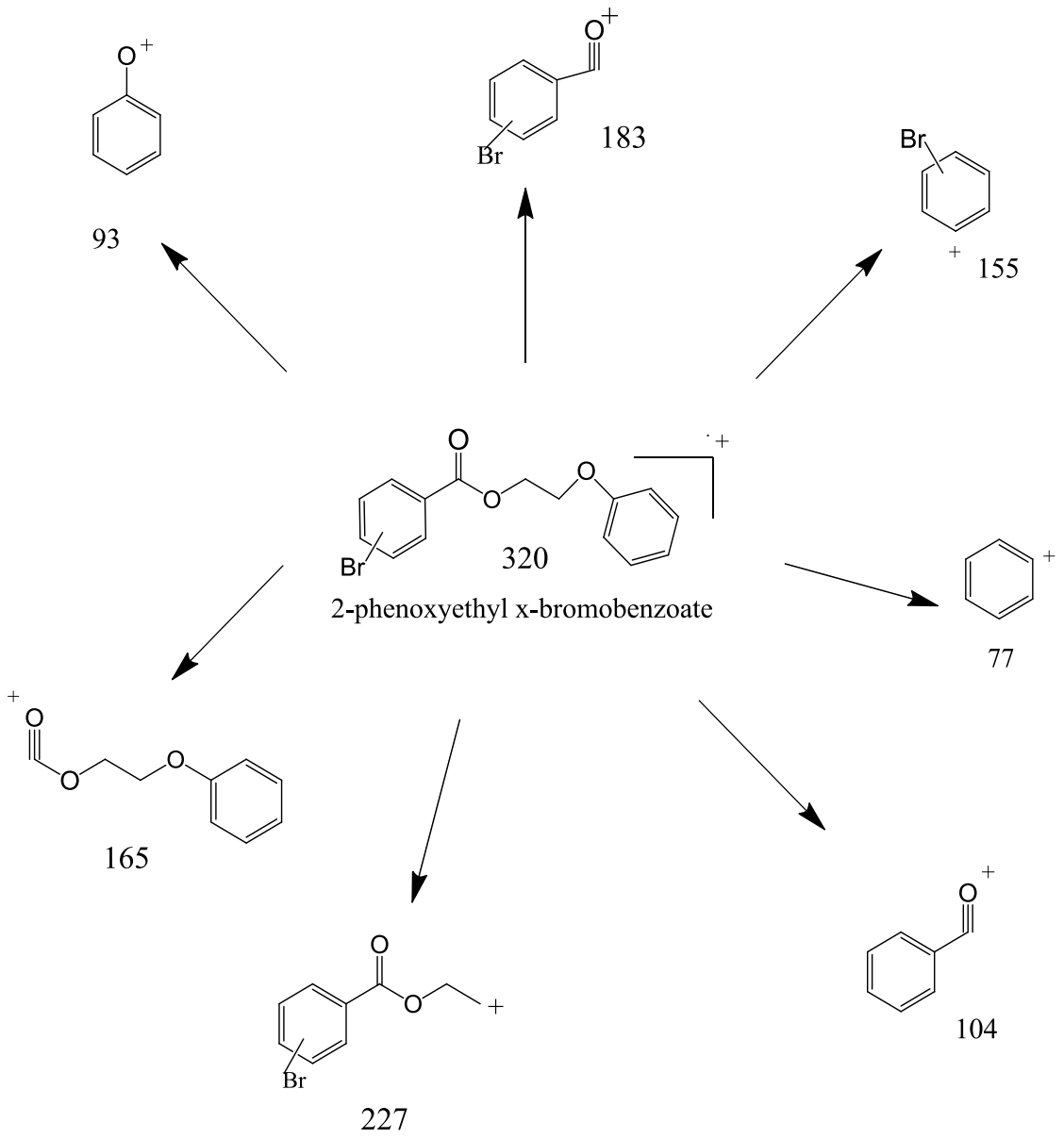
The molecular ions are relatively stable as a result of the high number of functional groups and the high number of lone pairs and π-bonds. The oxonium ion resulting from the ester dissociation is the base peak in most cases. The McLafferty rearrangement is appearing in most structures. All spectra show the two aromatic fragments phenyl-from the phenoxy-group and the X-phenyl- from the carboxylic part of the ester. Other specific peaks resulting from the dissociation of the substituent, also, have been seen.

**Table 3.1 Relative abundance of mass spectra of benzoate compounds in (%)**

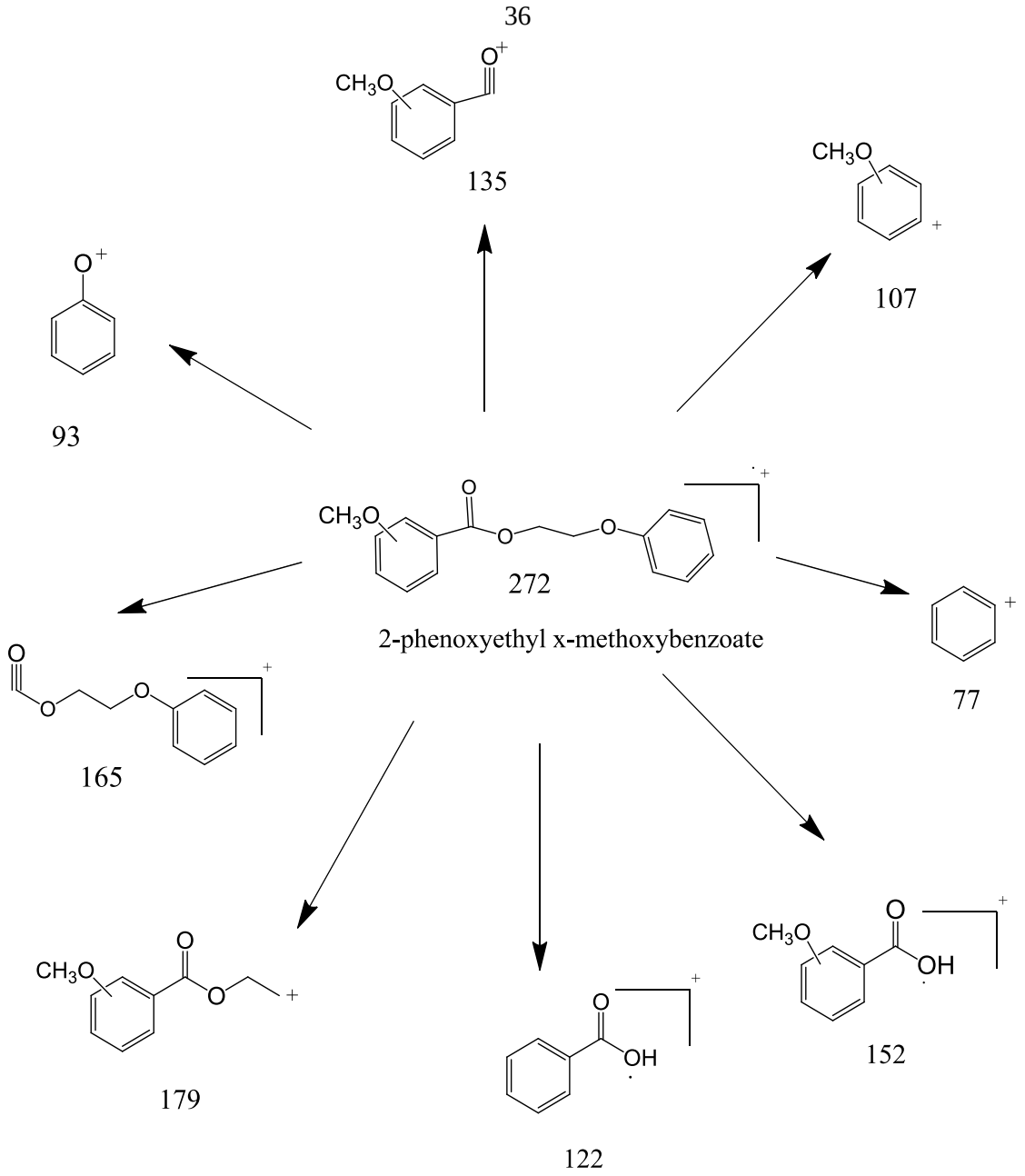
| Cpd | I | II | III | IV | V | VI | VII | VIII | IX | X | XI | XII |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $M^{+\cdot}$ | 4 | 5 | 1 | 2 | 1.5 | 1 | 2.2 | 3.1 | 0.3 | 9 | 2.8 | 2.5 |
| M-(*Ph-O*) | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| M-(*Ph-X*) | 1.3 | 3 | 2.2 | - | - | - | 0.1 | 0.1 | 0.1 | 8 | 11 | 3 |
| *phenoxy ion* | 6.2 | 5.11 | 2.8 | 2 | 1 | 1.2 | 4.6 | 3.1 | 1.5 | 5 | 5 | 10 |
| *aromatic ion* | 20.8 | 34 | 24.4 | 34 | 26 | 20 | 80.5 | 53 | 25.5 | 13 | 27 | 85 |
| $(X\text{-}Ph)^{+}$ | 2.2 | 2 | 3.6 | 19.5 | 25.5 | 21 | 2.1 | 57 | 10 | 34.5 | 34 | 11 |
| (*X-Ph-C-* | 46.2 | 100 | 53 | 61.5 | 59 | 60 | 100 | 100 | 76 | 58 | 91.5 | 100 |
| *mclafferty ion* | 4 | 0.5 | 0.5 | - | - | - | 0.1 | 6 | 2.1 | 8 | 1 | 0.1 |
| *others* | 120 (13%) 257 (2.2%) | 120 (13%) 257 (2.2%) | 120 (34%)257 (0.5%) | 104 (7.5%) | 104 (11.5%) | 104 (13.1%) | 122 (2%) | 122 (0.1%) | - | 122 (2.1%) | 122 (2%) | 146 (51.5%) 191 (4%), 283 (4%) |



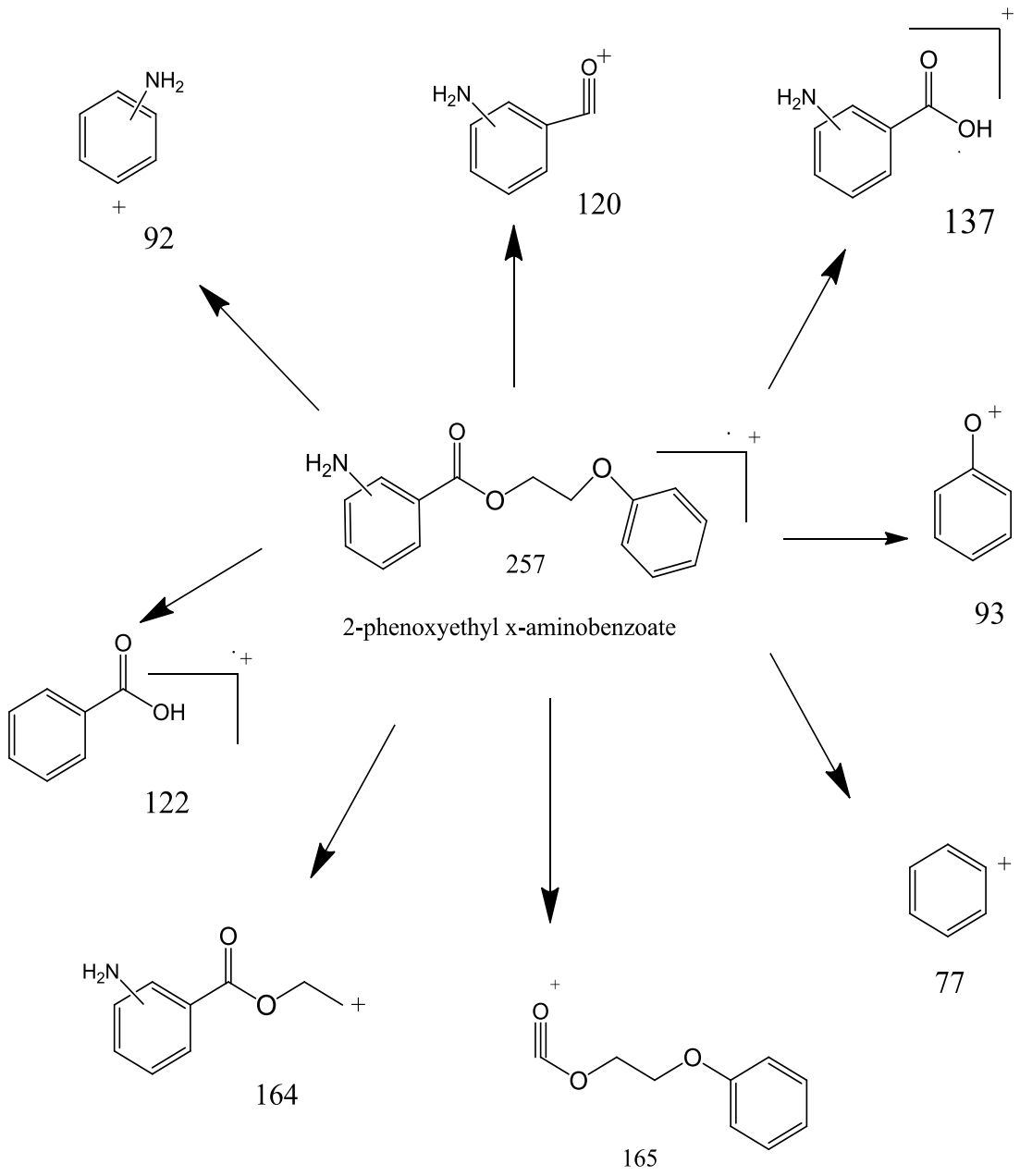

**Scheme 3.1** Fragmentations of 2-phenoxyethyl x-nitrobenzoate



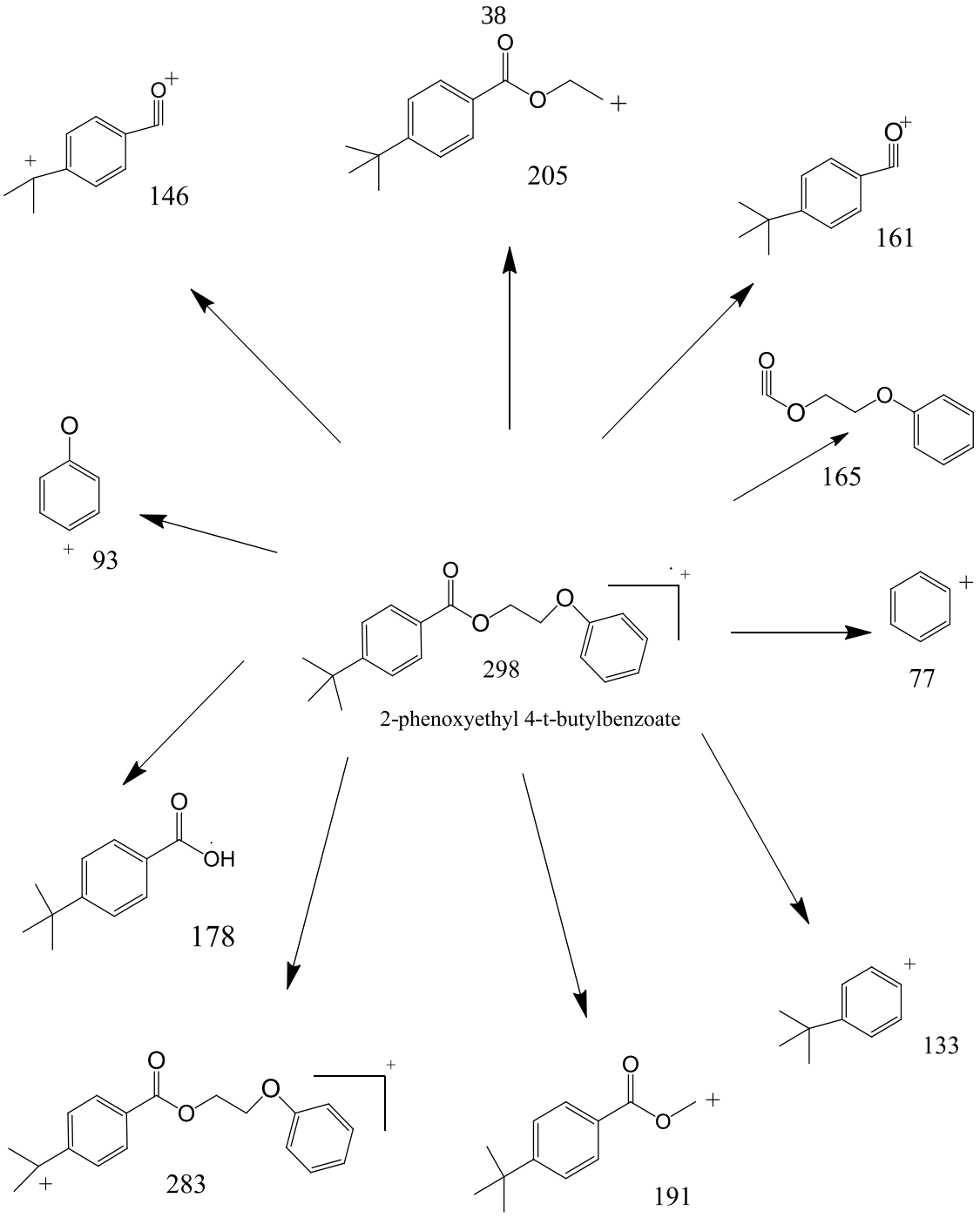

**Scheme 3.2** Fragmentations of 2-phenoxyethyl x-bromobenzoate




**Scheme 3.3** Fragmentations of 2-phenoxyethyl x-methoxybenzoate




**Scheme 3.4** Fragmentations of 2-phenoxyethyl x-aminobenzoate




**Scheme 3.5** Fragmentations of 2-phenoxyethyl 4-t-butylbenzoate

### 3.1.2 Infra-red

All IR spectra are in full agreement with the proposed structures **Table 3.2, Appendix I.**

All IR bands for all functional groups in the prepared compounds are seen obviously, even those small deviations due to the fine differences in structures can be explained. The -$CH_2$-$CH_2$- stretching (symmetric and asymmetric) bands appear clearly for all products in the range 2800-3000 $cm^{-1}$. The aromatic proton bond stretching bands are seen just above 3000 $cm^{-1}$ .The bands for the carbonyl groups vary according to the specific structure of each compound.

The conjugated carbonyl group, with an aromatic ring, is expected to show bands in the range 1700-1710 $cm^{-1}$,this has been seen with exceptions for the ortho- products. The bulkiness of these groups prevent an ideal conjugation by distorting the planarity required for that and increasing the wave number. The C-C stretching for aromatic rings are found around 1590 and around 1490$cm^{-1}$. The C-O single bond of the ester stretches around 1240 $cm^{-1}$, that of the C-O of that with the aromatic ring is about 1280$cm^{-1}$, while that of the alcoholic C-O stretching is found around 1040 – 1060 $cm^{-1}$, in accordance with those found for esters of primary alcohols [39]. The out of plane pending of the aromatic C-H bonds for the mono-substituted ring have been found at around 690 and 750 $cm^{-1}$and those for the di-substituted aromatic ring are clearly found at the expected frequency.

### 3.1.3 NMR

The proton NMR spectra of the esters I – XII have been obtained and analyzed. The high resolution of the machine (500 MHz) has approximated the expected very complex spectra, such as the AA'XX' and AA'BB' for aromatic system into simple $A_2X_2$, $AX_2$ and so on. The simple coupling constants can be calculated even for the aromatic protons. Each spectrum is in complete consistence with corresponding compound **Table 3.3**, **Appendix II**. And each carbon in the benzoate compound are named as **Fig 3.1**.

The coupling constant were averaged because the resolution isn't enough to show the para and meta coupling.

The alcoholic part of the ester is the same and show very similar signals in their charts. The ethylene group shows two triplets at δ 4.2 -4.6 ppm with an average coupling constant (4.2-4.5 Hz).

**Table 3.2 frequencies of main functional groups of benzoate compounds in $cm^{-1}$**

| Others | di- substituted | Mono-substituted | O-phenyl | O-C alcoholic | C-O carbonyl | Aromatic C-C | C=O ester | C-H aromatic | $CH_2CH_2$ stretching | cpd |
|---|---|---|---|---|---|---|---|---|---|---|
| N-O,1354 C-N,856 | 786 | 689 734 | 1281 | 1062 | 1236 | 1498 1536 | 1734 | 3030 | 2800 2927 | I |
| N-O,1306 C-N,849 | 606,799 | 679,749 | 1275 | 1061 | 1242 | 1486 1537 | 1718 | 3050 | 2831 2974 | II |
| N-O,1343 C-N,856 | 822 | 686,754 | 1274 | 1063 | 1240 | 1499 1522 | 1719 | 3053 | 2890 2970 | III |
| C-Br,598 | 796 | 688,743 | 1288 | 1063 | 1233 | 1486 1585 | 1728 | 3010 | 2944 2962 | IV |
| C-Br,599 | 670,760 | 688,722 | 1261 | 1064 | 1244 | 1489 1586 | 1715 | 3055 | 2854 2949 | V |
| C-Br,599 | 837 | 683,750 | 1267 | 1066 | 1235 | 1483 1585 | 1702 | 3047 | 2881 2954 | VI |
| CH3 bending 1380 | 522 | 693,760 | 1285 | 1062 | 1247 | 1490 1597 | 1722 | 3060 | 2810 2953 | VII |
| CH3 bending 1366 | 606,799 | 679,748 | 1275 | 1061 | 1243 | 1486 1581 | 1718 | 3050 | 2831 2942 | VIII |
| CH3 bending 1373 | 844 | 689,750 | 1279 | 1063 | 1249 | 1498 1604 | 1708 | 3040 | 2842 2927 | IX |
| N-H 3450 3371 | 606,791 | 688,748 | 1289 | 1043 | 1240 | 1454 1598 | 1702 | 3050 | 2875 2924 | X |
| N-H, 3349,3447 | 880 | 688,747 | 1271 | 1053 | 1271 | 1496,1599 | 1700 | 3035 | 2980 3000 | XI |
| CH3bending 1370 | 826 | 688,751 | 1279 | 1060 | 1240 | 1495,1597 | 1703 | - | 2850 2961 | XII |

The peaks in nitro compounds found at the highest values about 8.5 ppm because the nitro group move the electron density away from the proton "deshielding" and the signal moves downfield (to the left).

Bromo group also is electron withdrawing group but less than the nitro one, the value of its chemical shift is about 8 ppm.

Methoxy group give lower chemical shift around 7.5 ppm because it is considered as electron releasing group which shield the protons moving the shift up-field (to the right).

Amino and tertiary butyl groups also are electron donating groups which were found at 7 and 7.9 ppm respectively.

**Table 3.3:** chemical shift in ppm, coupling constant, and splitting type of NMR spectra

| cpd | C2-H | C3-H | C4-H | C5-H | C6-H | C7-H | C8-H | C10-H | C11-H | C12-H | X |
|---|---|---|---|---|---|---|---|---|---|---|---|
| I | – | 8.08,d,1H J=7.5Hz | 7.85,m Unresolvable | 7.85,m Unresolvable | 7.85,m Unresolvable | 4.62,t,2H J = 4.37Hz | 4.28,t,2H J = 4.37 Hz | 6.97,d,2H J=8.01Hz | 7.3,t,2H J=8.01Hz | 6.95,t,1H, J=8.01 | – |
| II | 8.62,s, 1H | – | 8.5, d,1H J=8.01Hz | 7.84, t,1H J=8.01Hz | 8.36,d,1H J=8.01Hz | 4.69,t,2H J = 4.50Hz | 4.38 ,t,2H J = 4.50 Hz | 7,t, 2H J=7.57Hz | 7.3,t,2H J=7.57Hz | 6.95,t, 1H J=7.57 Hz | – |
| III | 8.19,d,2H J=8.83Hz | 8.35,d,2H J=8.83Hz | – | 8.35,d,2H J=8.83Hz | 8.19,d,2H J=8.83Hz | 4.67,t,2H J = 4.4 Hz | 4.37,t,2H J = 4.4 Hz | 6.99,d,2H J=7.56Hz | 7.31,t, 2H J=7.56Hz | 6.96,t, 1H J=7.56 Hz | – |
| IV | – | 7.76, 1H Low resolution | 7.5, 1H low resolution | 7.5, 1H low resolution | 7.76,1H Low resolution | 4.33 Low resolution | 4.62 Low resolution | 6.98,d,2H J=7.66 Hz | 7.3,t,2H J=7.66 | 6.97,t,1H | – |
| V | 8.05, s, 1H | – | 7.96,d,1H J=8.06Hz | 7.51,t,1H J=8.06Hz | 7.89,d,1H J=8.06Hz | 4.36,t,2H J = 4.5 Hz | 4.62,t,2H J = 4.5 Hz | 7,d,2H J=7.74Hz | 7.31,t, 2H J=7.74Hz | 6.96,t, 1H J=7.74 Hz | – |
| VI | 7.75,d,2H, J=7.58Hz | 7.88,d,2H, J=7.58Hz | – | 7.88,d,2H, J=7.58Hz | 7.75,d,2H, J=7.58Hz | 4.34(2H) Low resolution | 4.61,(2H) Low resolution | 6.99(2H) Low resolution | 7.3(2H) Low resolution | 6.99(1H) Low resolution | – |
| VII | – | 7.14,d,1H J=7.67Hz | 7.02,t,1H J=7.67 Hz | 7.54,t,1H J=7.67Hz | 7.64,d,1H J=7.67Hz | 4.55,t,2H J = 4.3 Hz | 4.29,t,2H J = 4.3 Hz | 6.99,d,2H J=7.84Hz | 7.3,t,2H, J=7.84Hz | 6.95,t,1H J=7.84 Hz | 3.8,s 3H |
| VIII | 7.44 (1H,s) | – | 7.19,dd,1H $J_1$=1.9 Hz $J_2$=7.7 Hz | 7.55, t,1H J=7.7Hz | 7.23,dd,1H J=1.88 J=7.7 Hz | 4.34,t,2H J = 4.5 Hz | 4.61,t,2H J = 4.5 Hz | 7,d,2H J=7.55Hz | 7.3,t,2H J=7.55Hz | 6.96,t,1H J=7.55Hz | 3.81,s 3H. |
| IX | 7.92,d,2H J=8.85Hz | 7.05,d,2H J=8.85Hz | – | .05,d,2H J=8.85Hz | 7.92,d,2H J=8.85Hz | 4.33,t,2H J = 4.5 Hz | 4.57,t,2H J = 4.5 Hz | 6.99,d,2H J=7.76Hz | 7.3,t,2H J=7.76Hz | 6.96,t,1H J=7.76 Hz | 3.84,s 3H |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| X | 7.2, s,1H | – | 6.8,d,1H J=7.5 Hz | 7.11,t,1H J=7.5 Hz | 7.15,d,1H J=7.5 Hz | 4.3,t,2H J = 4.2Hz | 4.55,t,2H J = 4.2Hz | 6.99,d,2H J=8.03Hz | 7.31,t,2H J=8.03Hz | 6.94,t,1H J=8.03 Hz | 5.38,s 2H |
| XI | not measured | – | – | – | – | – | – | – | – | – | – |
| XII | 7.9,d,2H J=8.45Hz | 7.54,d,2H J=8.45Hz | – | 7.54,d,2H J=8.45Hz | 7.9,d,2H J=8.45Hz | 4.33,t,2H J = 4.5 Hz | 4.6,t,2H J = 4.5 Hz | 6.99,d,2H J=7.57Hz | 7.3,t,2H J=7.57Hz | 6.96,t,1H J=7.57 Hz | 1.3,s 9H |

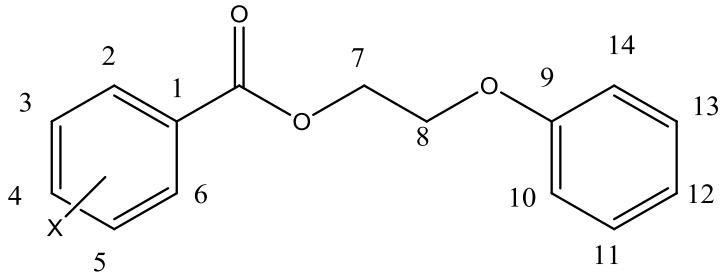



**Fig 3.1** General naming of each carbon in benzoate compounds

## 3.2 Anti-fungal activity

Many anti-fungal substances are known and available in a few markets when compared to the antibacterial substances.

Anti-fungal medications for skin are also relatively unsatisfactory. The goal of this study is to find new anti-fungal compounds that are more powerful than the known fungal antibiotics used to fight a specific infections, e.g., skin infections. In drug discovery, the first aim is to find a '*lead* compound' that works as the 'active ingredient' of future medications that provoke fungal death. If our 'lead' compounds were found to cause fungal death, this may lead to the discovery of antifungal medicines as new chemical entities (NCE) that can have strong effect in killing some fungi [40].

Our compounds were tested for their antifungal activities against *M. canis,T. rubrum,* and *E. flaccosum*. **Tables 3.4, 3.4.1, 3.4.2**, respectively. The twelve tested compounds showed results as explained next. 2-phenoxyethyl-4-nitrobenzoate showed complete inhibition against *M. canis* at 750 µg/ml, while the other two nitro compounds didn't show significant activity. 2-phenoxyethyl-3-bromobenzoate showed complete inhibition against *M. canis* at 1500 µg/ml acid and complete inhibition against *T. rubrum* at 750 µg/ml and at 1500 µg/ml for *E. flaccosum*. 2-phenoxyethyl 4-bromobenzoate showed complete inhibition against *M. canis* at 1500 µg/ml only, while the last bromo compound didn't show significant activity. 2-phenoxyethyl 2-methoxy benzoate showed complete inhibition against *M. canis* at 1500 µg/ml only while 4-methoxybenzoateshowed

complete inhibition against *T. rubrum*, and *E. flaccosum* at 1500 µg/m. However, the last methoxy compound didn't show significant activity.

2-phenoxyethyl-3-aminobenzoate showed complete inhibition against *M. canis* at 1500 µg/ml, while*T. rubrum at 750*, and *E. flaccosum* at 1500 µg/ml. Fig 3.2.1.On the other hand, 2-phenoxyethyl-4-aminobenzoate showed complete inhibition only against *M. canis* at 1500 µg/ml. 2-phenoxyethyl-4-t-butylbenzoate showed complete inhibition against *M. canis*for the three concentrations and at 750 µg/ml for *T. rubrum* and for *E. flaccosum***Fig 3.2, 3.2.2, and 3.2.3.**

The type and the position of the functional group on the ring seems to affect the activity of the compound, although the three compounds have the same molecular weights and formulas.

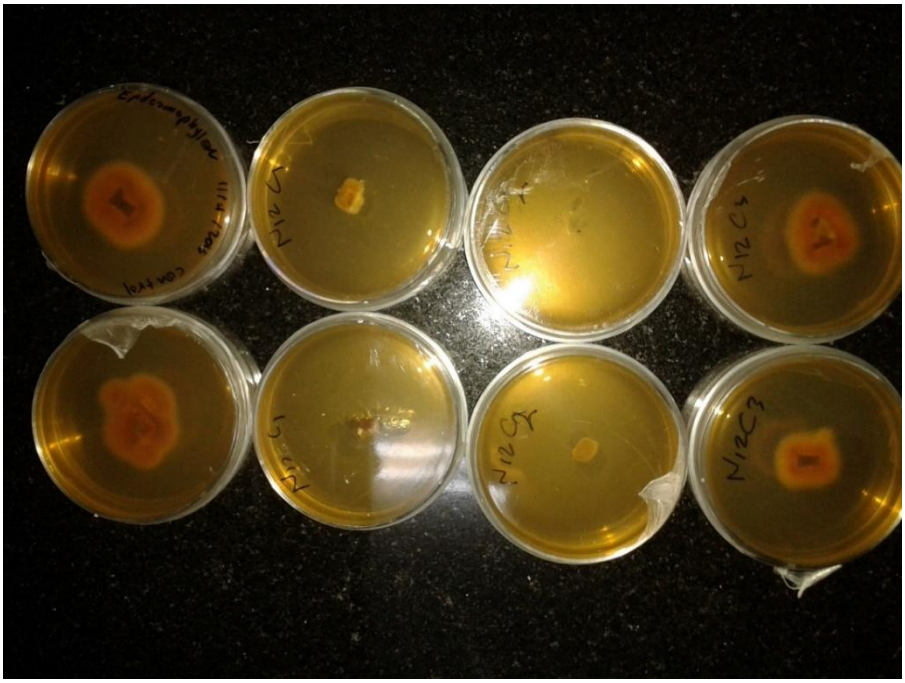


**Figure 3.2:** Anti-fungal testing of compound number12 against *E. flaccosum*

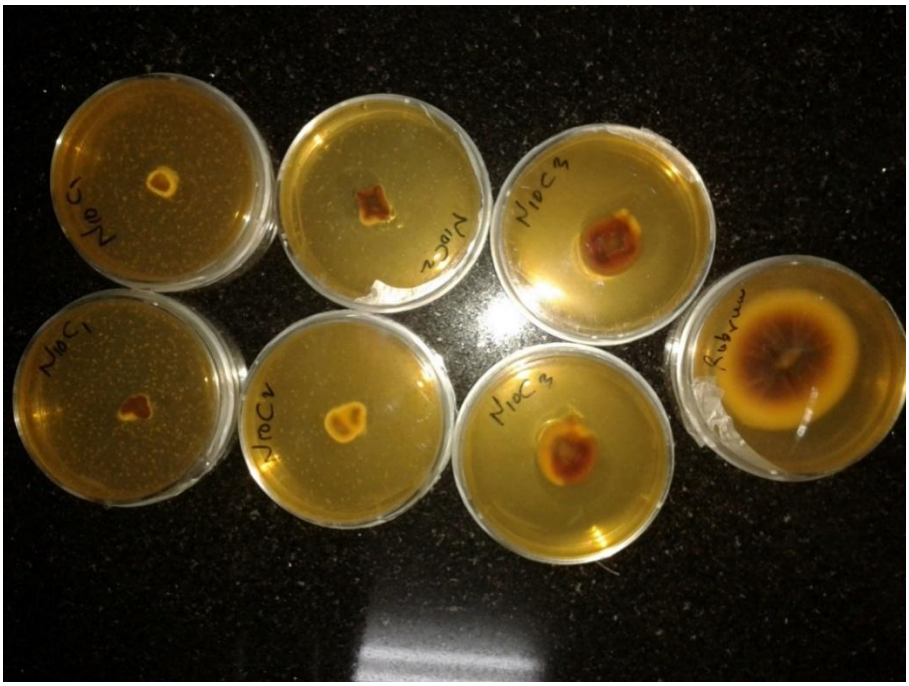


**Figure 3.2.1 :** Anti-fungal testing of compound number 10 against *T. rubrum*

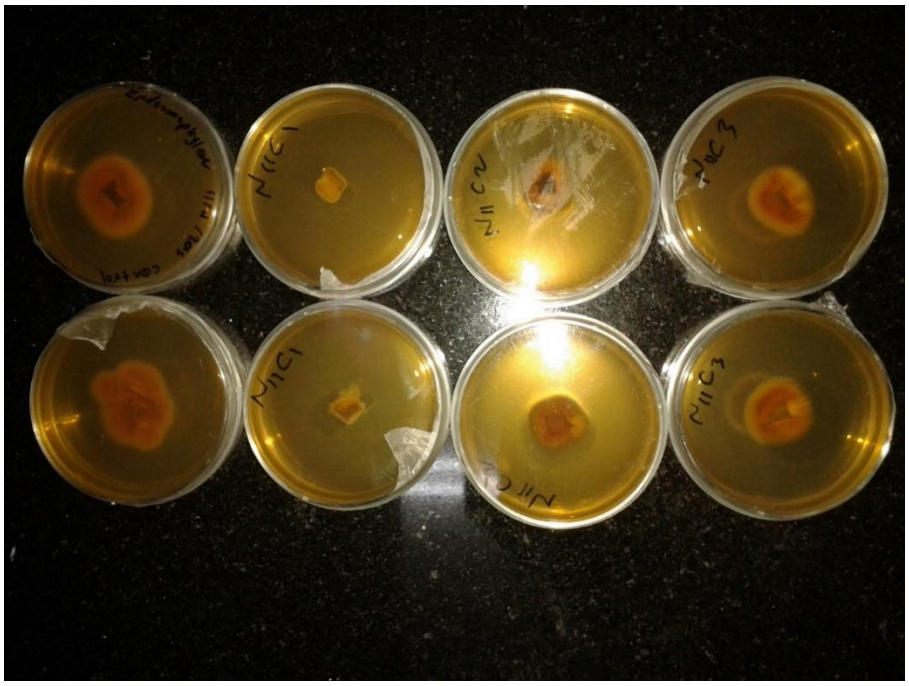


**Figure 3.2.2 :** Anti-fungal testing of compound number 11 against *E. flaccosum*

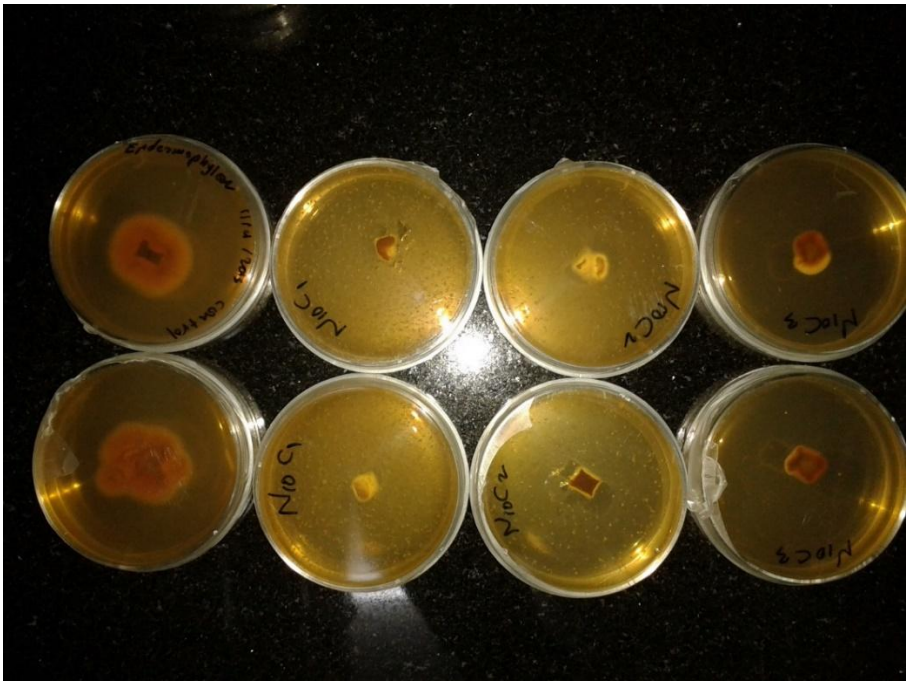


**Figure 3.2.3** Anti-fungal testing of compound number 10 against *E. flaccosum*

## Table 3.4Anti-fungal activity of benzoate compound against *M. canis at three concentrations*

| | | ***M. canis*** | | |
|---|---|---|---|---|
| **no.** | **compound** | **375** µg/ml | **750** µg/ml | **1500** µg/ml |
| 1 | 2-phenoxyethyl2-nitrobenzoate | 29.7 | 35.3 | 52.9 |
| 2 | 2-phenoxyethyl3-nitrobenzoate | 6.5 | 30.5 | 64.8 |
| 3 | 2-phenoxyethyl4-nitrobenzoate | 63.2 | 100 | 100 |
| 4 | 2-phenoxyethyl2-bromobenzoate | 4.9 | 22.5 | 45.7 |
| 5 | 2-phenoxyethyl3-bromobenzoate | 61.7 | 68.8 | 100 |
| 6 | 2-phenoxyethyl4-bromobenzoate | 0.9 | 35.3 | 100 |
| 7 | 2-phenoxyethyl2-methoxy benzoate | 20.1 | 67.2 | 100 |
| 8 | 2-phenoxyethyl3-methoxy benzoate | 52.9 | 61.7 | 64.8 |
| 9 | 2-phenoxyethyl4-methoxy benzoate | 0.159 | 33.7 | 56.1 |
| 10 | 2-phenoxyethyl3-aminobenzoate | 66.4 | 70.4 | 100 |
| 11 | 2-phenoxyethyl4-aminobenzoate | 4.1 | 28.9 | 100 |
| 12 | 2-phenoxyethyl4-t-butyl benzoate | 100 | 100 | 100 |

**Table 3.4.1Anti-fungal activity of benzoate compound against *T. rubrum at three concentrations***

| | | ***T. rubrum*** | | |
|---|---|---|---|---|
| **no.** | **compound** | **375** µg/ml | **750** µg/ml | **1500** µg/ml |
| 1 | 2-phenoxyethyl2-nitrobenzoate | 19.3 | 37.2 | 50.7 |
| 2 | 2-phenoxyethyl3-nitrobenzoate | 20.4 | 37.2 | 55.2 |
| 3 | 2-phenoxyethyl4-nitrobenzoate | 22.6 | 47.3 | 64.1 |
| 4 | 2-phenoxyethyl2-bromobenzoate | 5.8 | 24.9 | 41.7 |
| 5 | 2-phenoxyethyl3-bromobenzoate | 46.2 | 100 | 100 |
| 6 | 2-phenoxyethyl4-bromobenzoate | 10.3 | 23.8 | 47.3 |
| 7 | 2-phenoxyethyl2-methoxy benzoate | 17 | 26 | 55.1 |
| 8 | 2-phenoxyethyl3-methoxy benzoate | 19.3 | 41.7 | 55.1 |
| 9 | 2-phenoxyethyl4-methoxy benzoate | 30.5 | 42.8 | 100 |
| 10 | 2-phenoxyethyl3-aminobenzoate | 67.5 | 100 | 100 |
| 11 | 2-phenoxyethyl4-aminobenzoate | 27.1 | 41.7 | 66.4 |
| 12 | 2-phenoxyethyl4-t-butyl benzoate | 31.6 | 100 | 100 |

**Table 3.4.2 Anti-fungal activity of benzoate compound against *E. flaccosum at three concentrations***

| | | ***E. flaccosum*** | | |
|---|---|---|---|---|
| **no.** | **compound** | **375** µg/ml | **750** µg/ml | **1500** µg/ml |
| 1 | 2-phenoxyethyl 2-nitrobenzoate | 18.9 | 36.9 | 50.4 |
| 2 | 2-phenoxyethyl3-nitrobenzoate | 20 | 36.9 | 54.9 |
| 3 | 2-phenoxyethyl4-nitrobenzoate | 22.3 | 47.1 | 64 |
| 4 | 2-phenoxyethyl2-bromobenzoate | 5.4 | 24.5 | 41.4 |
| 5 | 2-phenoxyethyl3-bromobenzoate | 45.9 | 100 | 100 |
| 6 | 2-phenoxyethyl4-bromobenzoate | 9.9 | 23.4 | 47.1 |
| 7 | 2-phenoxyethyl2-methoxy benzoate | 16.7 | 25.7 | 54.9 |
| 8 | 2-phenoxyethyl3-methoxy benzoate | 18.9 | 27.9 | 50.4 |
| 9 | 2-phenoxyethyl4-methoxy benzoate | 30.2 | 40.3 | 100 |
| 10 | 2-phenoxyethyl3-aminobenzoate | 67.3 | 100 | 100 |
| 11 | 2-phenoxyethyl4-aminobenzoate | 26.8 | 41.4 | 66.2 |
| 12 | 2-phenoxyethyl4-t-butyl benzoate | 31.3 | 100 | 100 |

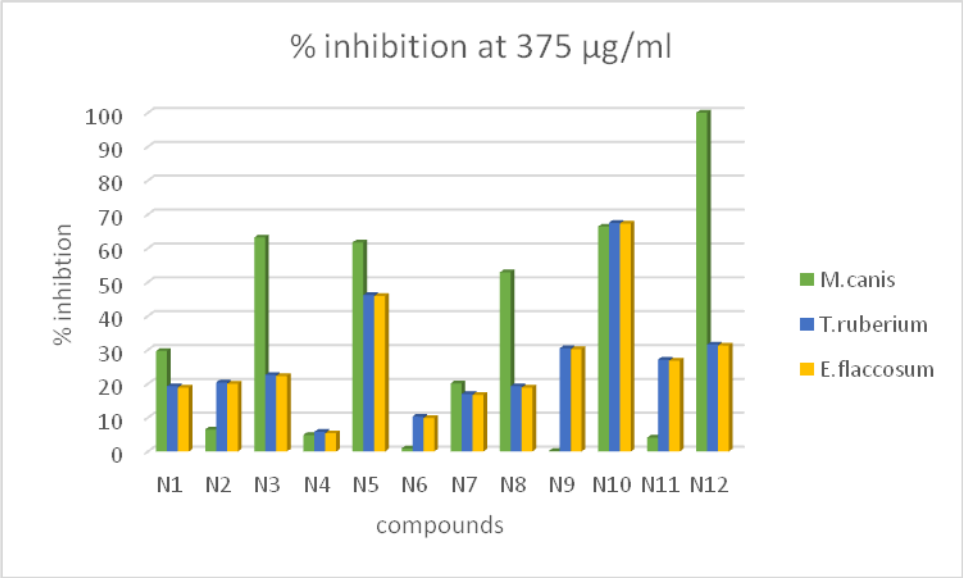



**Figure 3.3:** % Inhibition of benzoate compounds against three fungus at 375 µg/ml

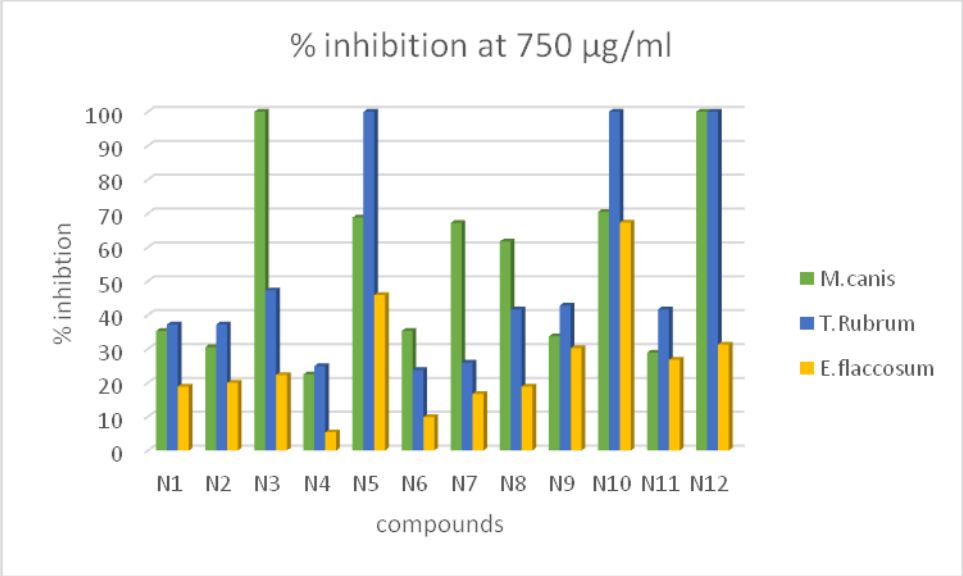



**Figure3.3.1:** % Inhibition of benzoate compounds against three fungus at 750µg/ml

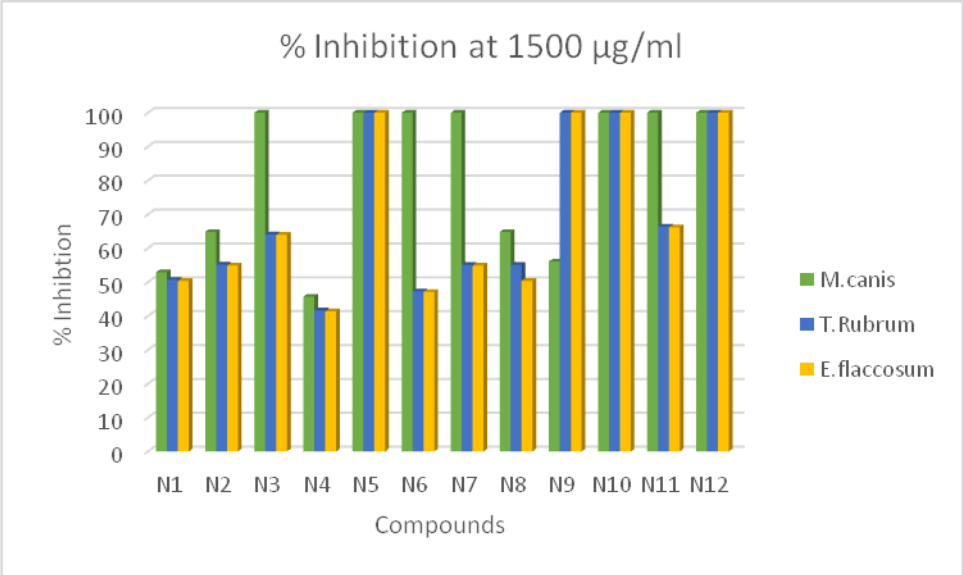



**Figure 3.3.2 :** % Inhibition of benzoate compounds against three fungus at 1500µg/ml

## 3.3 Anti-oxidant activity

DPPH (1,1-Diphenyl-2-picryl-hydrazyl) method was used to measure the anti-oxidant activity of benzoate compounds. Our compounds showed a reduction in the absorption of DPPH, but the differences in anti-oxidant activity between them were not sharp **Table 3.5.**

When antioxidants donate hydrogen atoms to the radicals, they lose their purple color. This in turn leads to a decreased absorption. The decrease in absorption is taken as a measure of the extent of radical scavenging. None of the compounds showed significant free radical scavenging activity, except compound XII which showed $IC_{50}$ at 22 µg/ml this mean that the efficiency of compound XII is more than ascorbic acid. **Fig. (3.4), (3.5).** We also found that values of percent inhibition increased with increasing

concentrations. The values for free radical scavenging given by our compounds were lower than that of ascorbic acid.

The position of functional group as ortho-, *para*- or *meta*- has no or slight effect on the antioxidant activity. Our results are in good agreement with literature done on polyphenolic compounds, which showed that the structure not affect the antioxidant activity [41]. The 2-phenoxyethyl 4-t-butyl benzoate showed the highest anti-oxidant activity of our compounds.

**Table 3.5Percent inhibition of radicals by benzoate compounds at different concentrations**

| no. | Concentration µg/ml | %Inhibition | | | | |
|---|---|---|---|---|---|---|
| | | 25 | 50 | 100 | 200 | 400 |
| I | 2-phenoxyethyl 2-nitrobenzoate | 43 | 45 | 46 | 47 | 63 |
| II | 2-phenoxyethyl 3-nitrobenzoate | 43 | 46 | 47 | 58 | 61 |
| III | 2-phenoxyethyl 4-nitrobenzoate | 42 | 46 | 47 | 48 | 62 |
| IV | 2-phenoxyethyl 2-bromobenzoate | 43 | 44 | 47 | 58 | 60 |
| V | 2-phenoxyethyl 3-bromobenzoate | 43 | 44 | 46 | 55 | 60 |
| VI | 2-phenoxyethyl 4-bromobenzoate | 43 | 45 | 46 | 48 | 61 |
| VII | 2-phenoxyethyl 2-methoxy benzoate | 43 | 46 | 48 | 49 | 61 |
| VIII | 2-phenoxyethyl 3-methoxy benzoate | 44 | 45 | 46 | 48 | 61 |
| IX | 2-phenoxyethyl 4-methoxy benzoate | 44 | 46 | 47 | 48 | 63 |
| X | 2-phenoxyethyl 3-aminobenzoate | 44 | 46 | 50 | 53 | 61 |
| XI | 2-phenoxyethyl 4-aminobenzoate | 43 | 46 | 47 | 49 | 60 |
| XII | 2-phenoxyethyl 4-t-butyl benzoate | 53 | 59 | 64 | 65 | 71 |

## 3.4 Antibacterial activity

The benzoate compounds were tested against six bacteria that cause dermic and mucosal infections [42]. Results were negative and there was no

activity against any of the tested types of bacteria at the concentration (10mg/ml) when compared with gentamicin **fig 3.6, 3.6.1**.

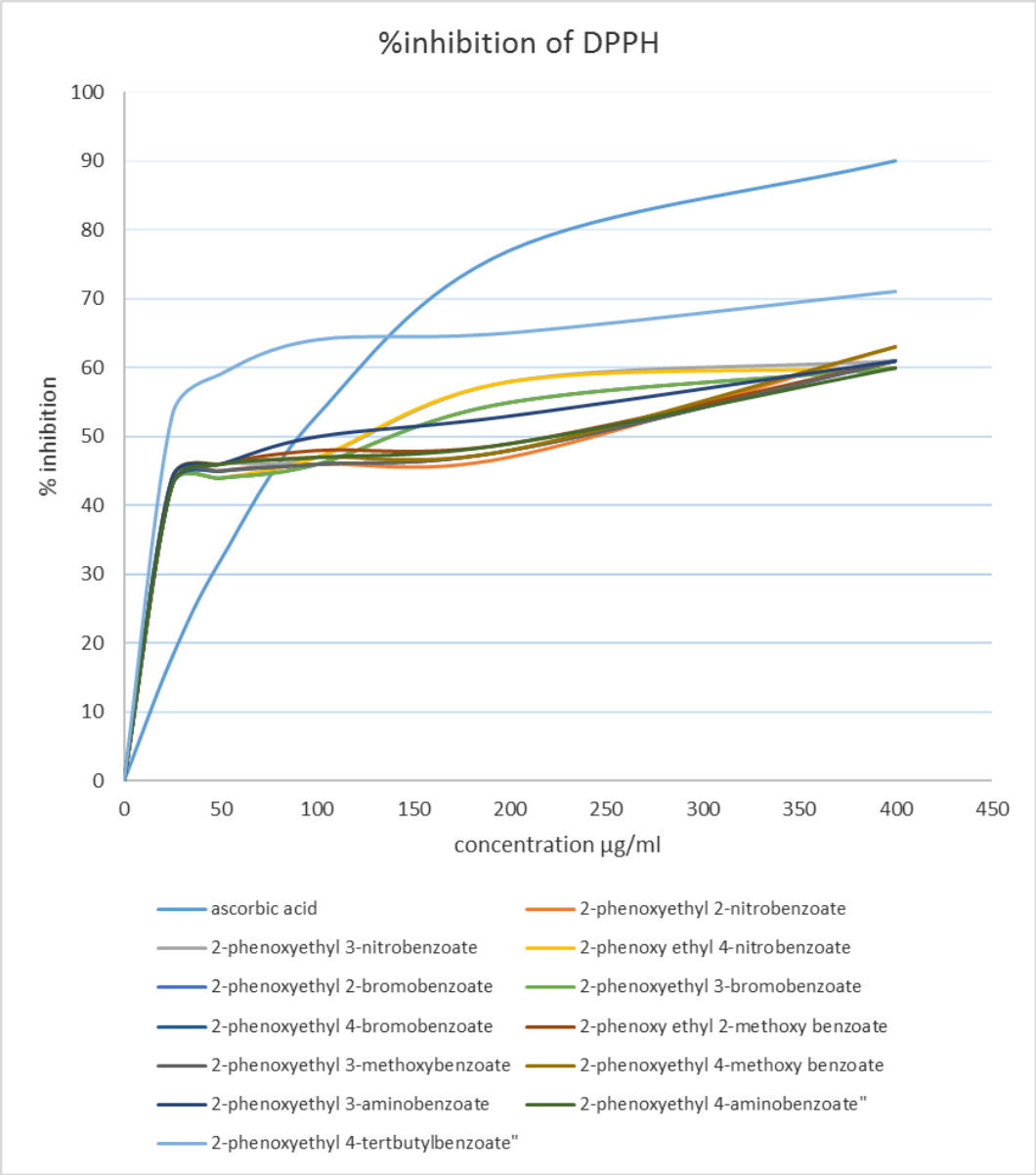



**Figure3.4 :** %Inhibition of DPPH for the tested compounds

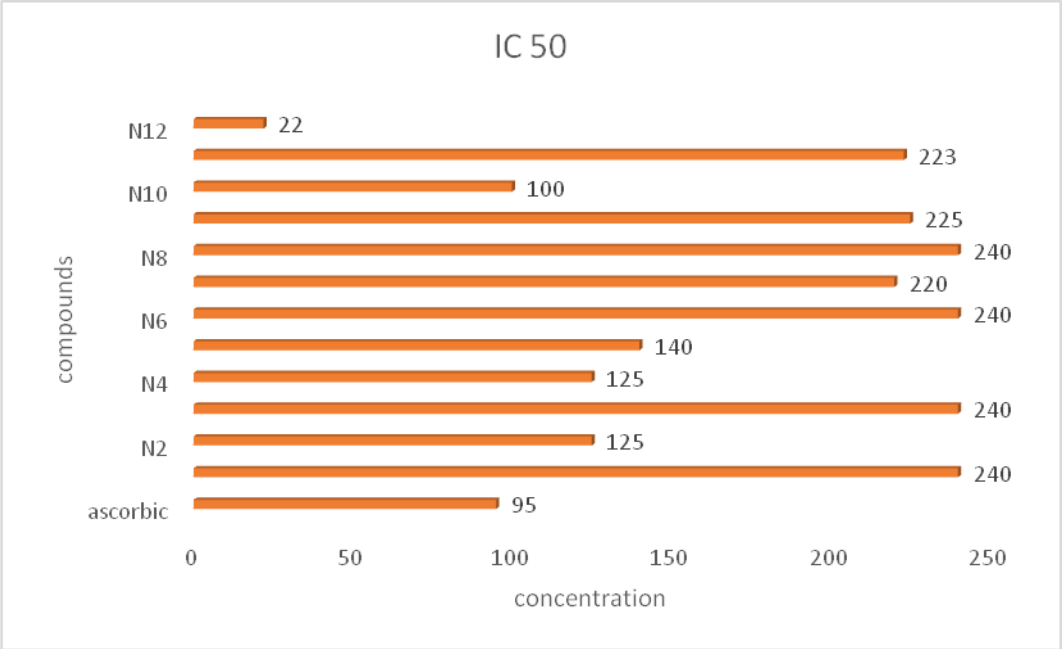



**Figure 3.5**: $IC_{50}$ for tested compounds

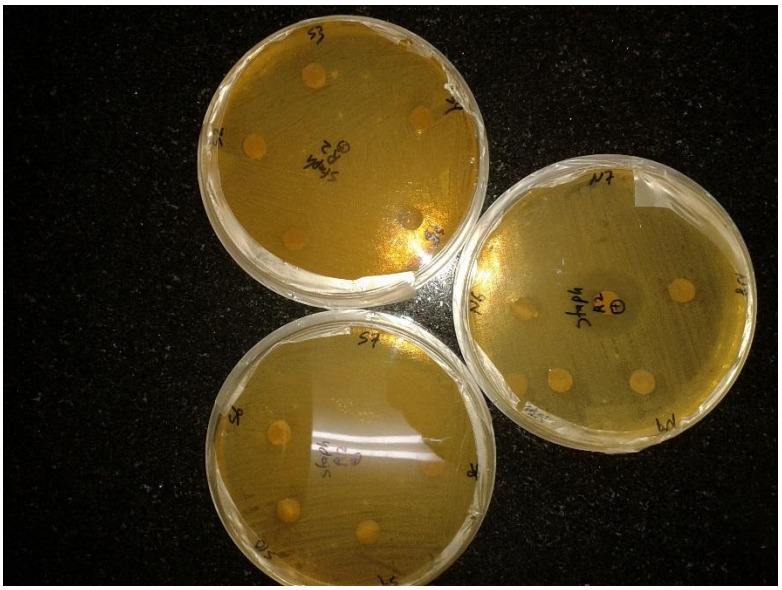


**Figure 3.6 :** Anti-bacterial testing of benzoate compounds against *Staphylococcus aureus*

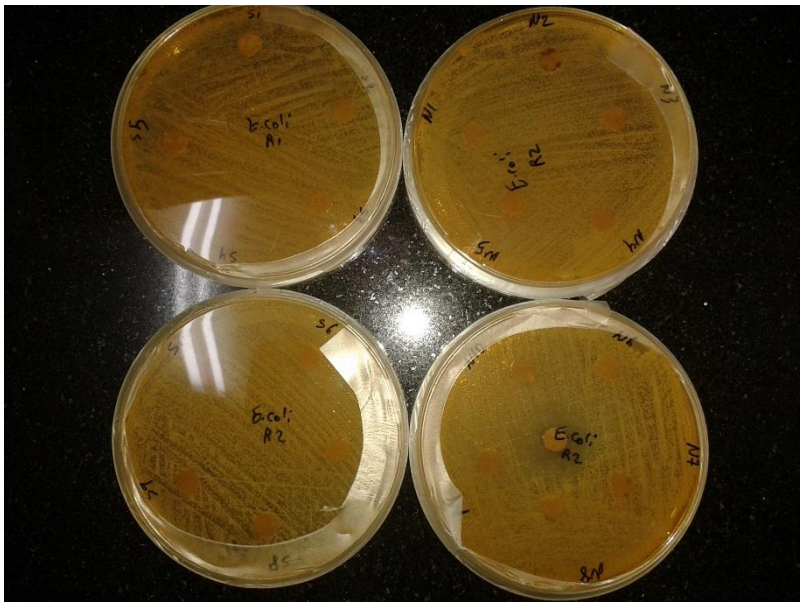



**Figure 3.6.1:** Anti-bacterial testing of benzoate compounds against Escherichia coli

## Suggestion for further work

1- To prepare modified esters by adding functional group to the phenoxyethanol and react it with benzoic acid.

2- To prepare modified esters by exchanging the phenoxyethanol to 2-(phenylthio)ethanol

3- To do more tests on compound XII for example against internal fungi.

4- To test the compounds in the agrochemical industry, such as pesticides.

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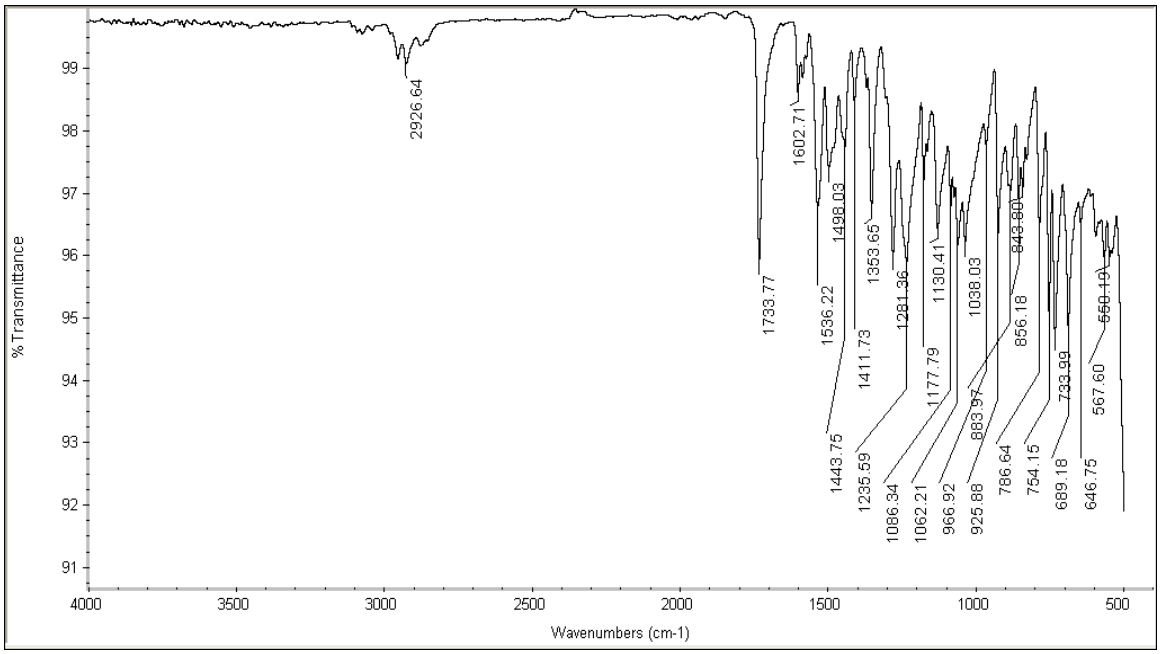
# Appendices

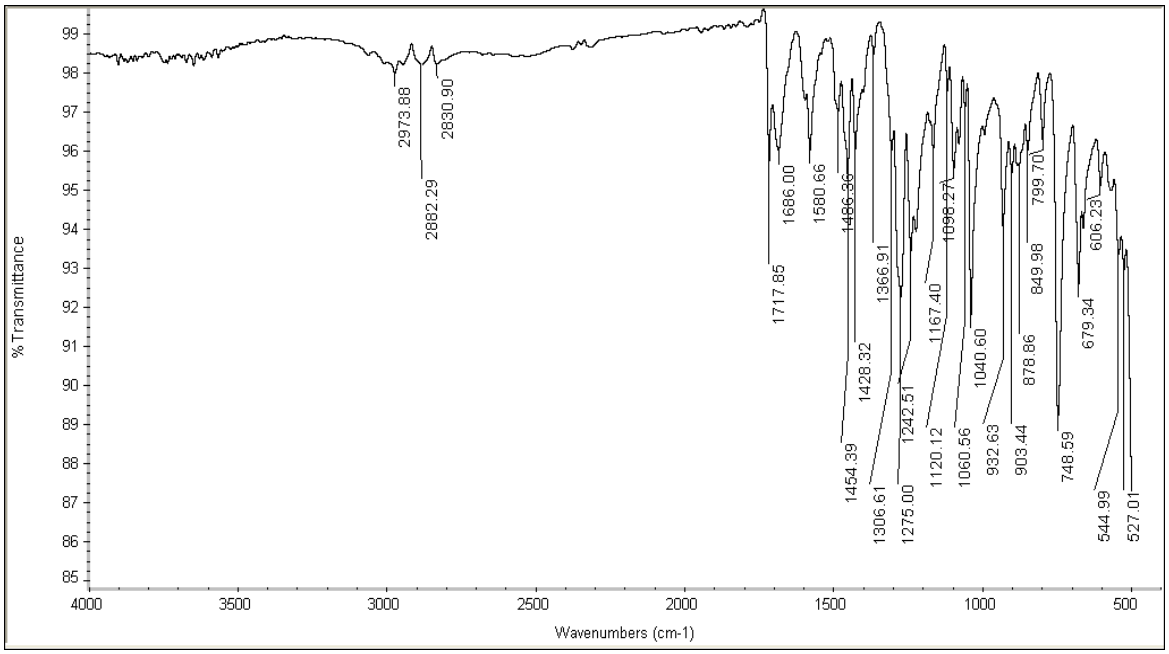
## Appendix I: Infra-Red Spectroscopy (IR)

### A1 2-phenoxyethyl 2-nitrobenzoate



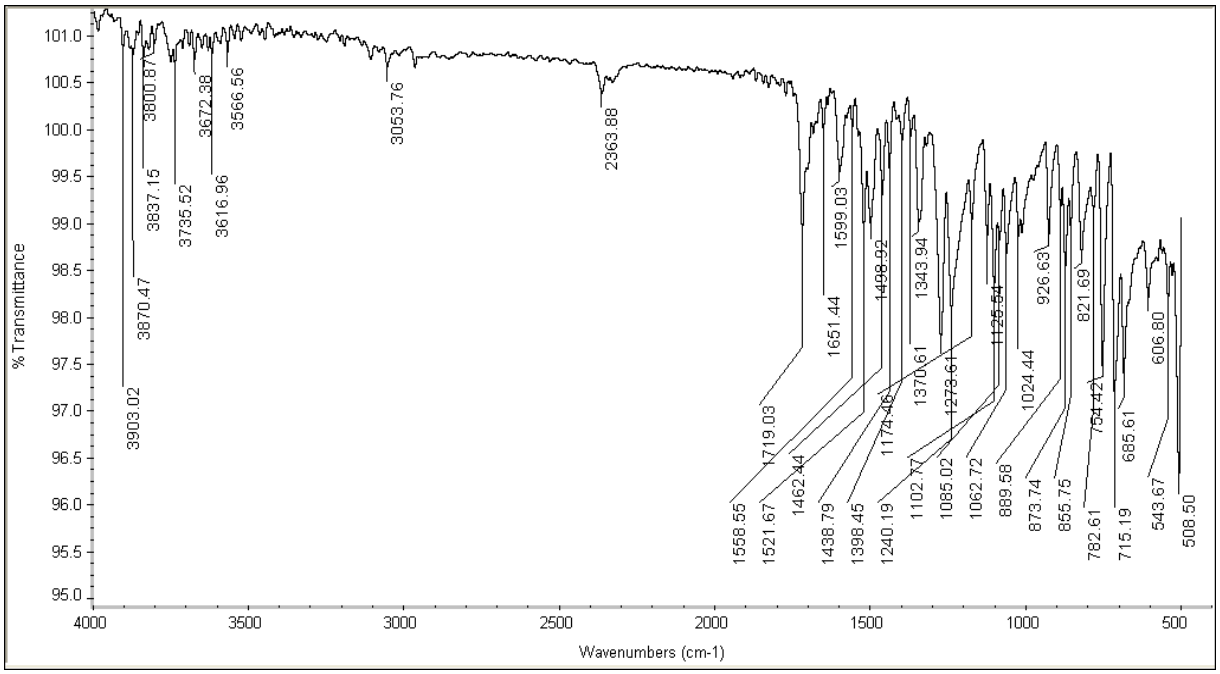

IR spectra of2-phenoxyethyl 2-nitrobenzoate

### A2 2-phenoxyethyl 3-nitrobenzoate



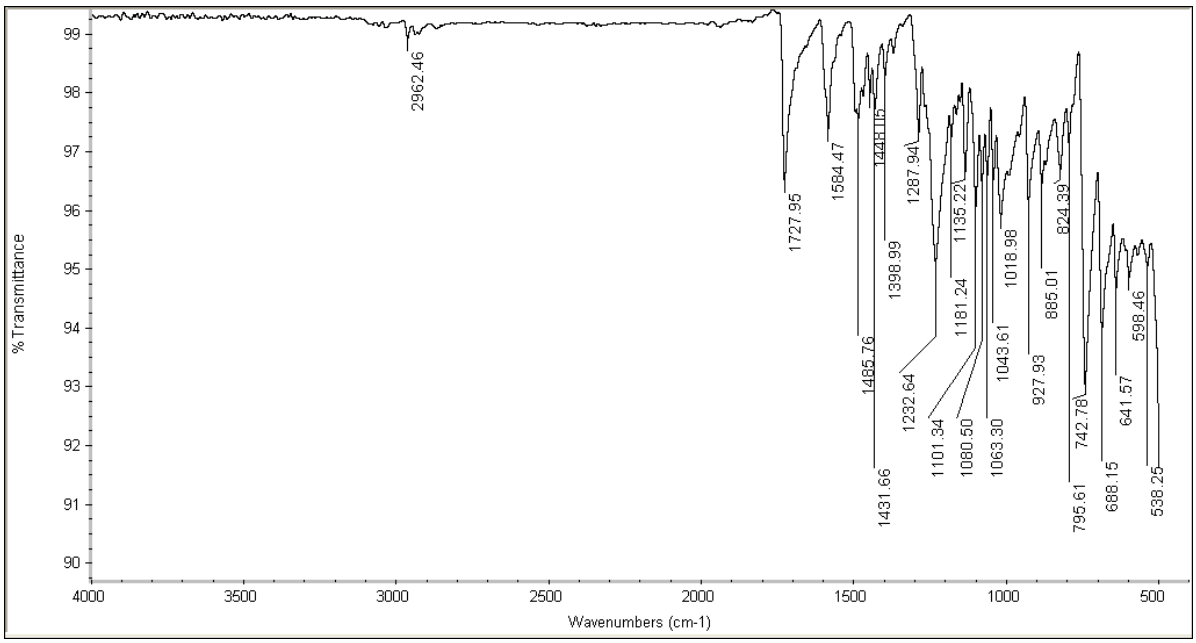

IR spectra of2-phenoxyethyl 3-nitrobenzoate

## A3 2-phenoxyethyl 4-nitrobenzoate



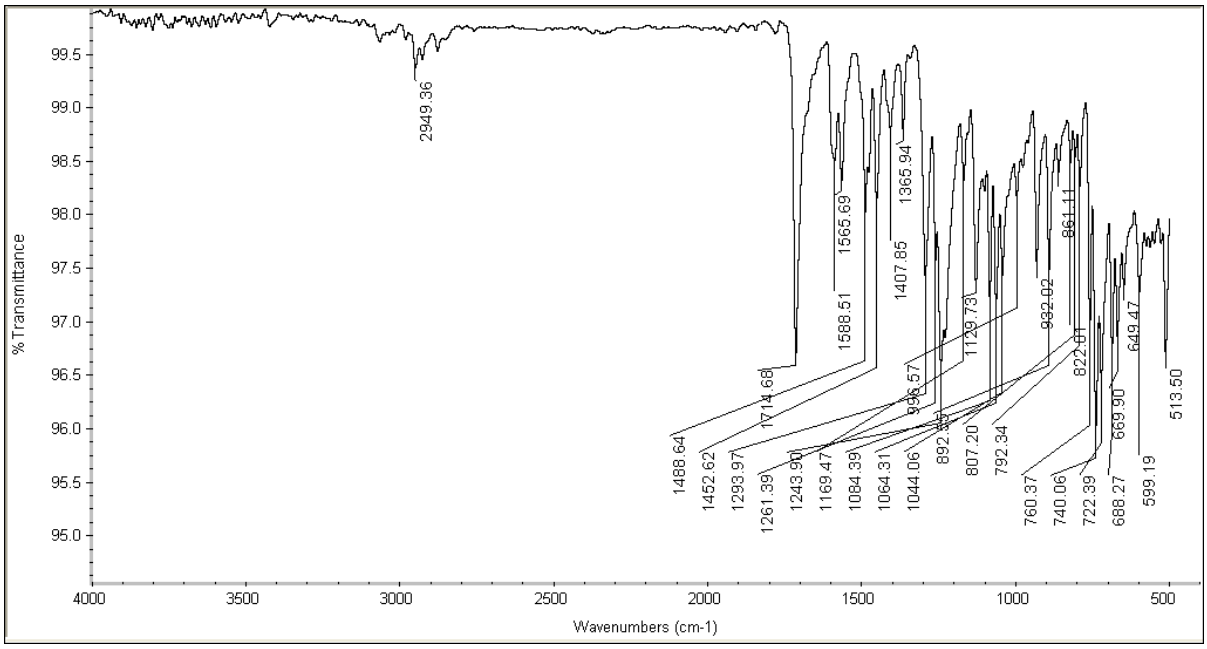

**IR spectra of 2-phenoxyethyl 4-nitrobenzoate**

## A4 2-phenoxyethyl 2-bromobenzoate



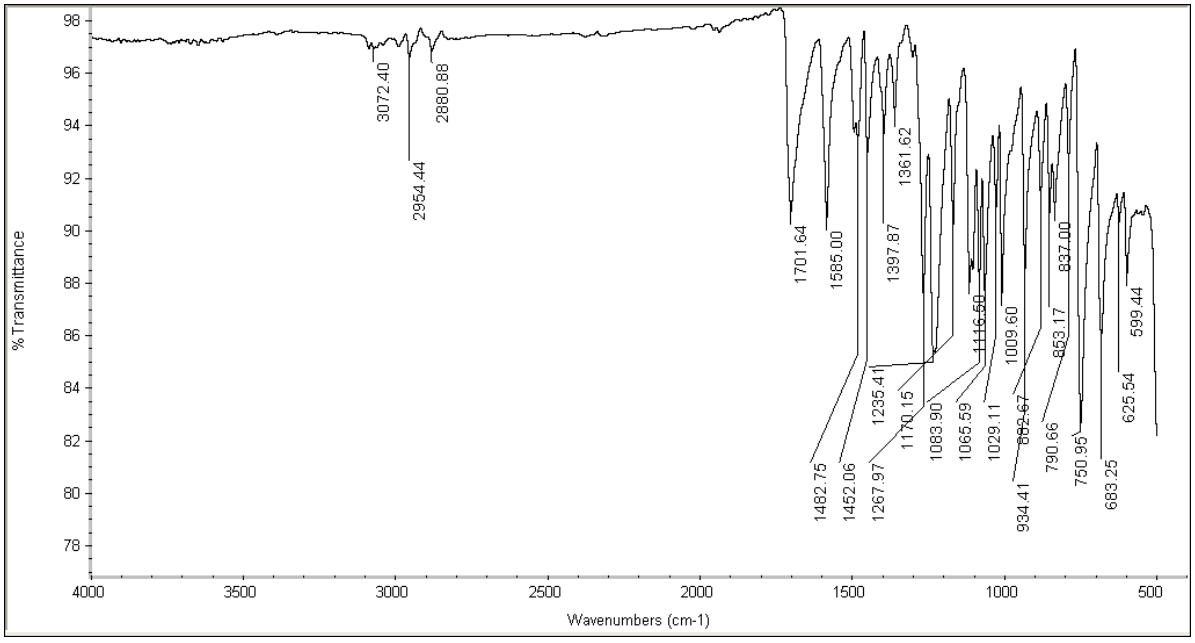

**IR spectra of 2-phenoxyethyl 2-bromobenzoate**

## A5 2-phenoxyethyl 3-bromobenzoate



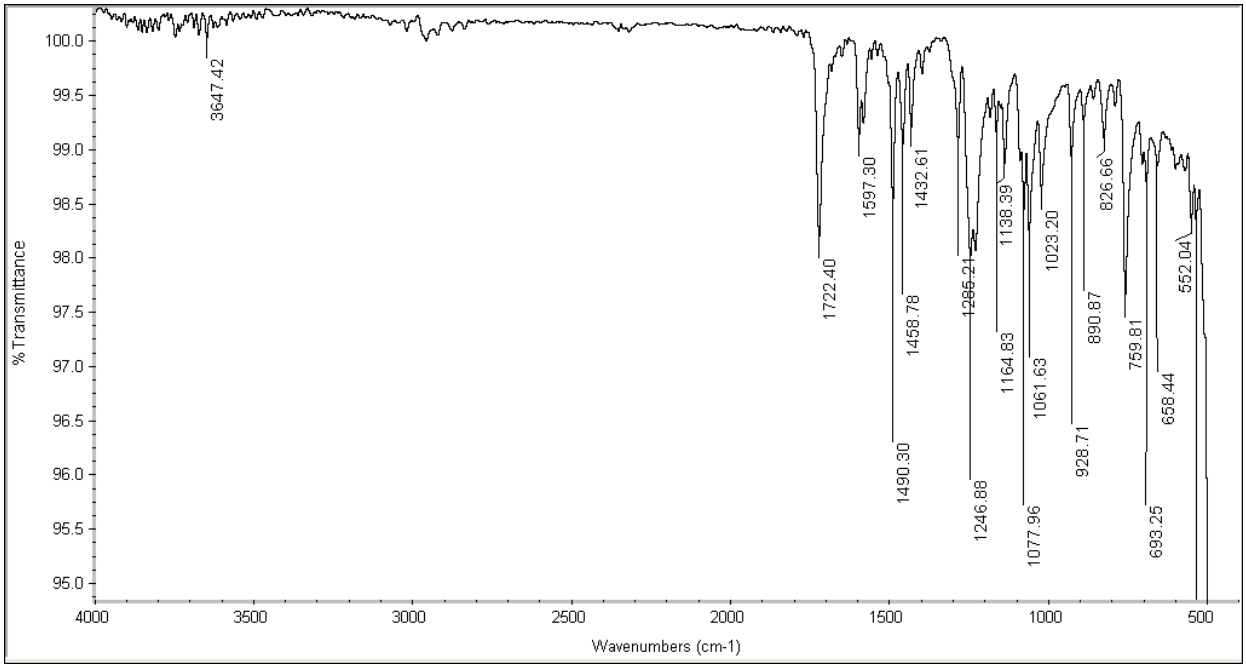

**IR spectra of 2-phenoxyethyl 3-bromobenzoate**

## A6 2-phenoxyethyl 4-bromobenzoate



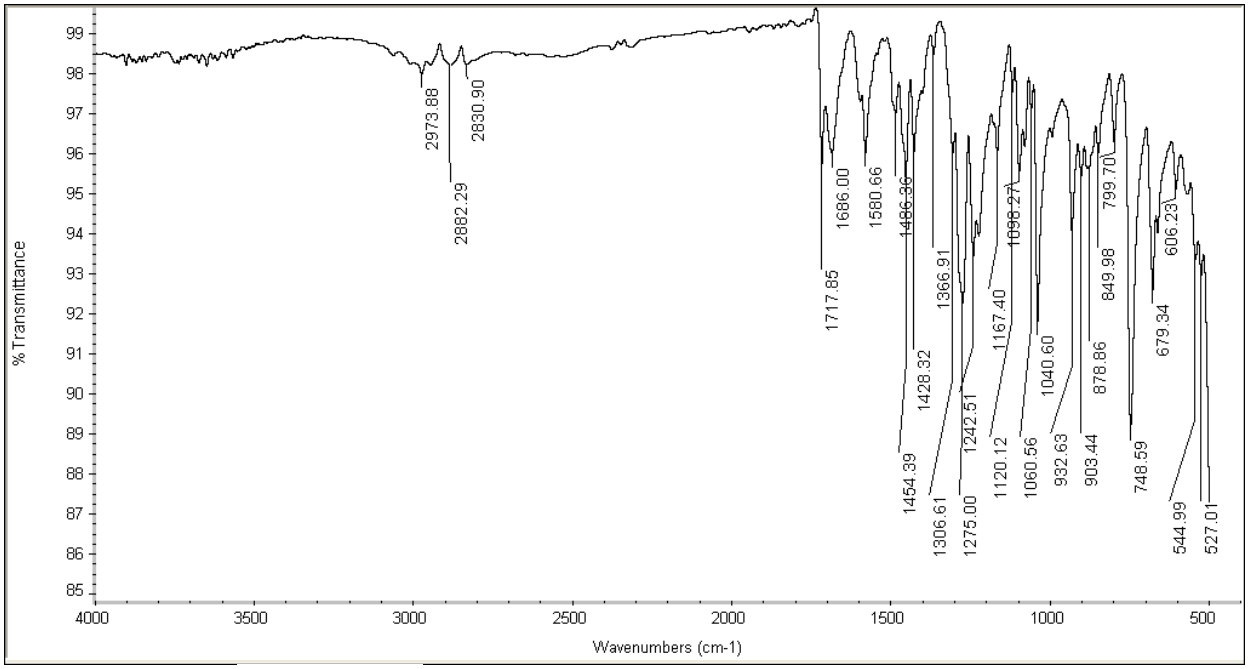

**IR spectra of 2-phenoxyethyl 4-bromobenzoate**

## A7 2-phenoxyethyl 2-methoxybenzoate



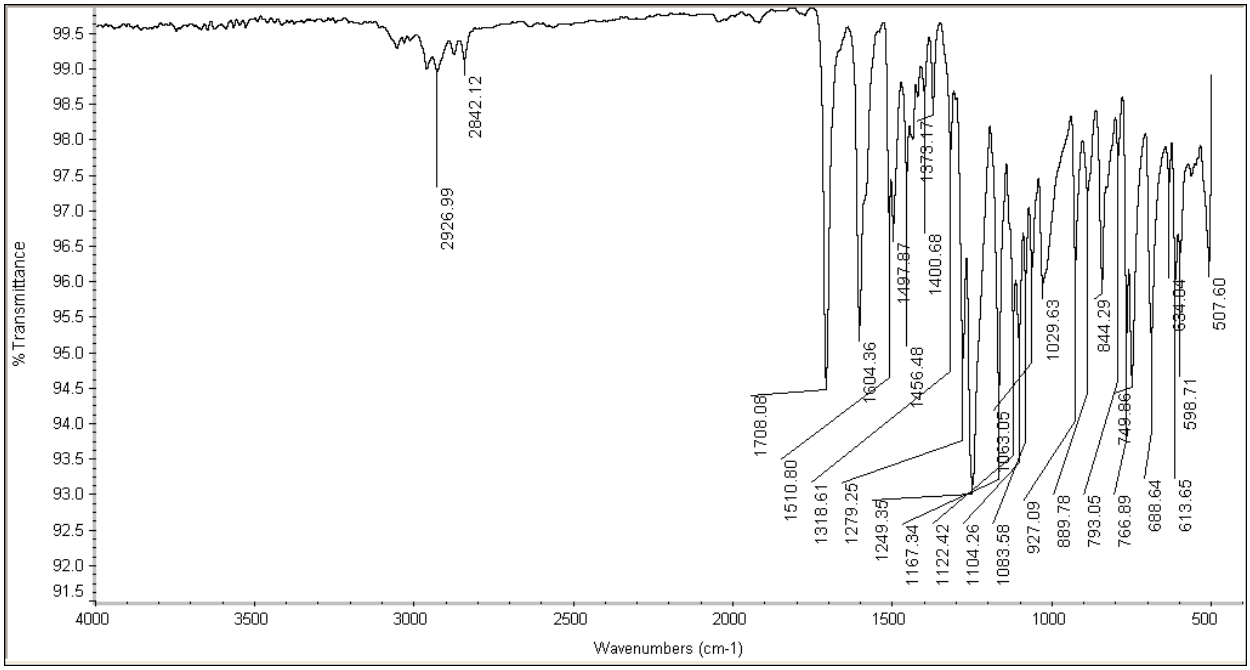

**IR spectra of 2-phenoxyethyl 2-methoxybenzoate**

## A8 2-phenoxyethyl 3-methoxybenzoate



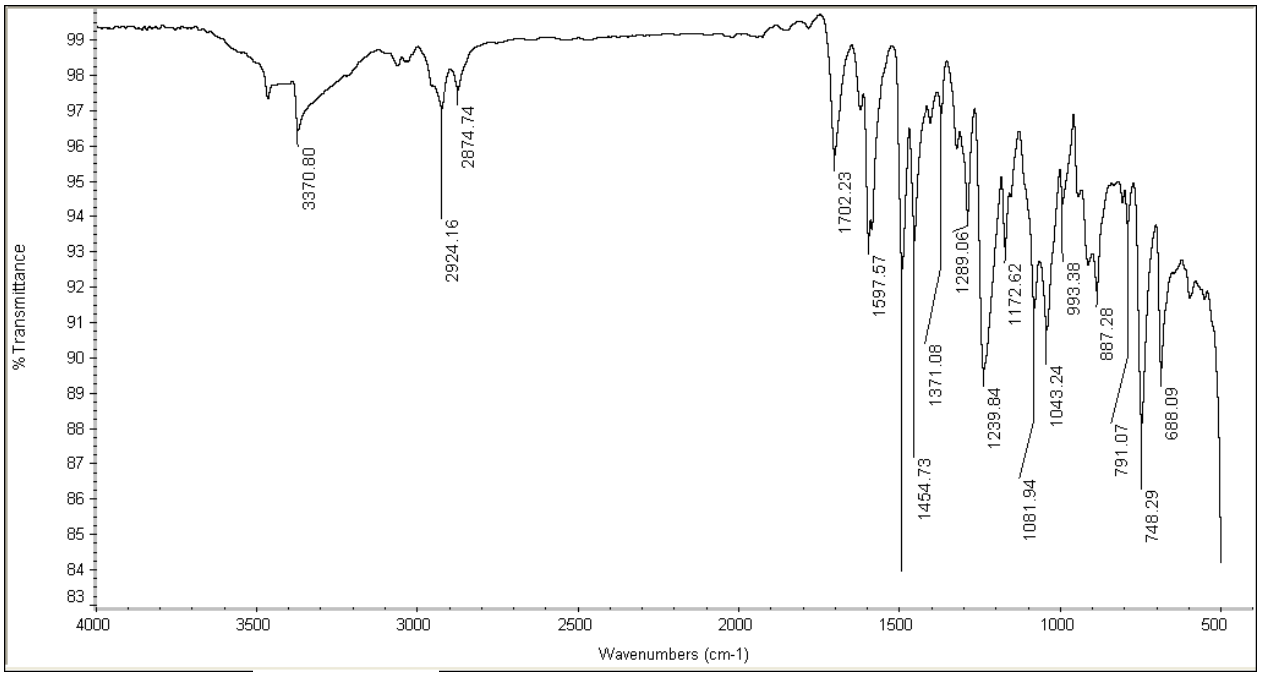

**IR spectra of 2-phenoxyethyl 3-methoxybenzoate**

## A9 2-phenoxyethyl 4-methoxybenzoate



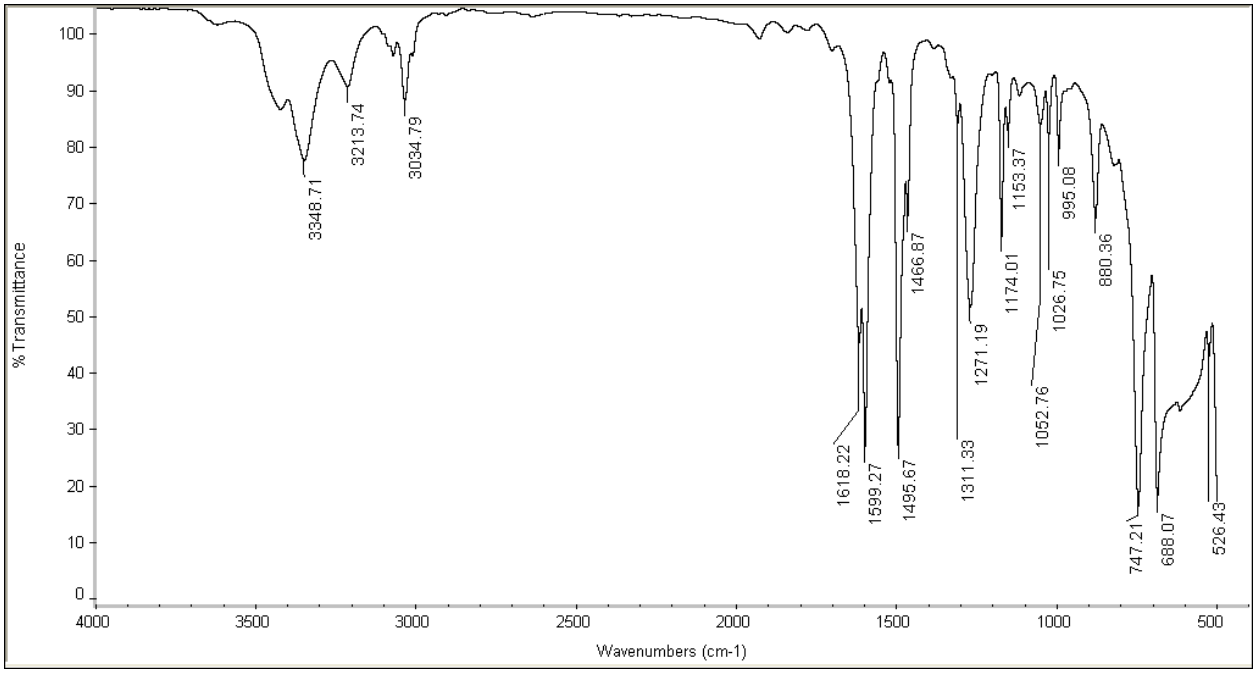

**IR spectra of 2-phenoxyethyl 4-methoxybenzoate**

## A10 2-phenoxyethyl 3-aminobenzoate



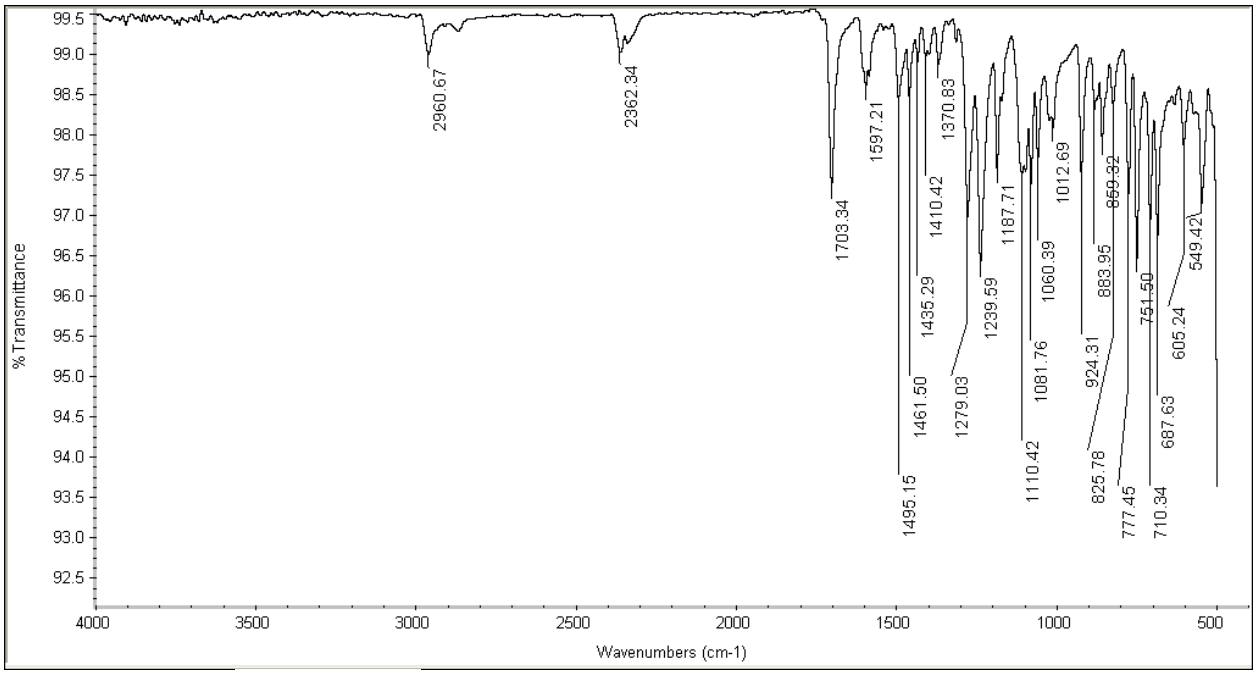

**IR spectra of 2-phenoxyethyl 3-aminobenzoate**

## A11 2-phenoxyethyl 4-aminobenzoate




**IR spectra of 2-phenoxyethyl 4-aminobenzoate**

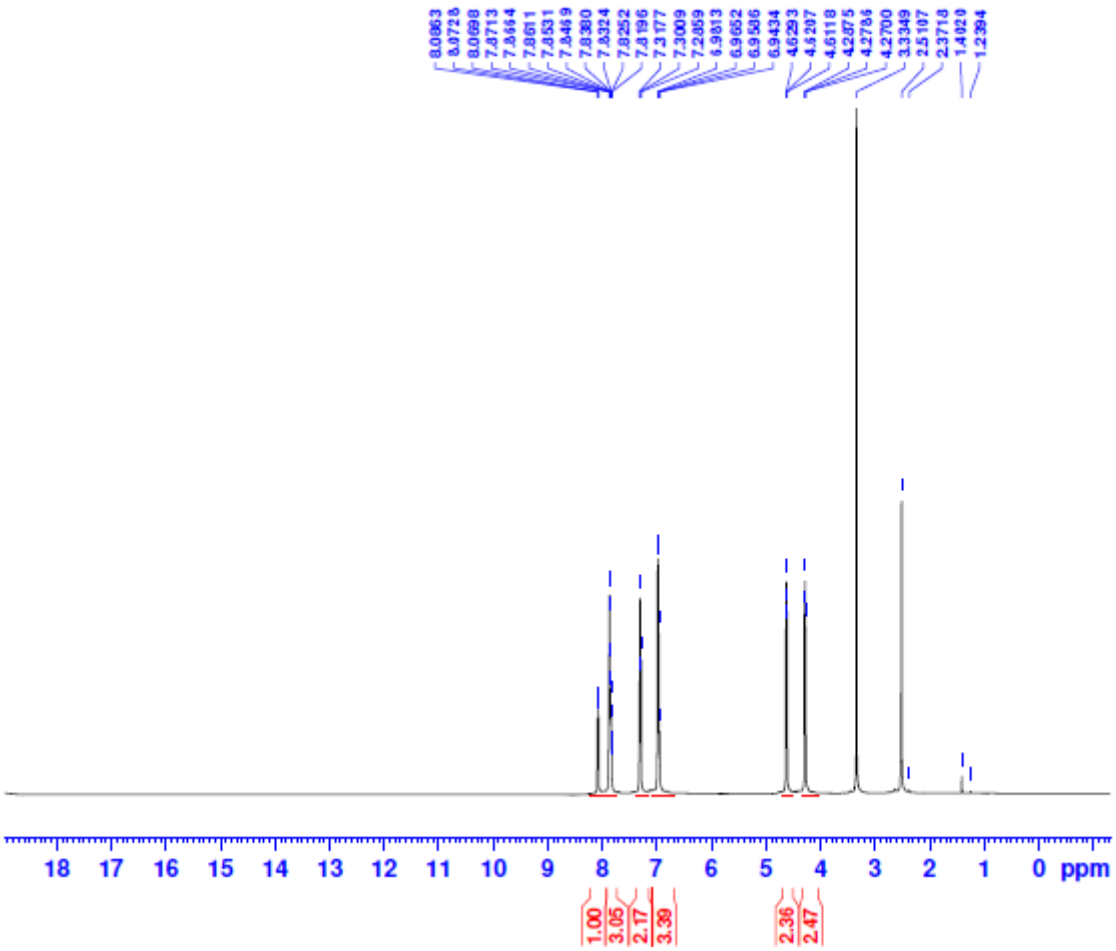
## A12 2-phenoxyethyl 4-tertbutylbenzoate



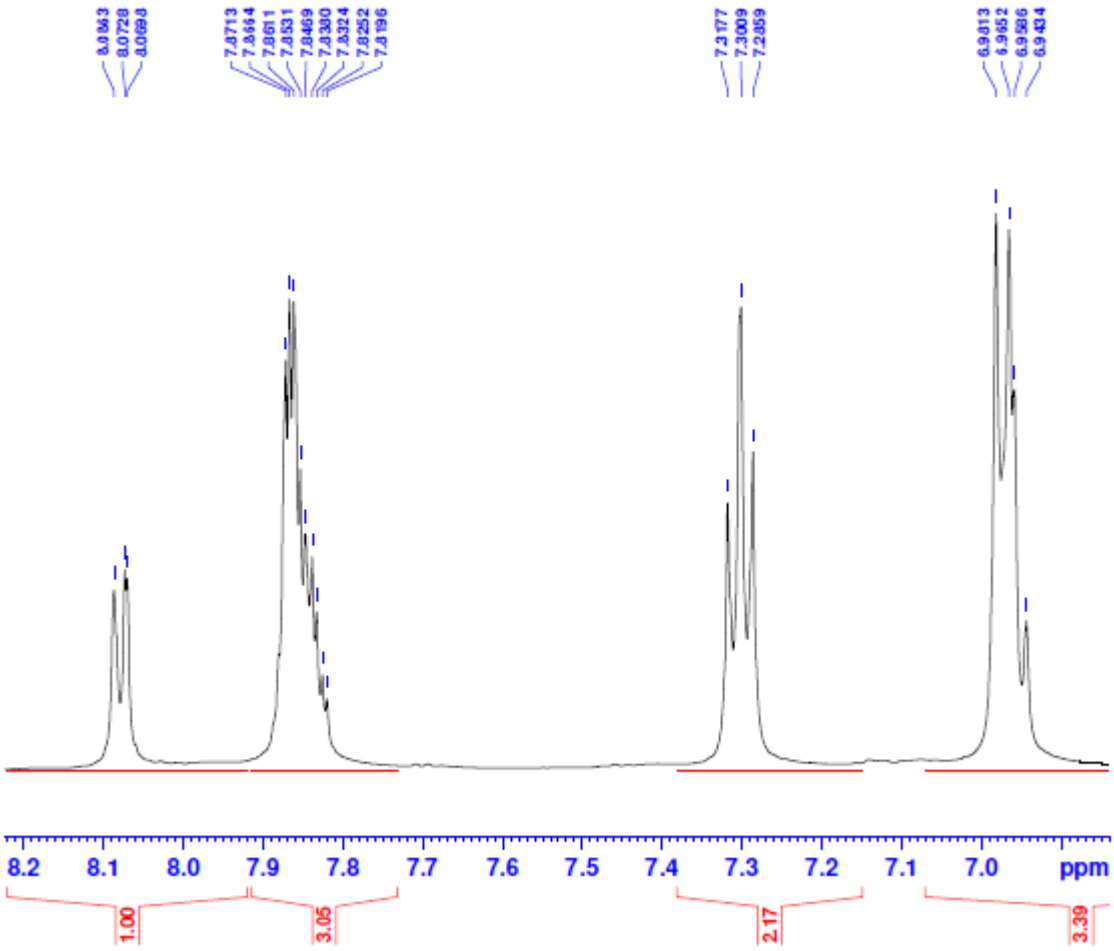

**IR spectra of 2-phenoxyethyl 4-tertbutylbenzoate**

# Appendix II: nuclear magnetic resonance Spectroscopy ($^1$H-NMR)

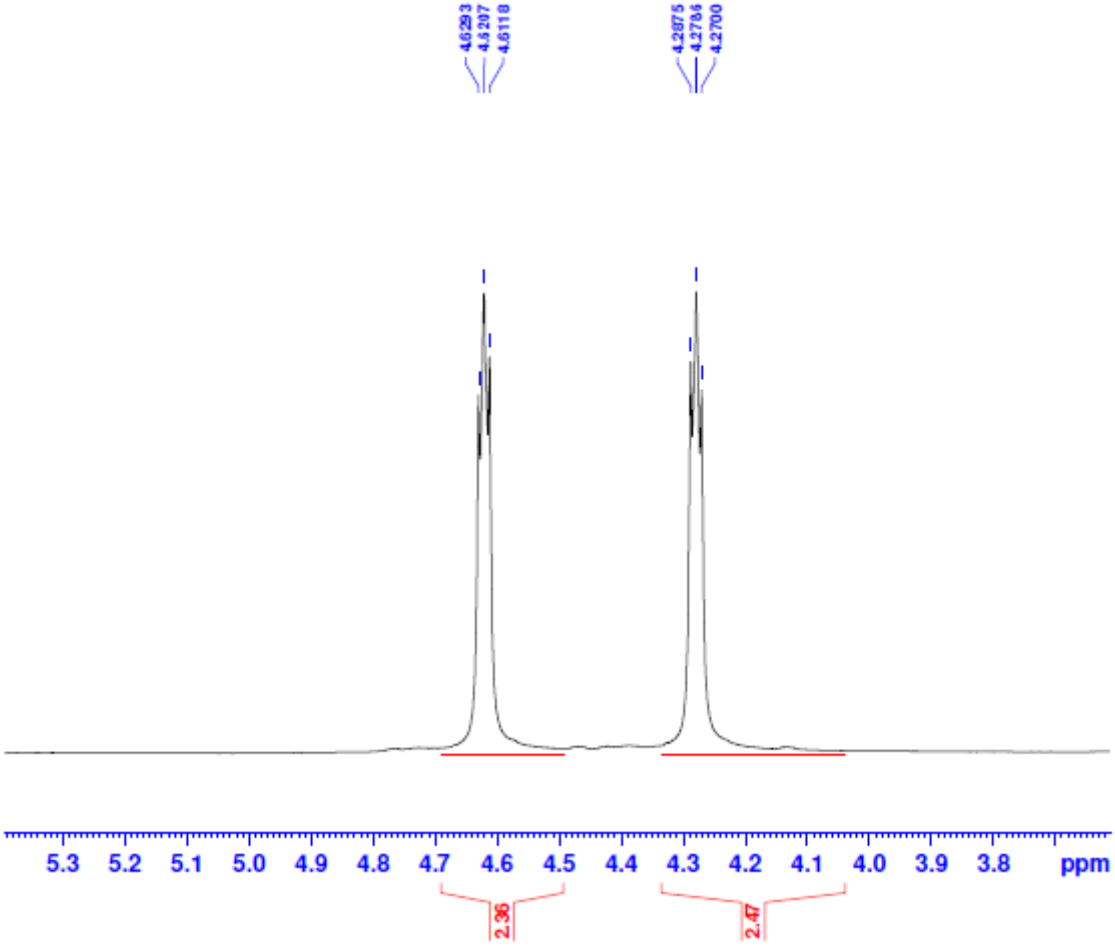
## B1 2-phenoxyethyl 2-nitrobenzoate




$^1$H-NMR spectrum of 2-phenoxyethyl 2-nitrobenzoate

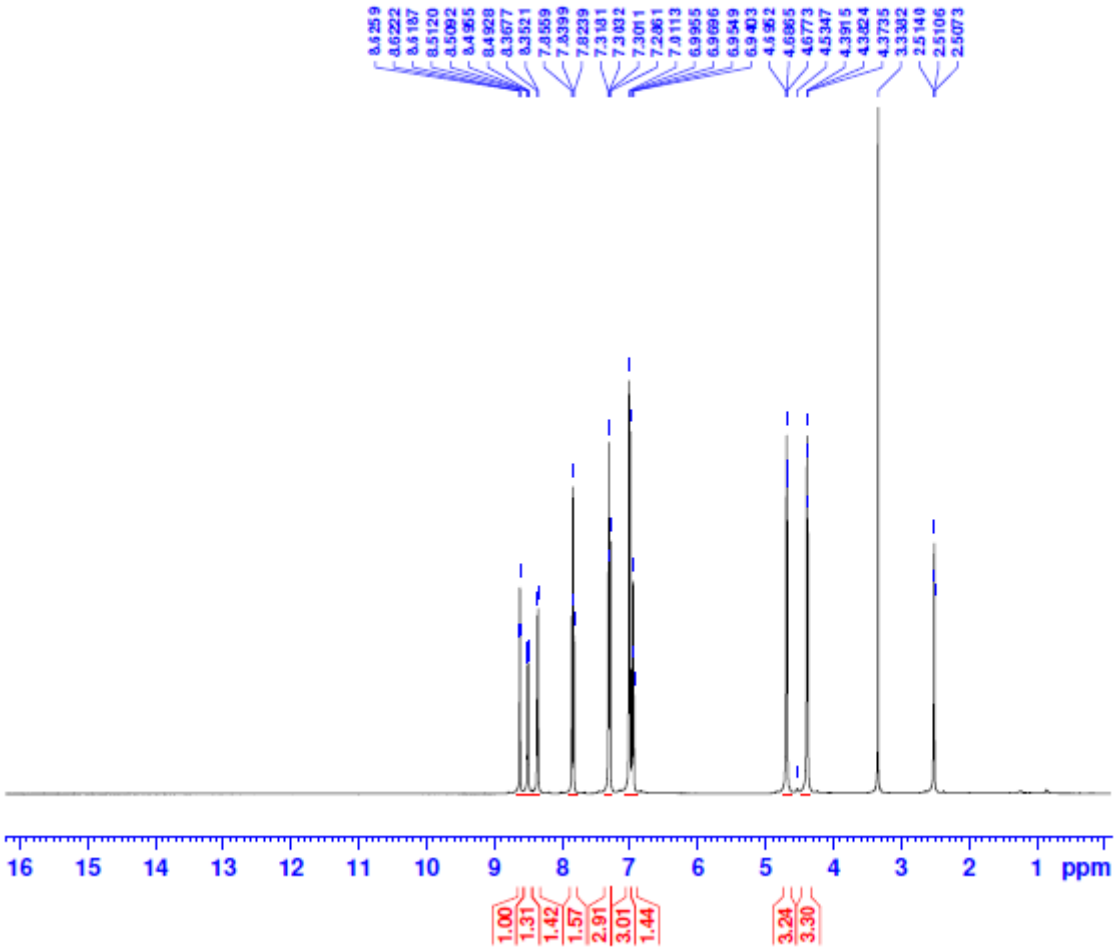



**Expansion of aromatic region of $^{1}$H- NMR spectrum of 2-phenoxyethyl 2-nitrobenzoate**

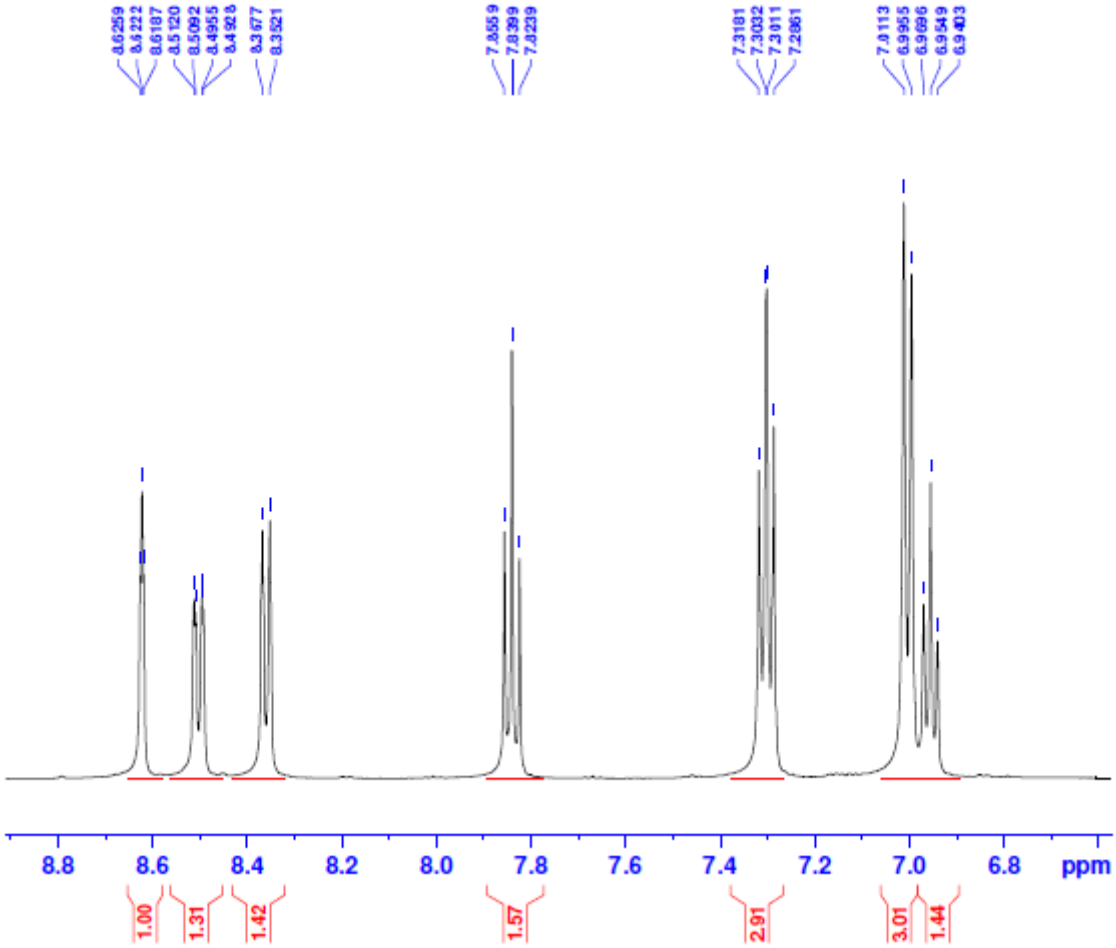



**Expansion of aliphatic region $^{1}$H-NMR spectrum of 2-phenoxyethyl 2-nitrobenzoate**

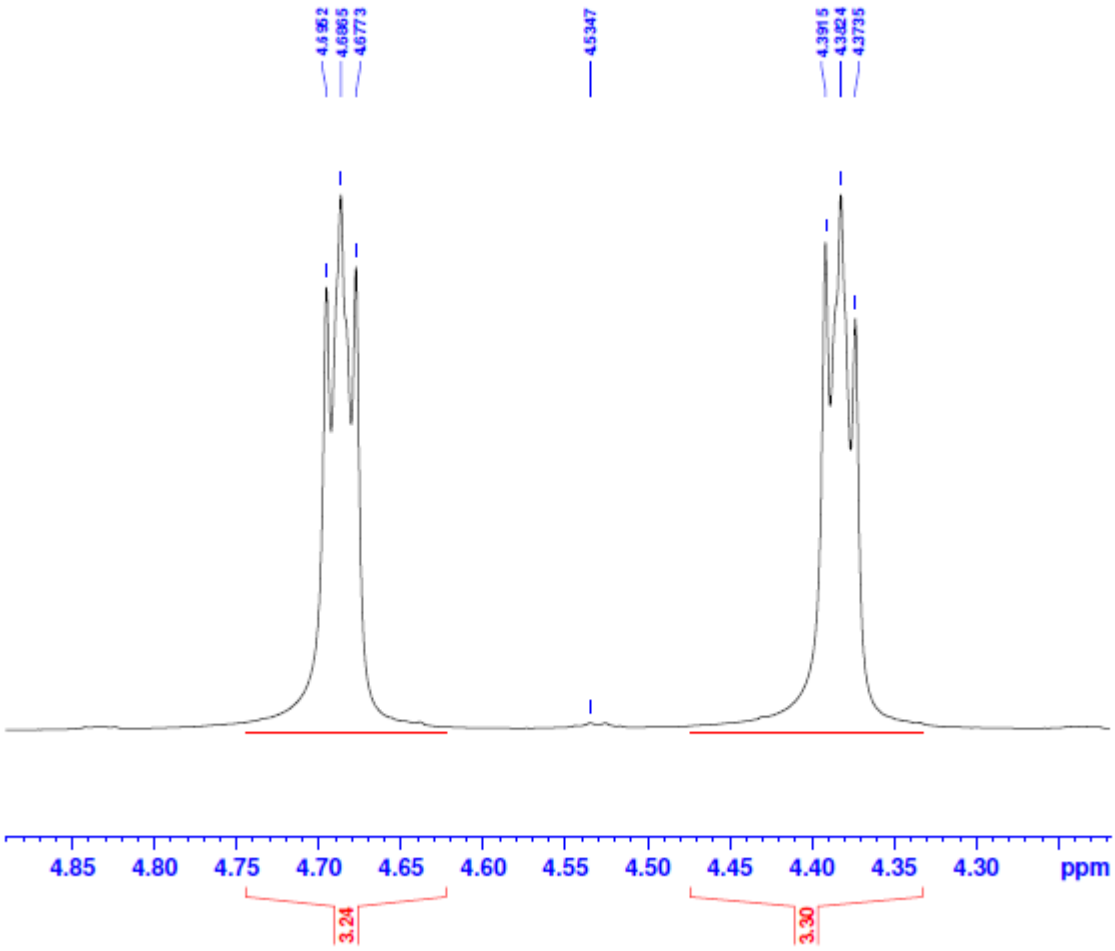
## B2 2-phenoxyethyl 3-nitrobenzoate




**$^{1}$H-NMR spectrum of 2-phenoxyethyl 3-nitrobenzoate**

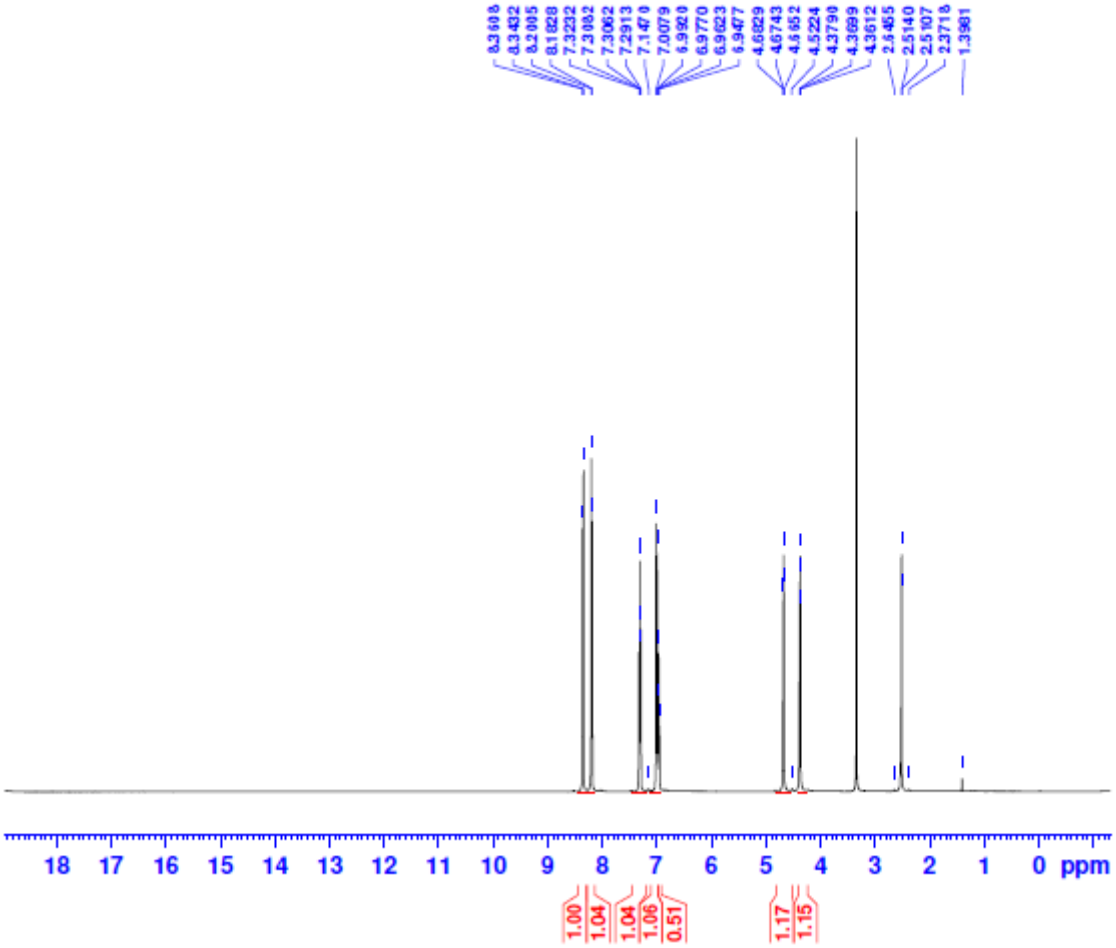



**Expansion of aromatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 3-nitrobenzoate**

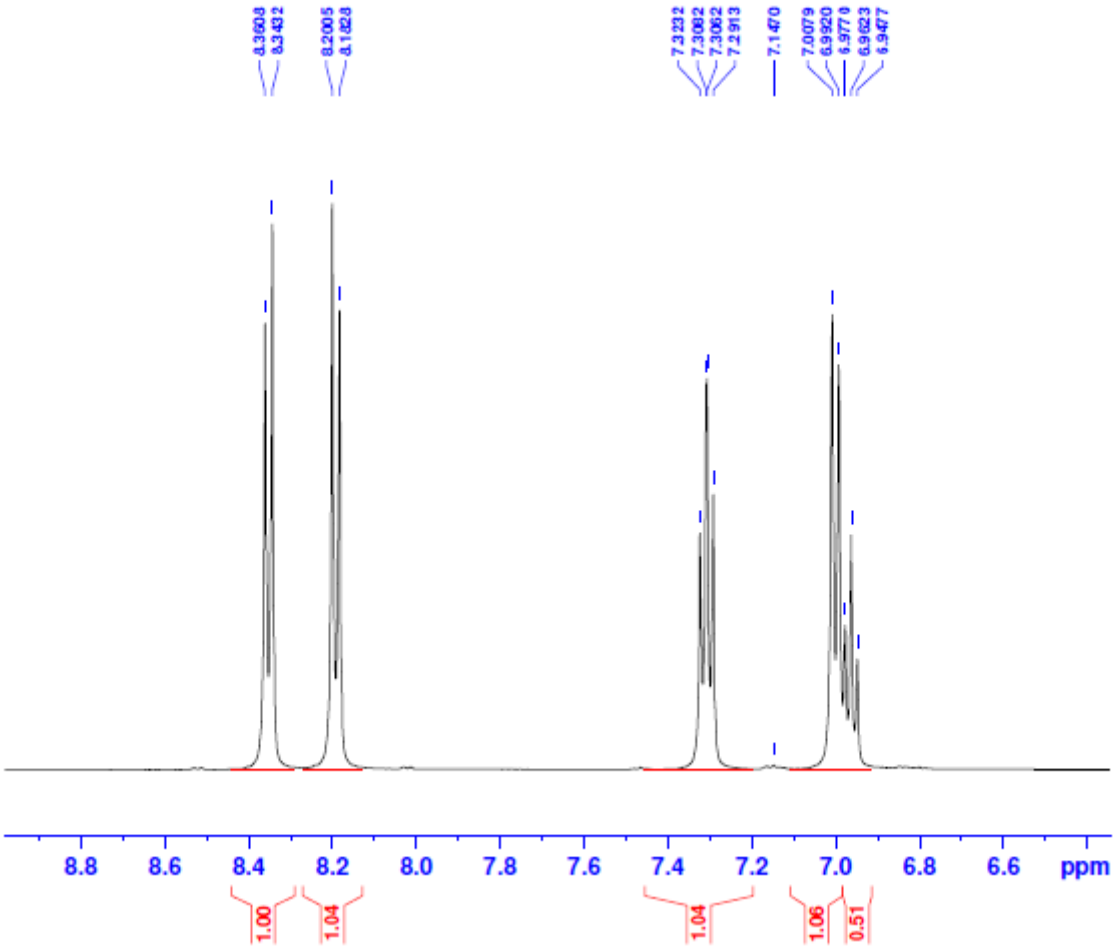



**Expansion of aliphatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 3-nitrobenzoate**

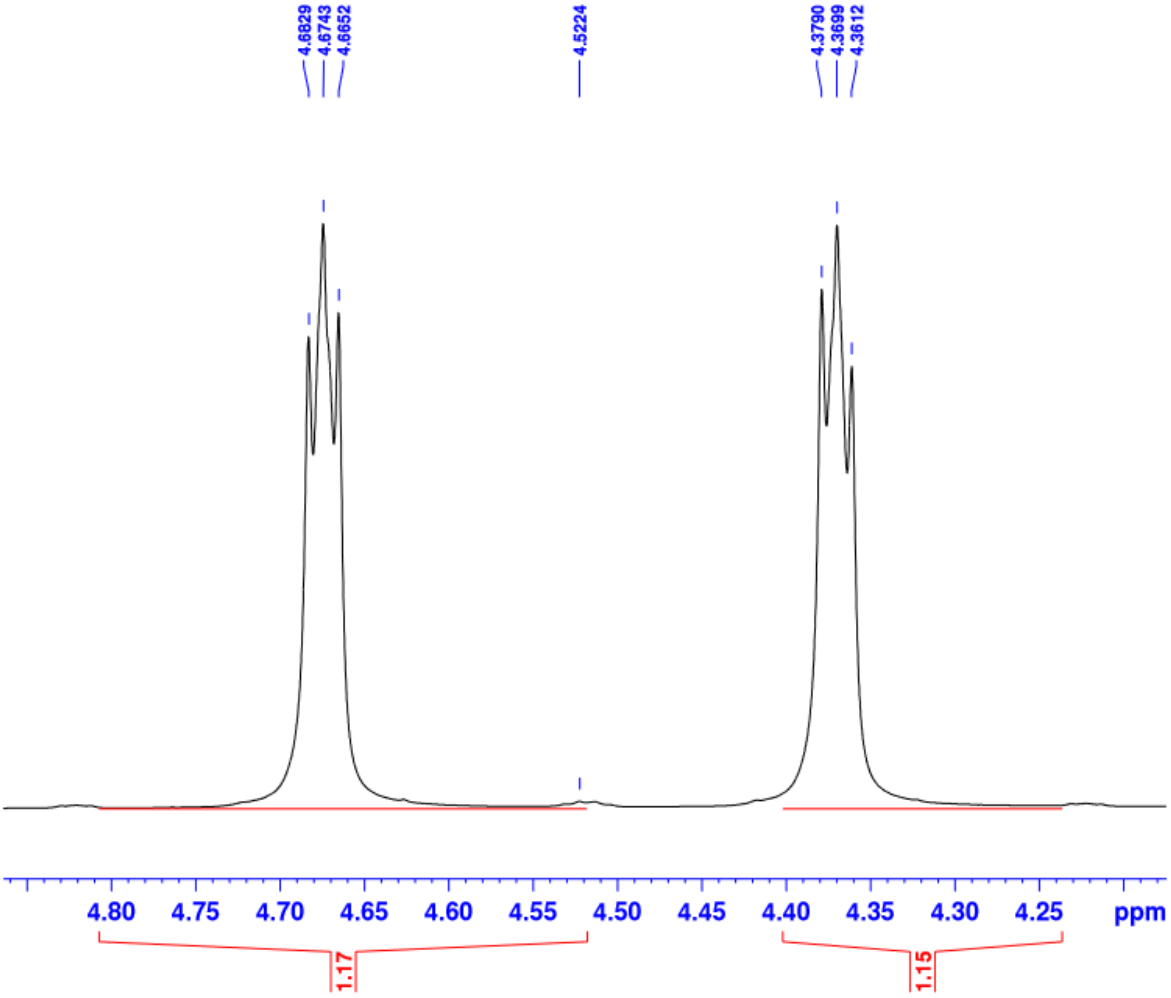
## B3 2-phenoxyethyl 4-nitrobenzoate




**$^{1}$H-NMR spectrum of 2-phenoxyethyl 4-nitrobenzoate**

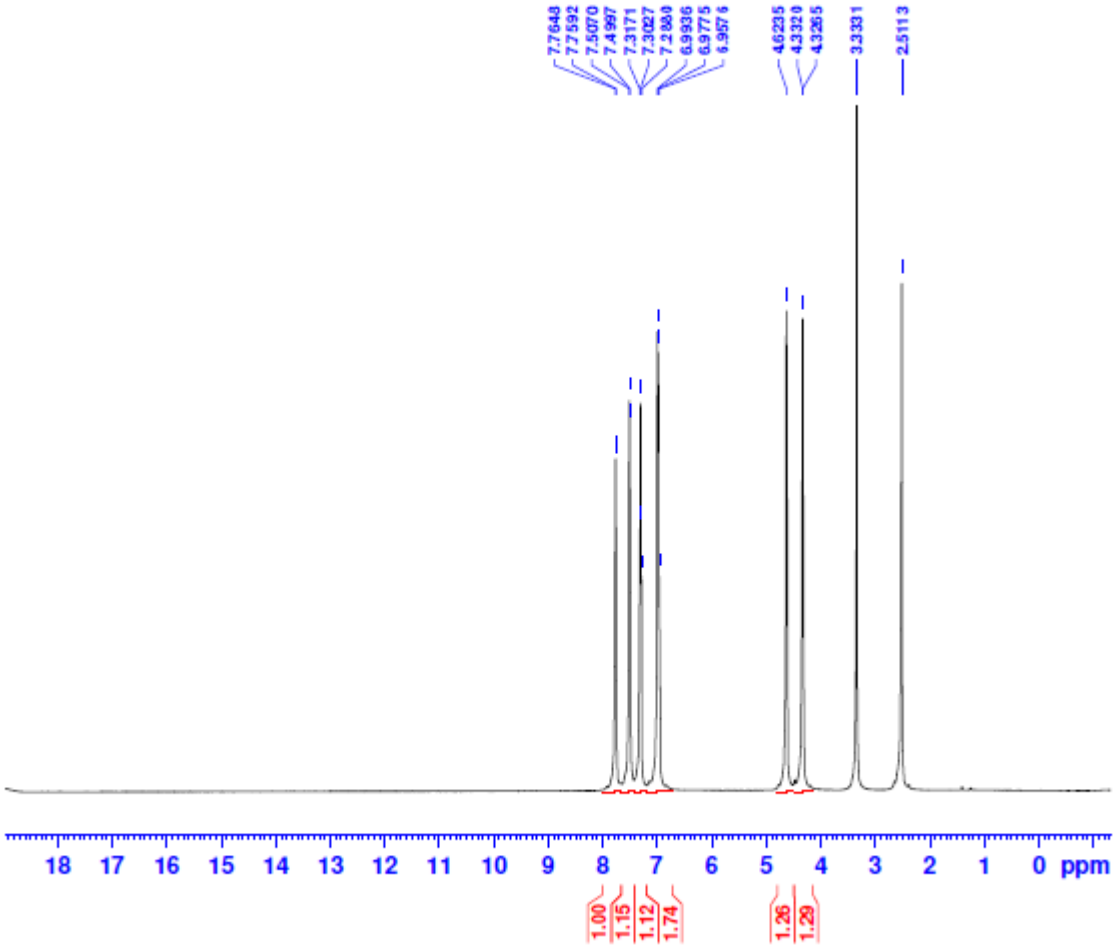



**Expansion of aromatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 4-nitrobenzoate**

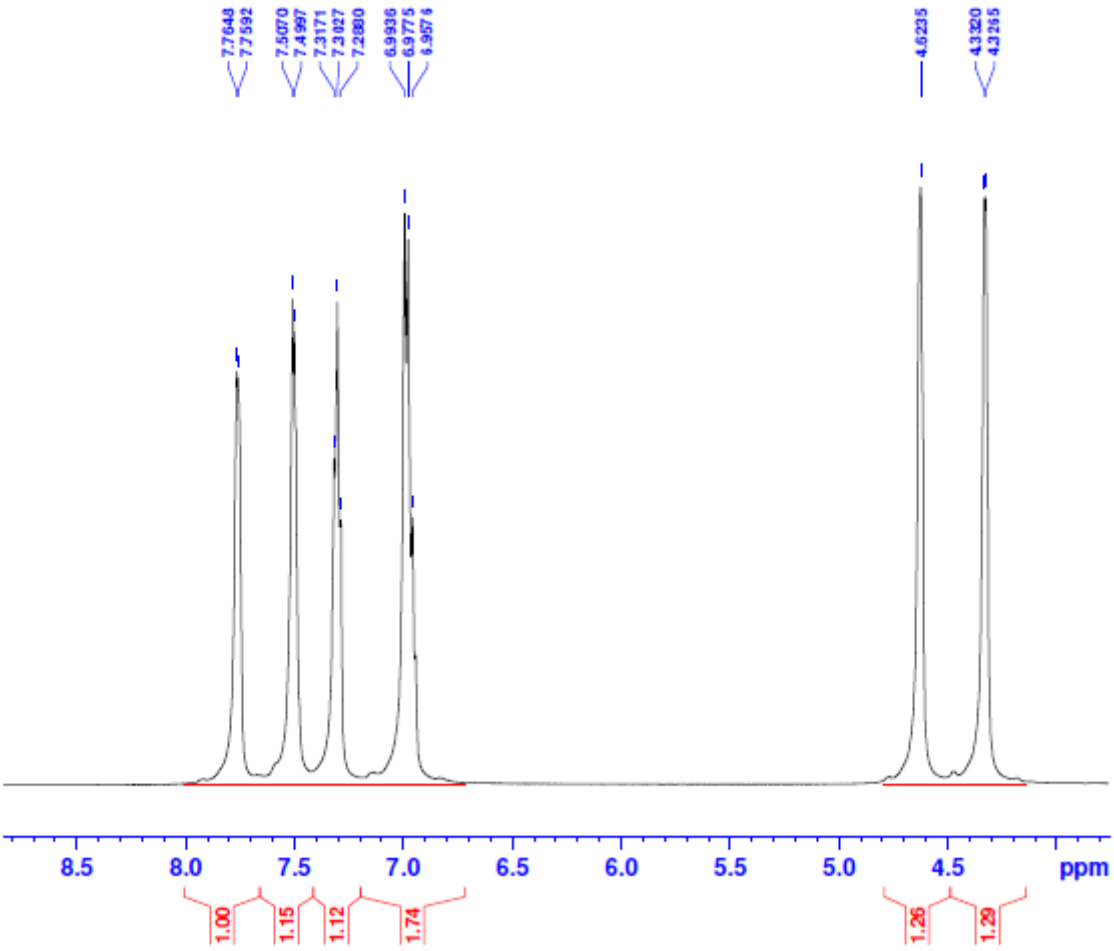



**Expansion of aliphatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 4-nitrobenzoate**

## B4 2-phenoxyethyl 2-bromobenzoate

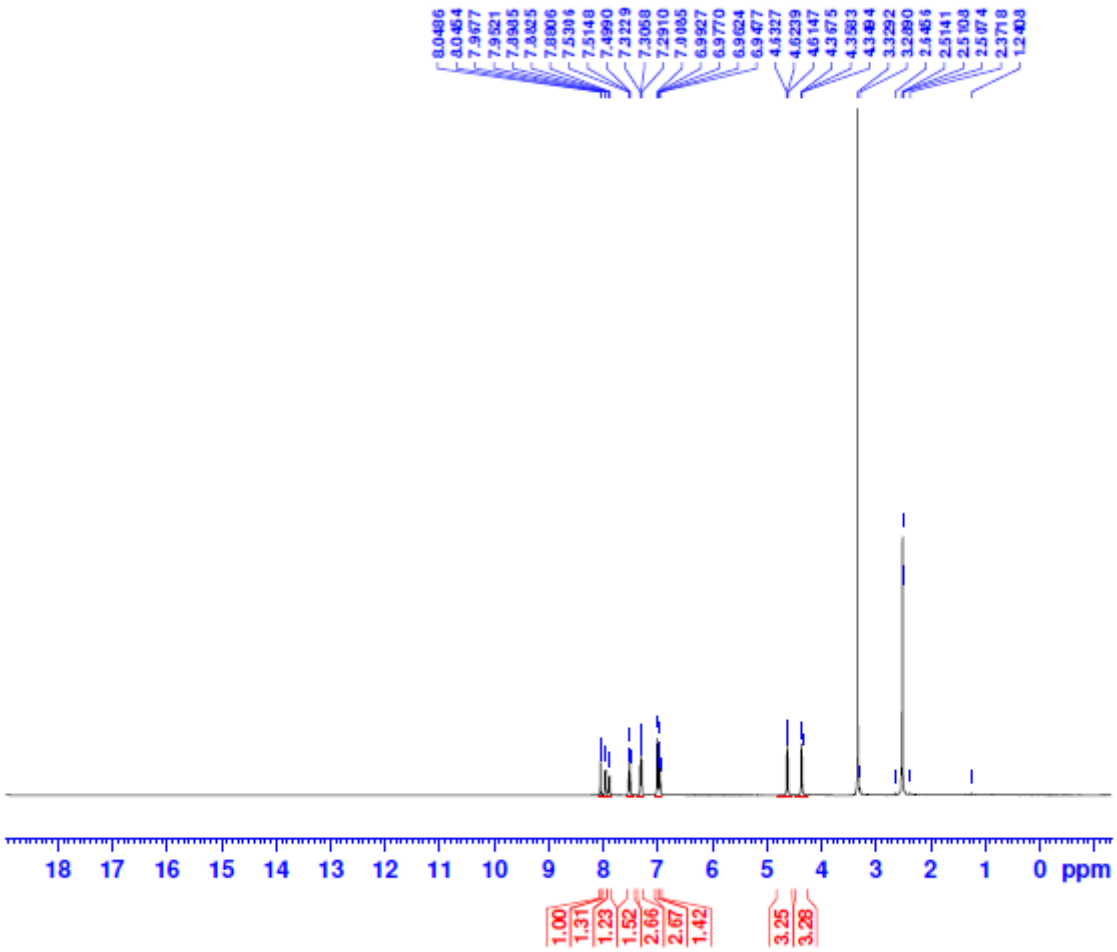



**$^{1}$H-NMR spectrum of 2-phenoxyethyl 2-bromobenzoate**

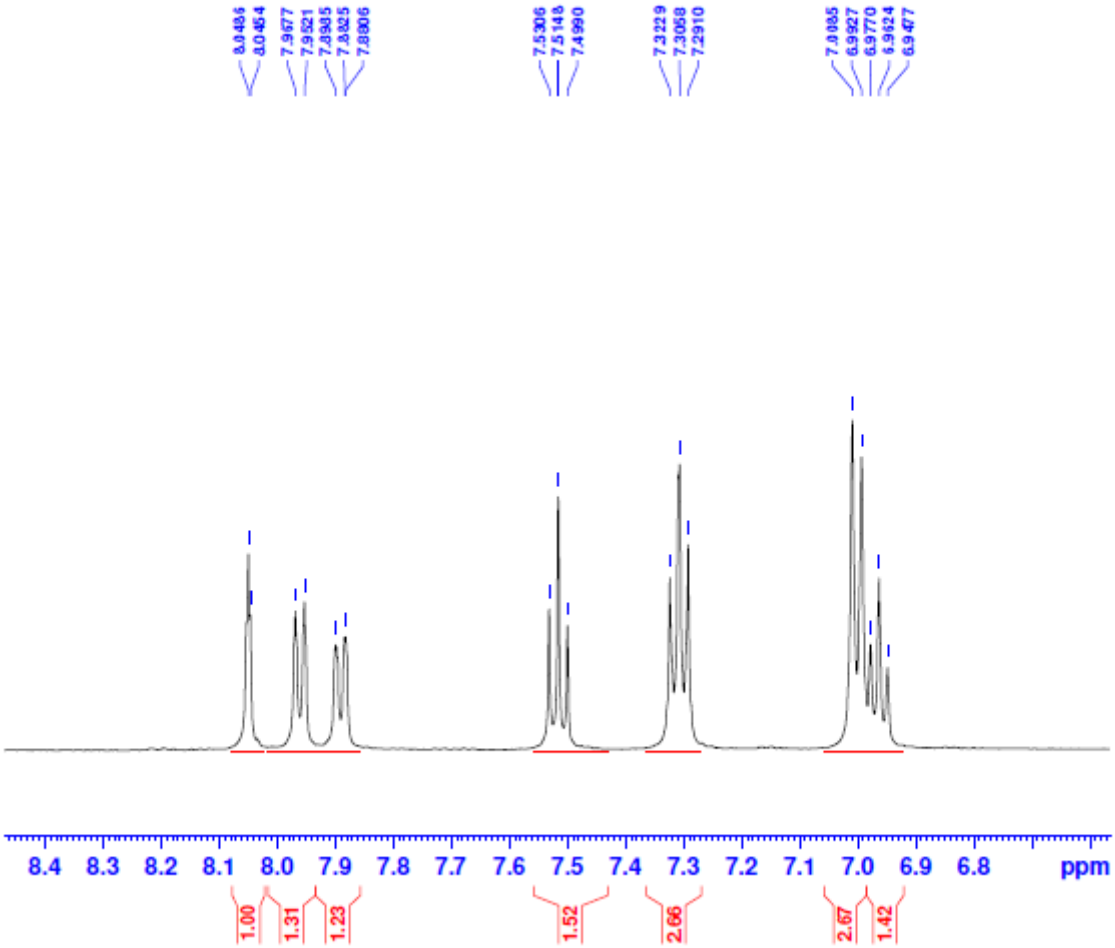



**Expansion of aromatic and aliphatic regions of $^{1}$H- NMR spectrum of 2-phenoxyethyl 2-bromobenzoate**

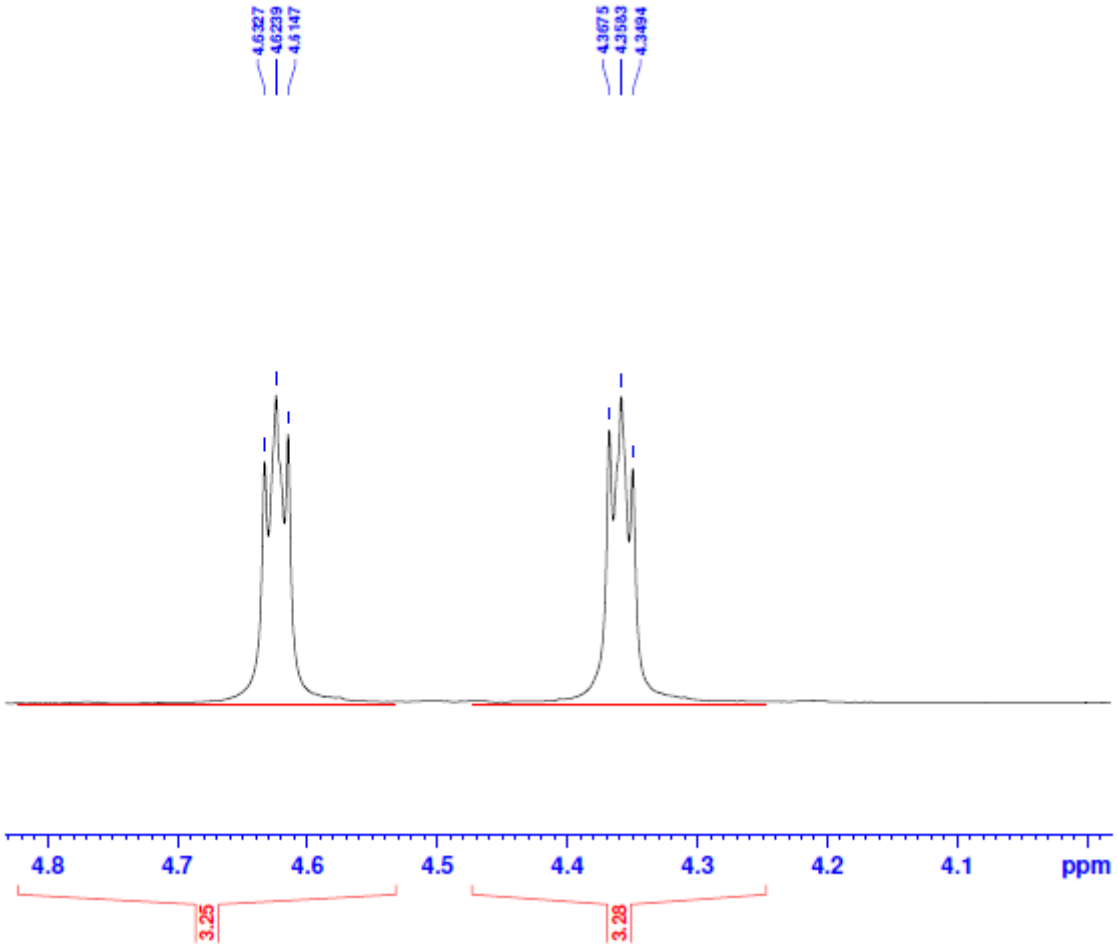
## B5 2-phenoxyethyl 3-bromobenzoate




**$^{1}$H-NMR spectrum of 2-phenoxyethyl 3-bromobenzoate**

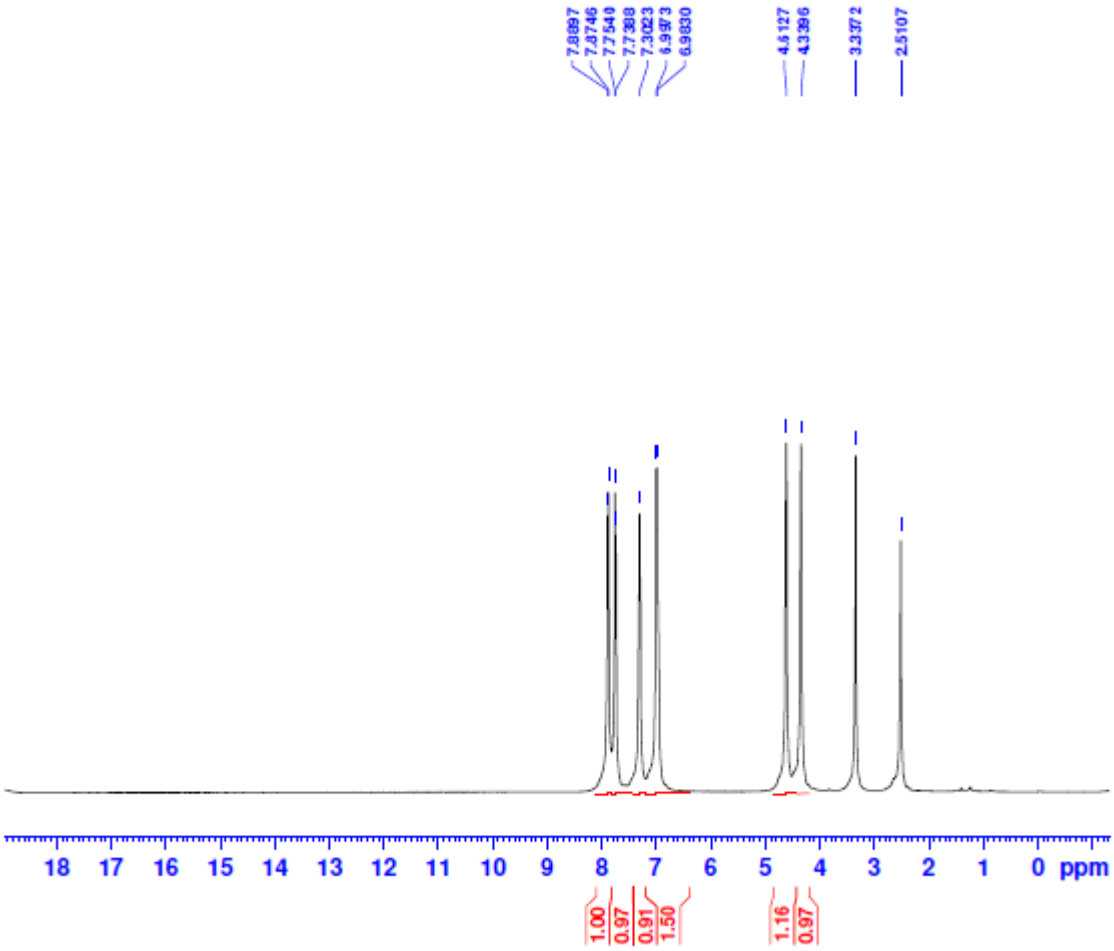



**Expansion of aromatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 3-bromobenzoate**

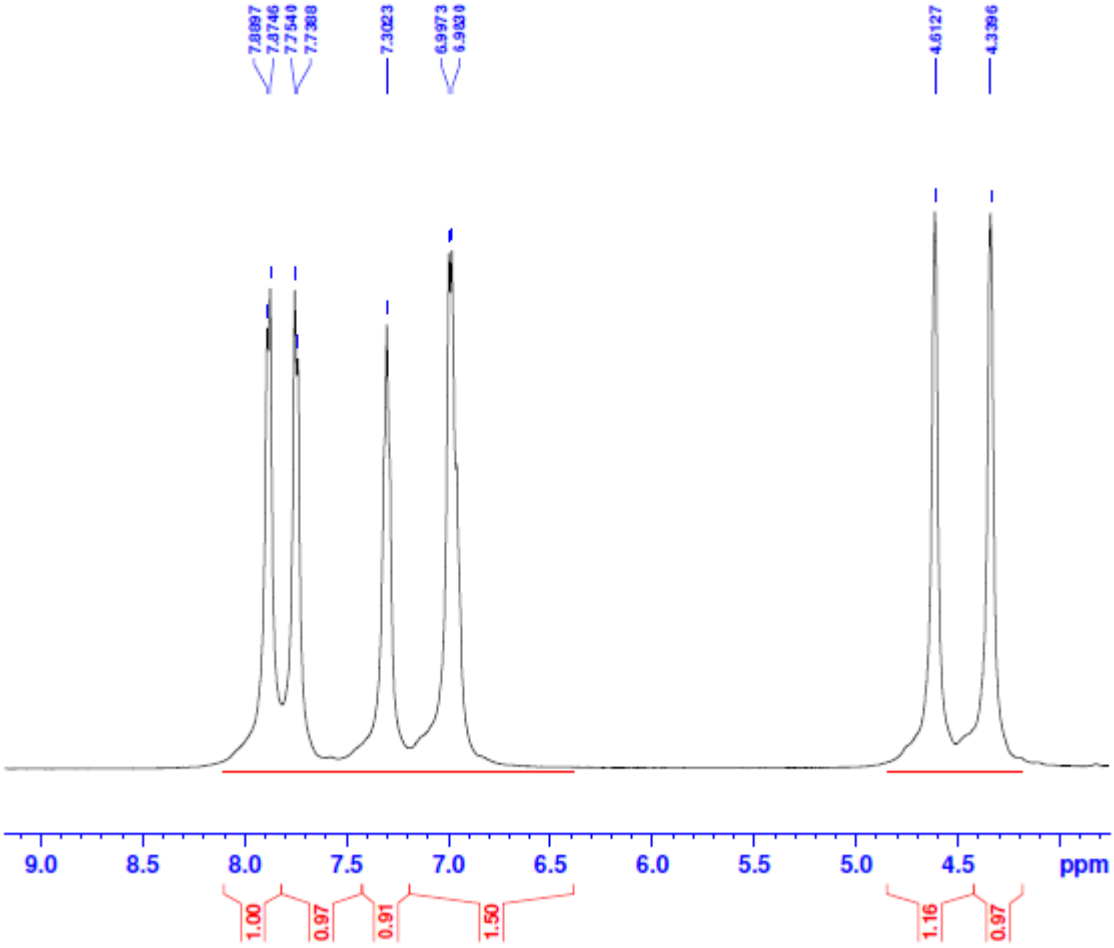



**Expansion of aliphatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 3-bromobenzoate**

**B62-phenoxyethyl 4-bromobenzoate**

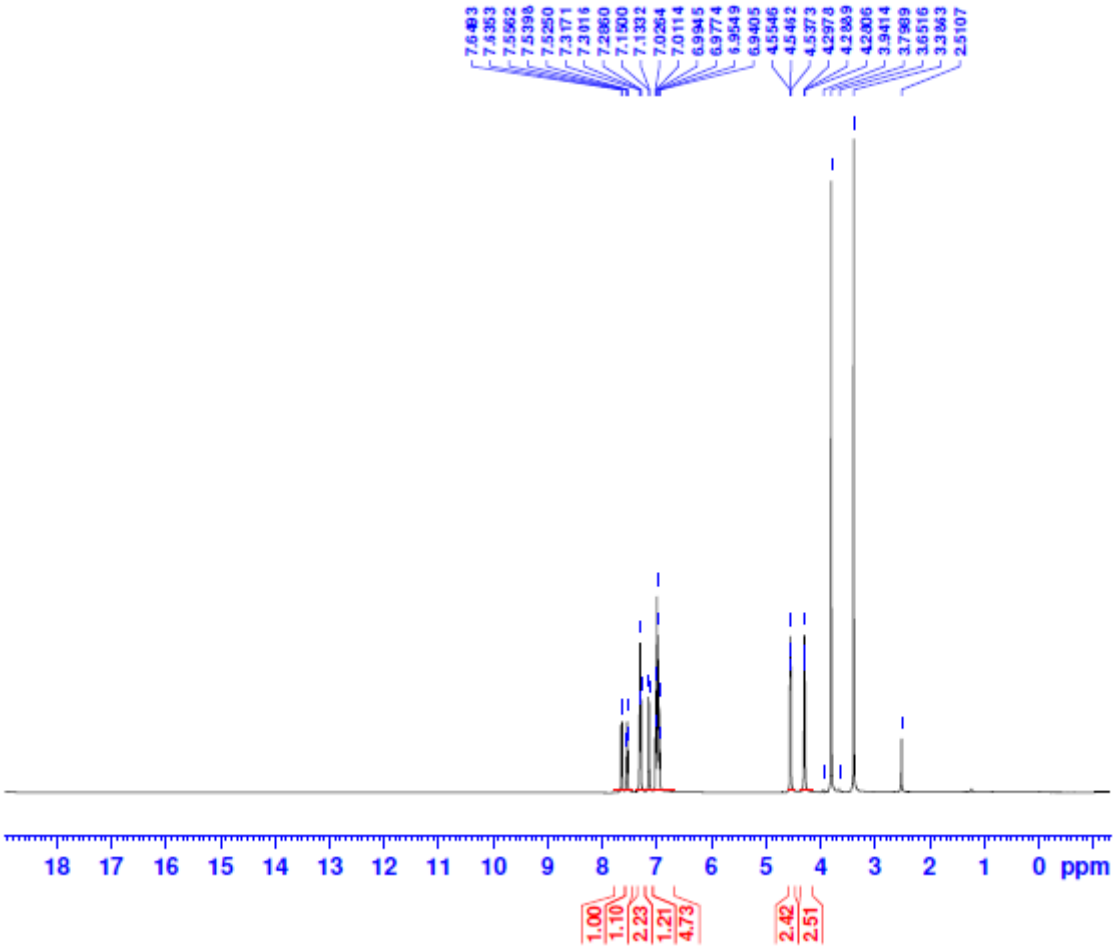



**$^{1}$H-NMR spectrum of 2-phenoxyethyl 4-bromobenzoate**

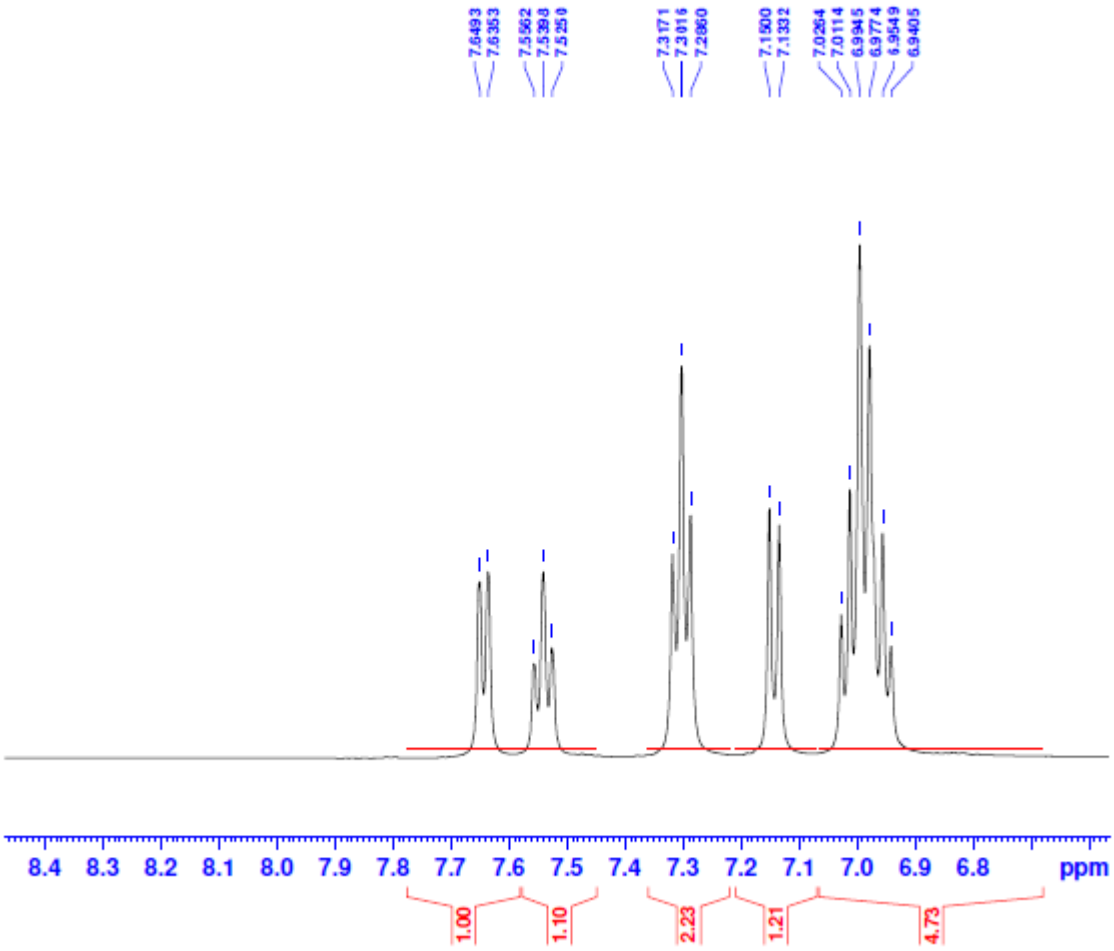



**Expansion of aromatic and aliphatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 4-bromobenzoate**

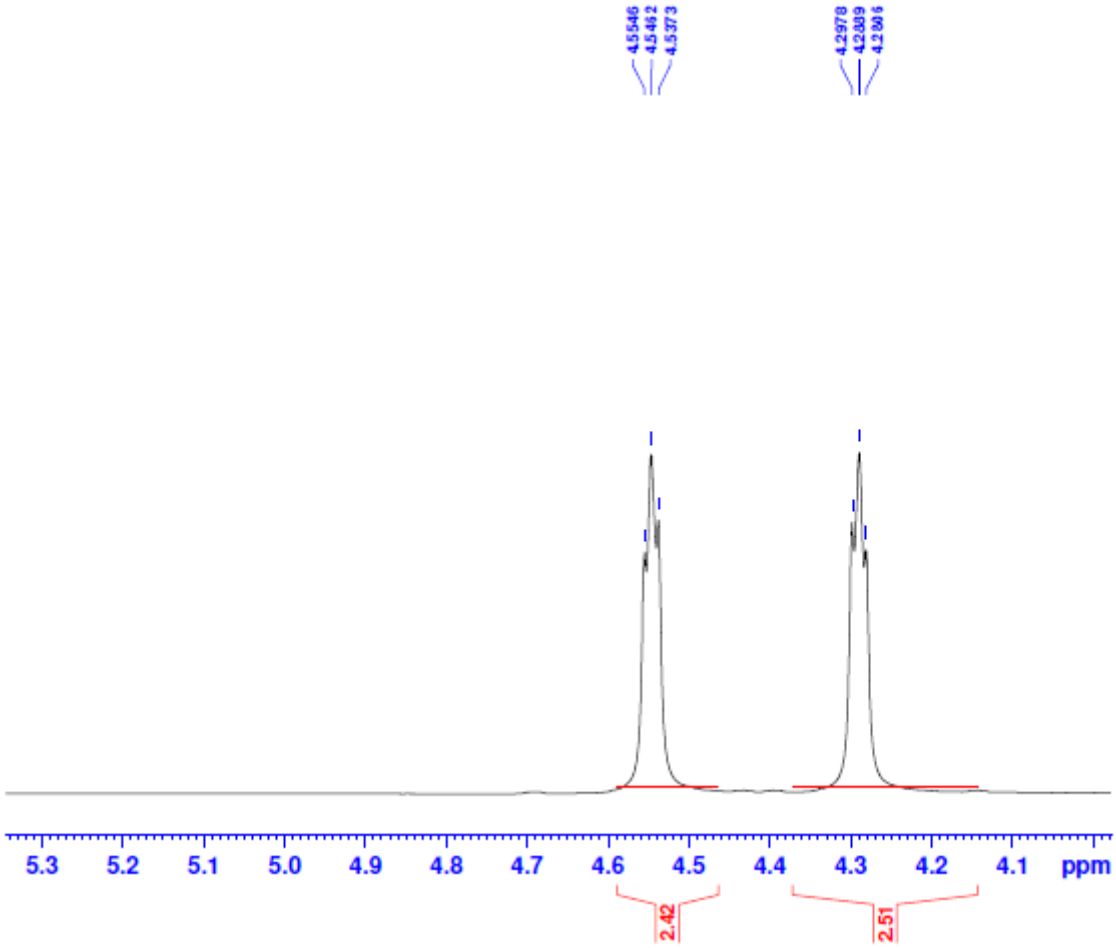
## B7 2-phenoxyethyl 2-methoxybenzoate




**[1]H-NMR spectrum of 2-phenoxyethyl 2-methoxybenzoate**

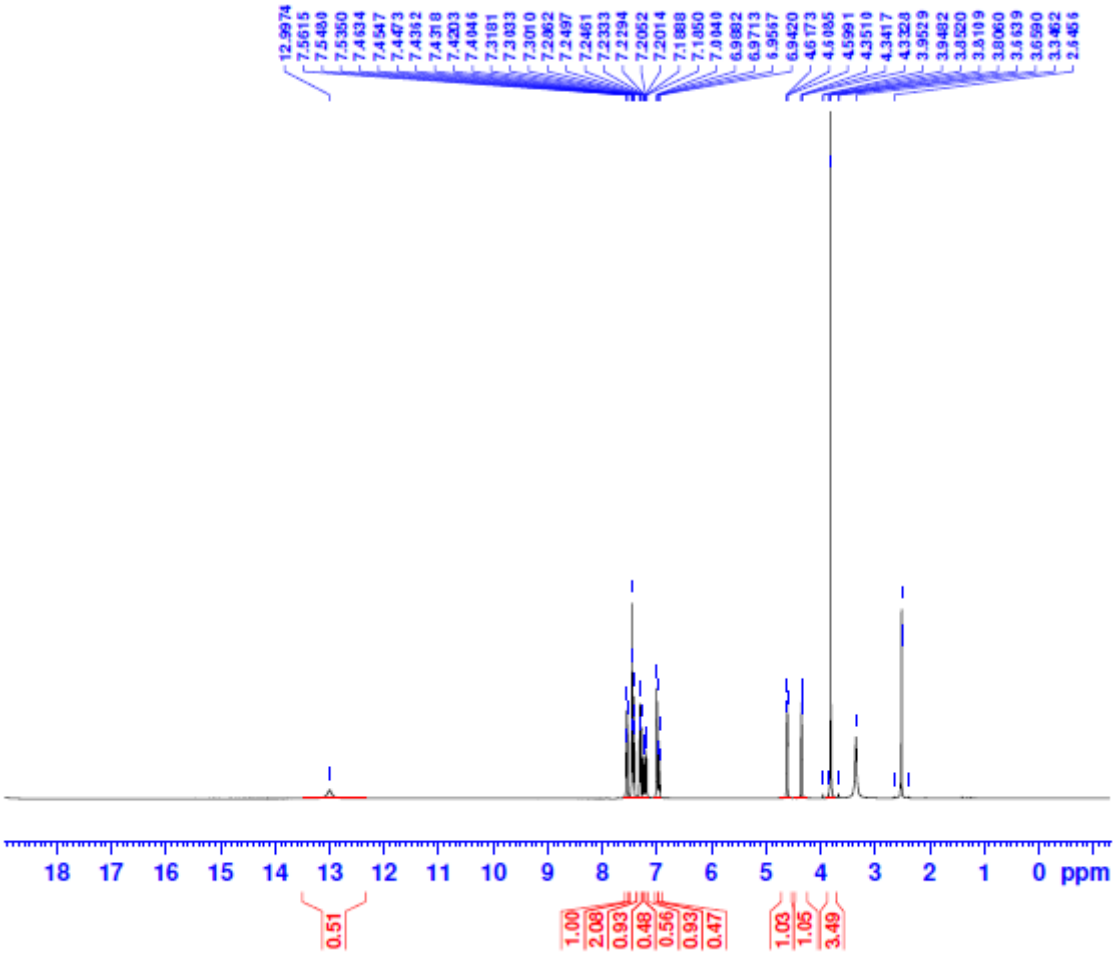



**Expansion of aromatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 2-methoxybenzoate**

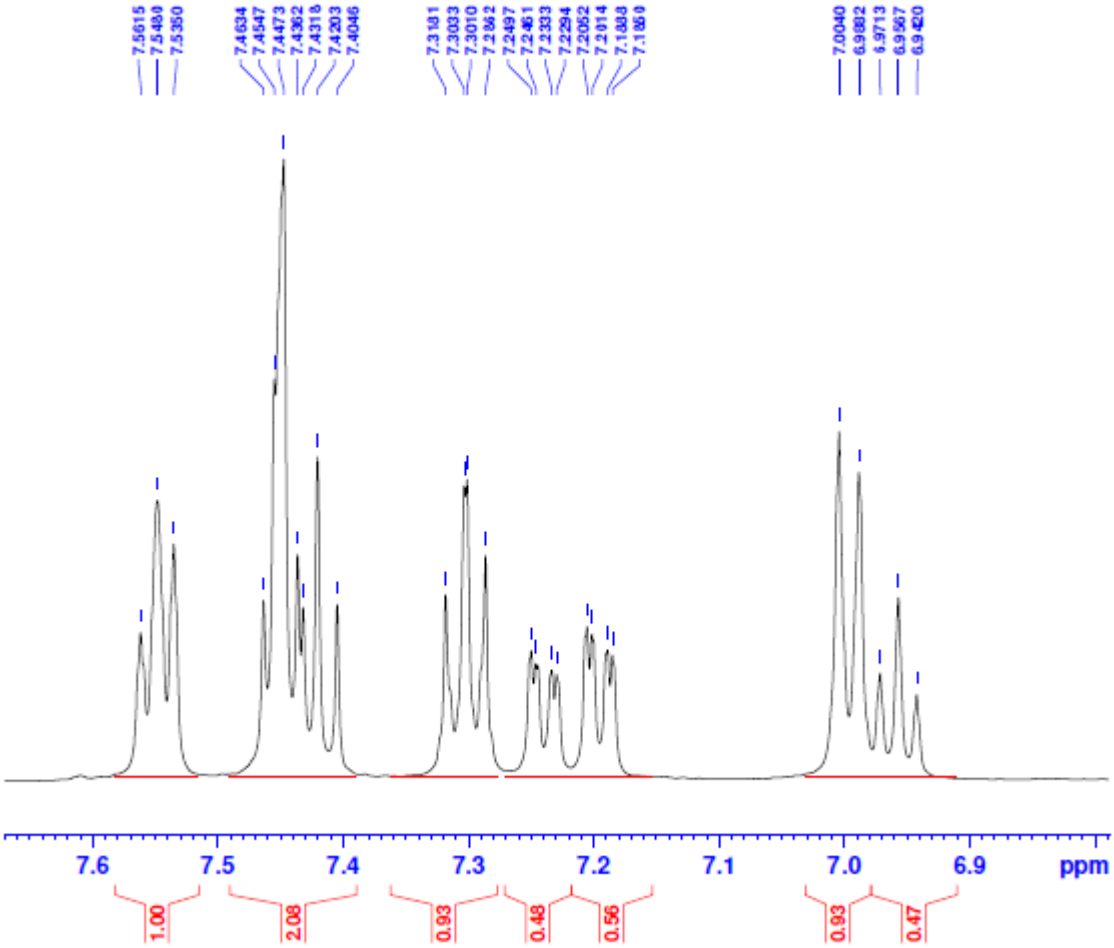



**Expansion of aliphatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 2-methoxybenzoate**

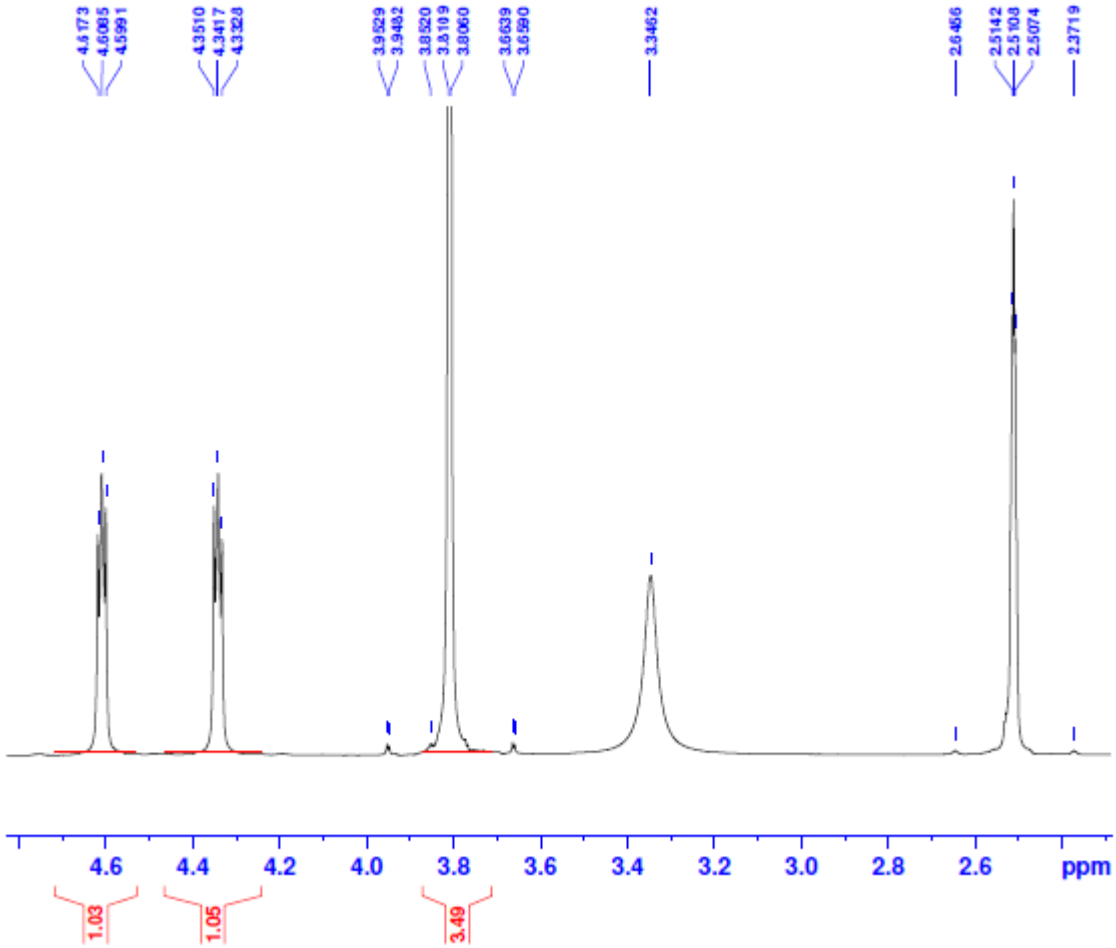
## B8 2-phenoxyethyl 3-methoxybenzoate




**[1]H-NMR spectrum of 2-phenoxyethyl 3-methoxybenzoate**

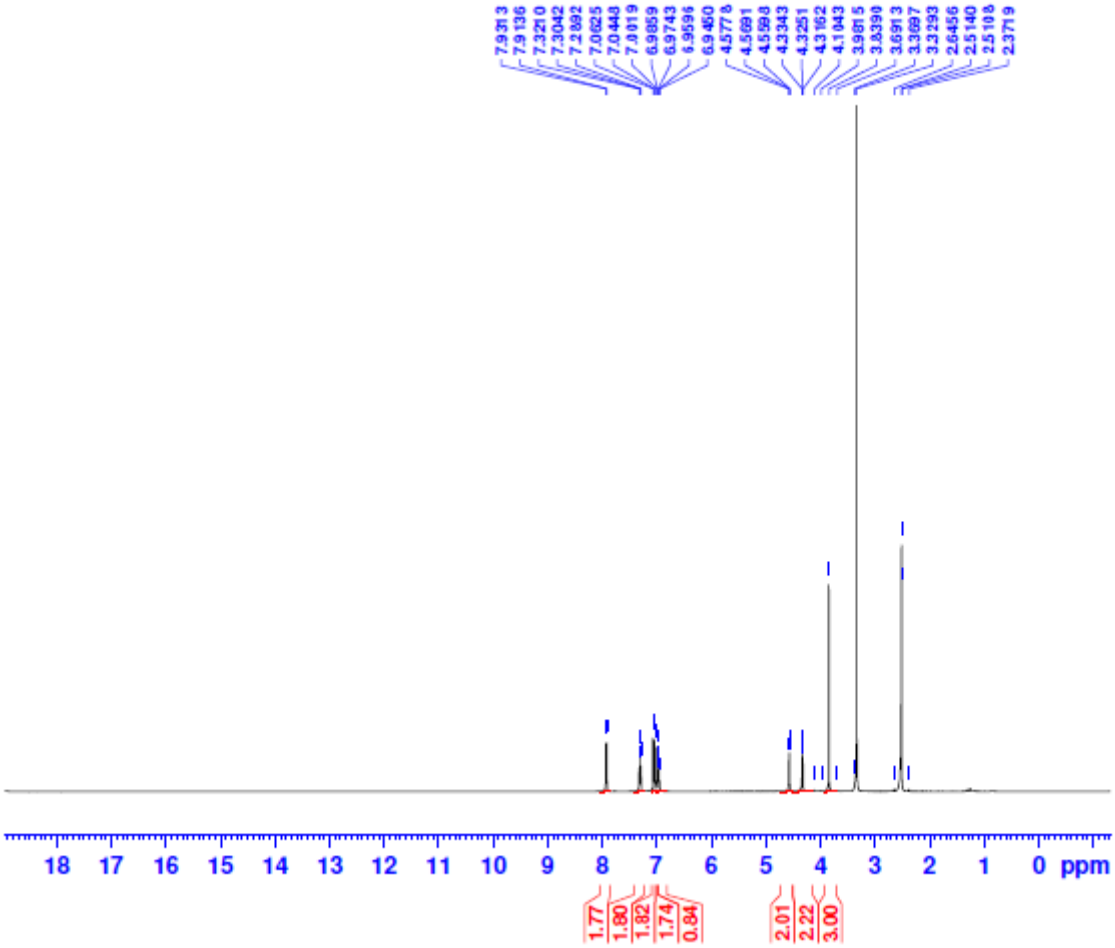



**Expansion of aromatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 3-methoxybenzoate**

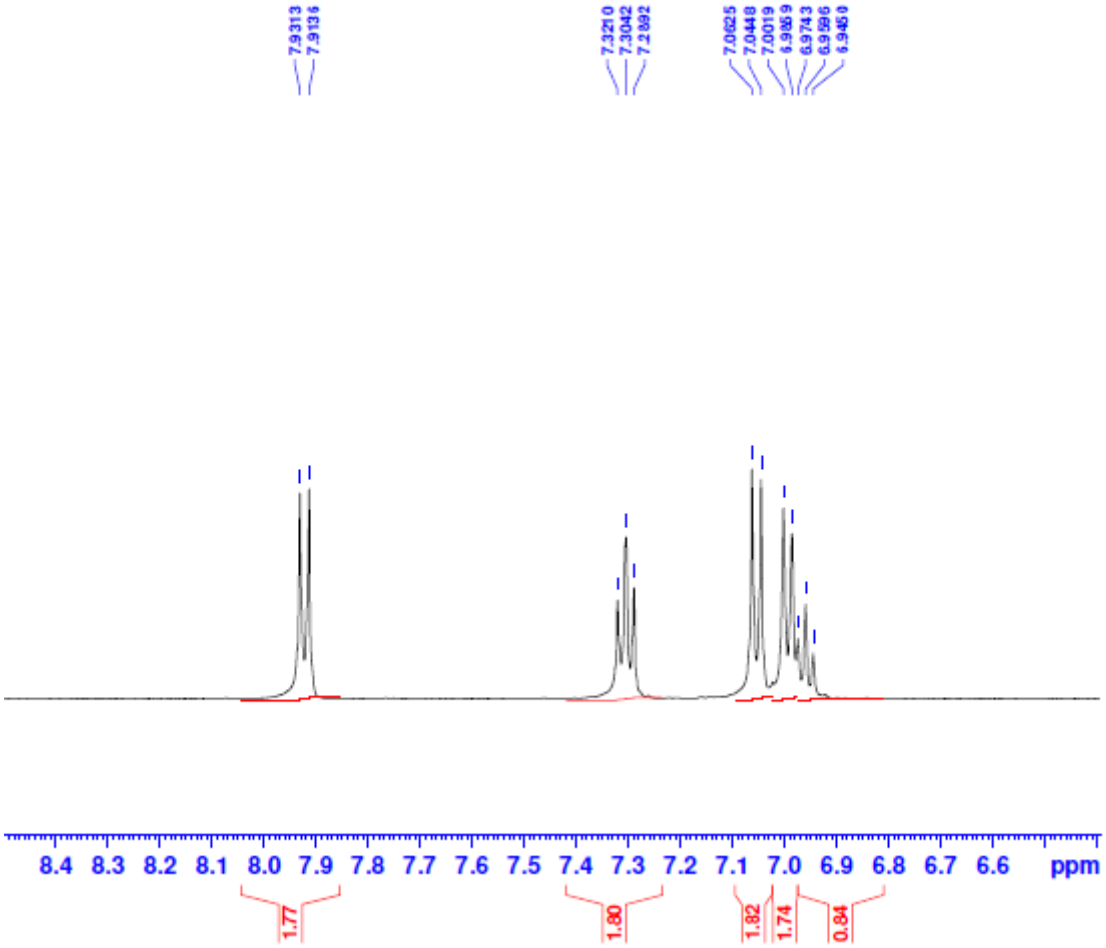



**Expansion of aliphatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 3-methoxybenzoate**

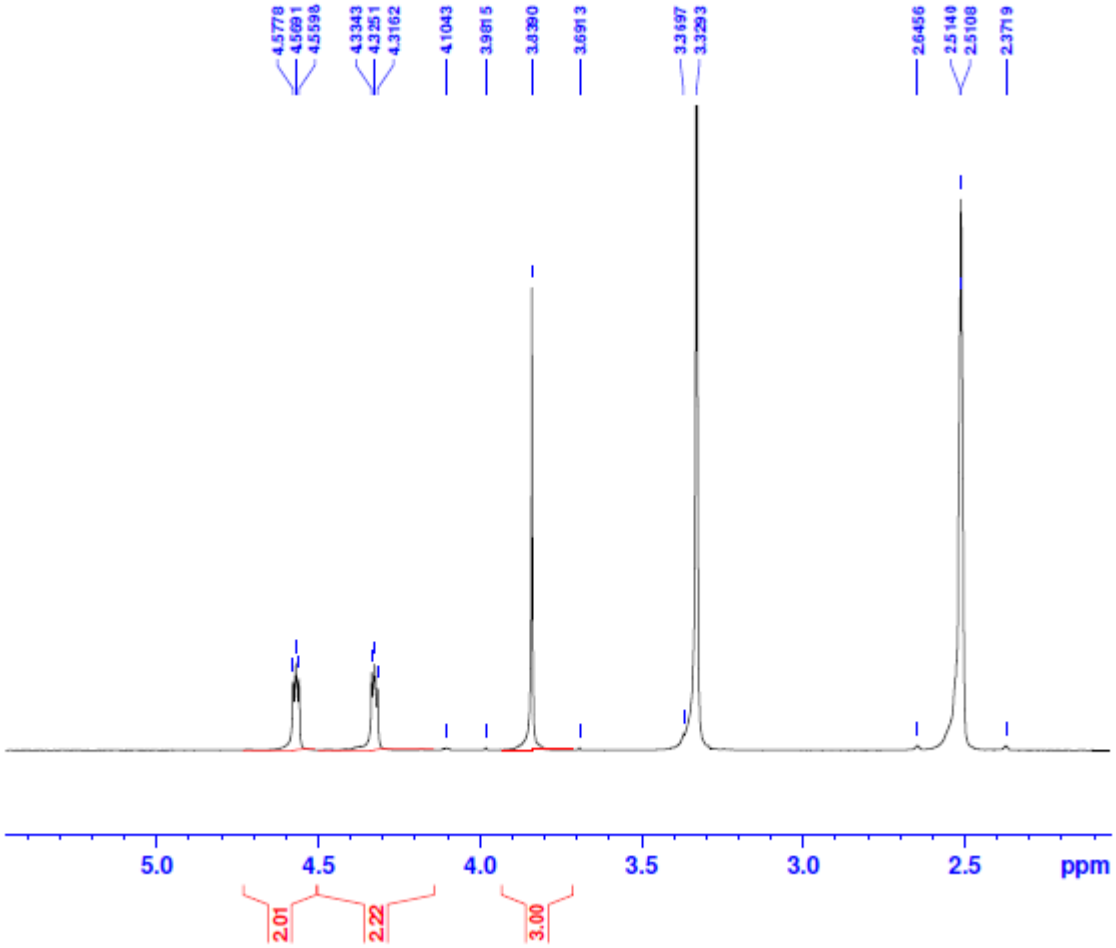
## B9 2-phenoxyethyl 4-methoxybenzoate




**$^{1}$H-NMR spectrum of 2-phenoxyethyl 4-methoxybenzoate**

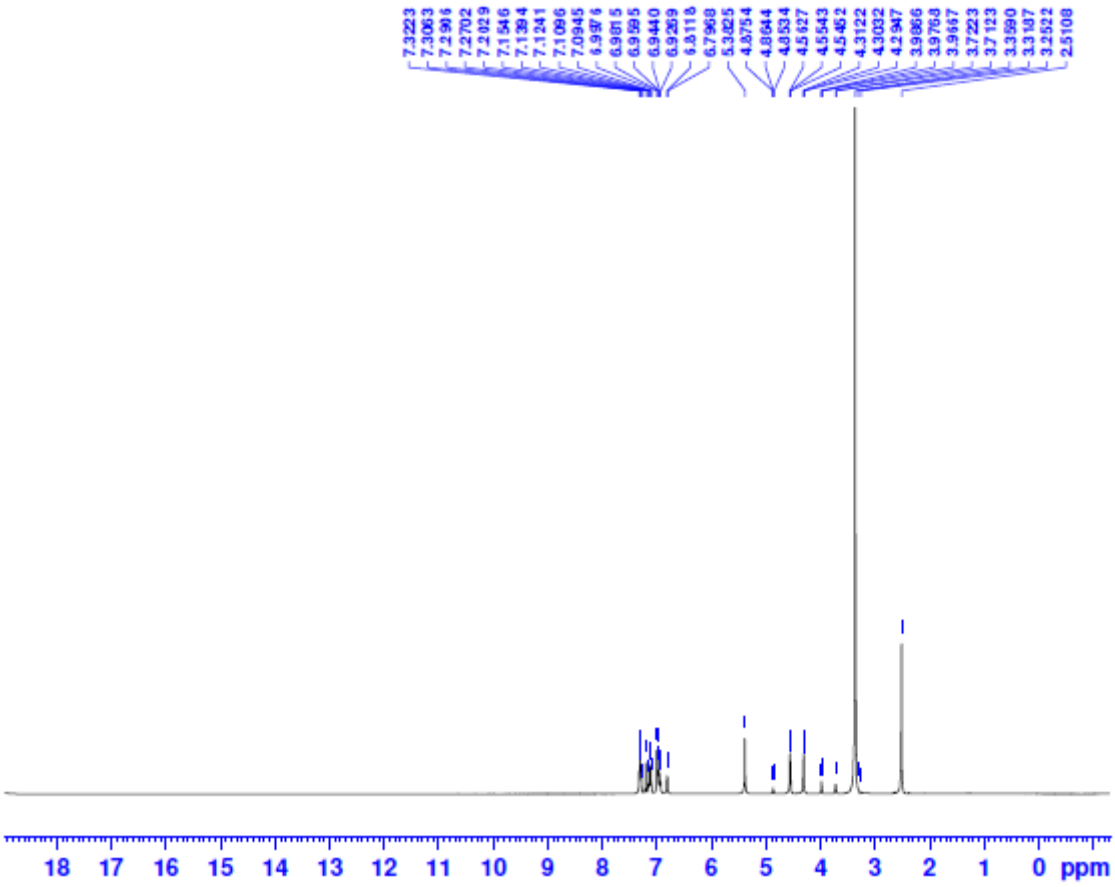



**Expansion of aromatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 4-methoxybenzoate**

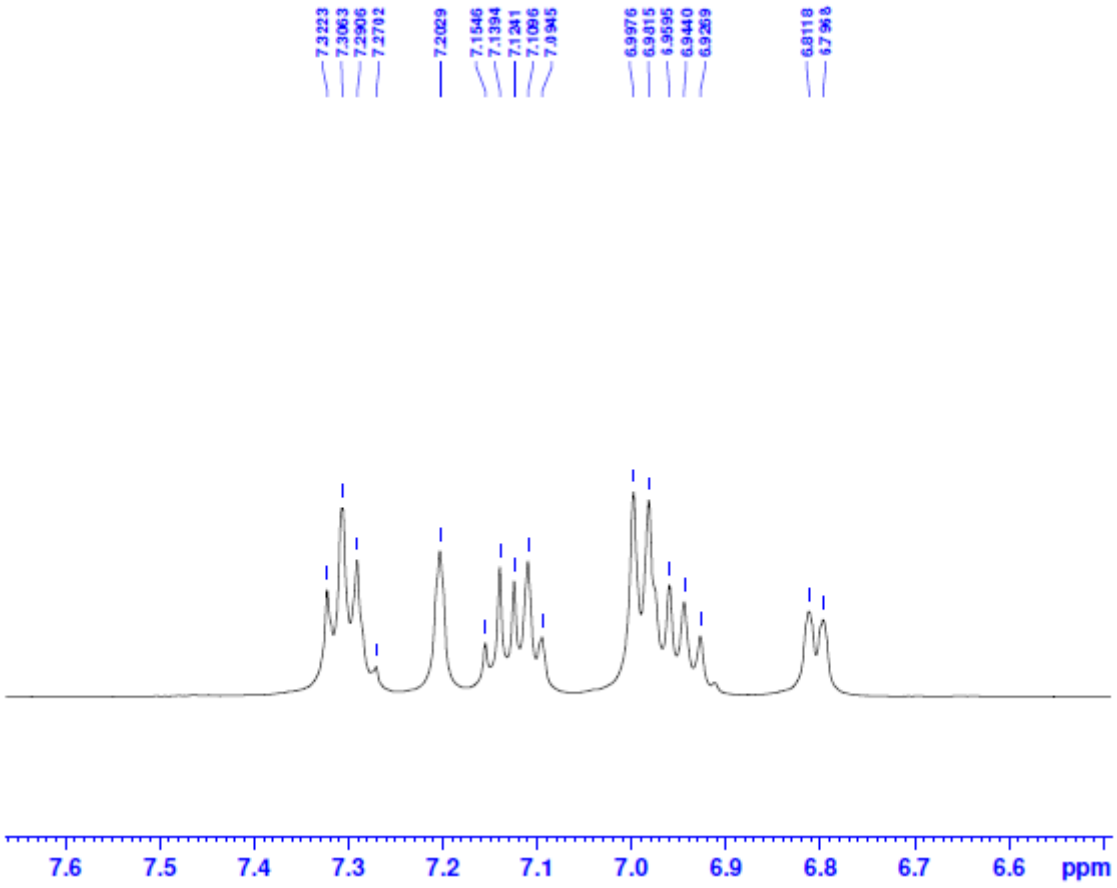



**Expansion of aliphatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 4-methoxybenzoate**

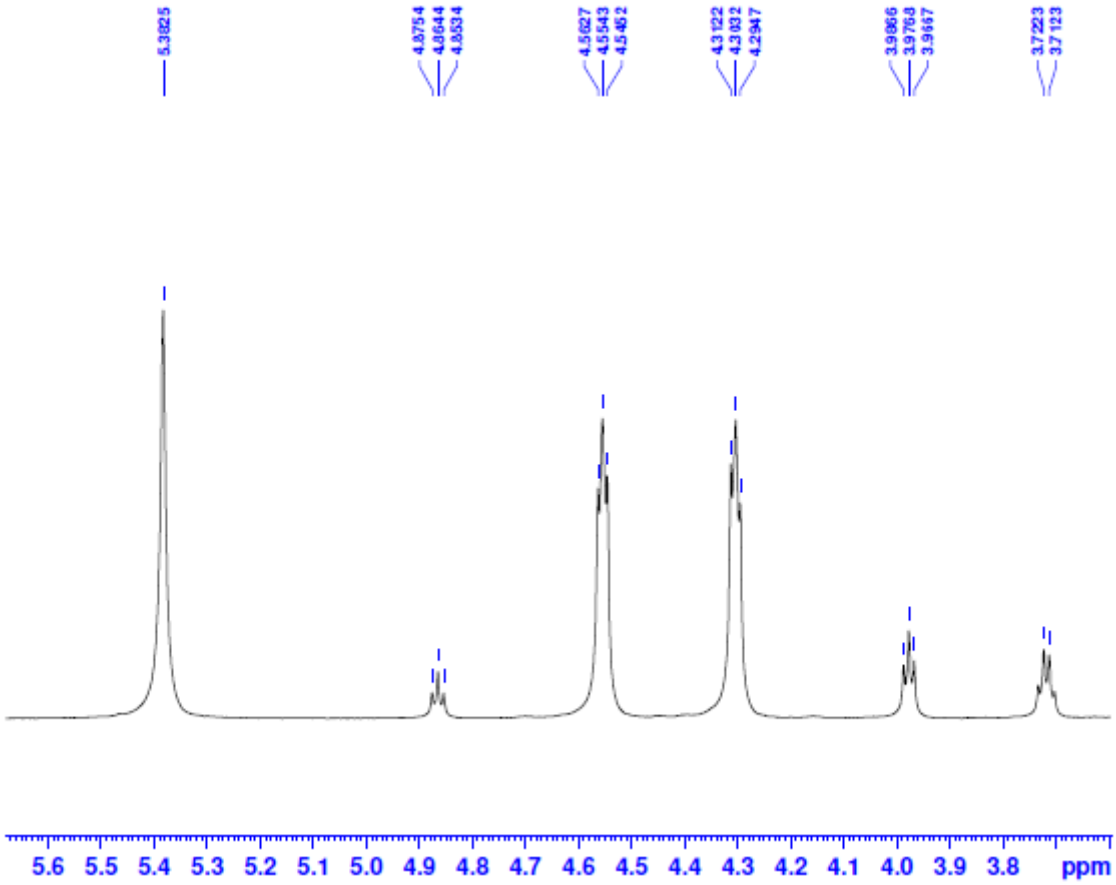
## B10 2-phenoxyethyl 3-aminobenzoate




**$^{1}$H-NMR spectrum of 2-phenoxyethyl 3-aminobenzoate**

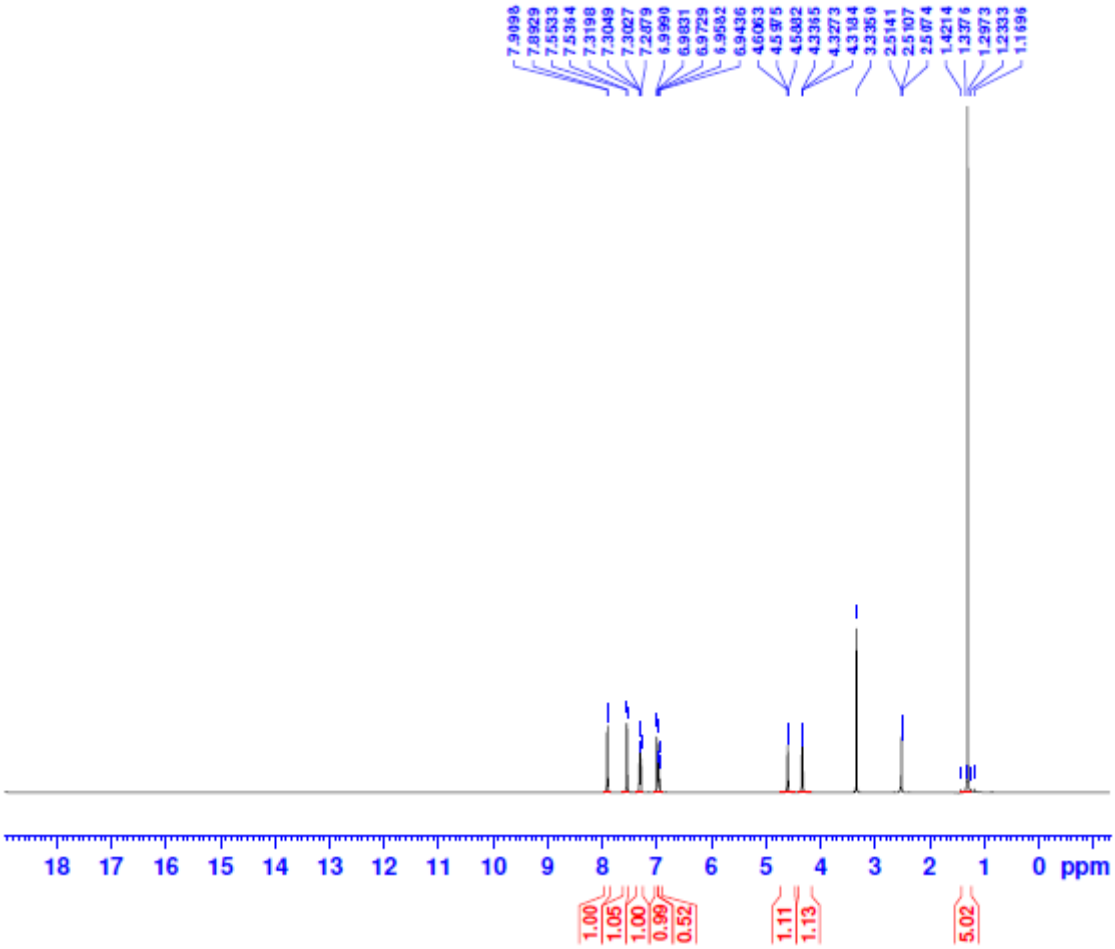



**Expansion of aromatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 3-aminobenzoate**

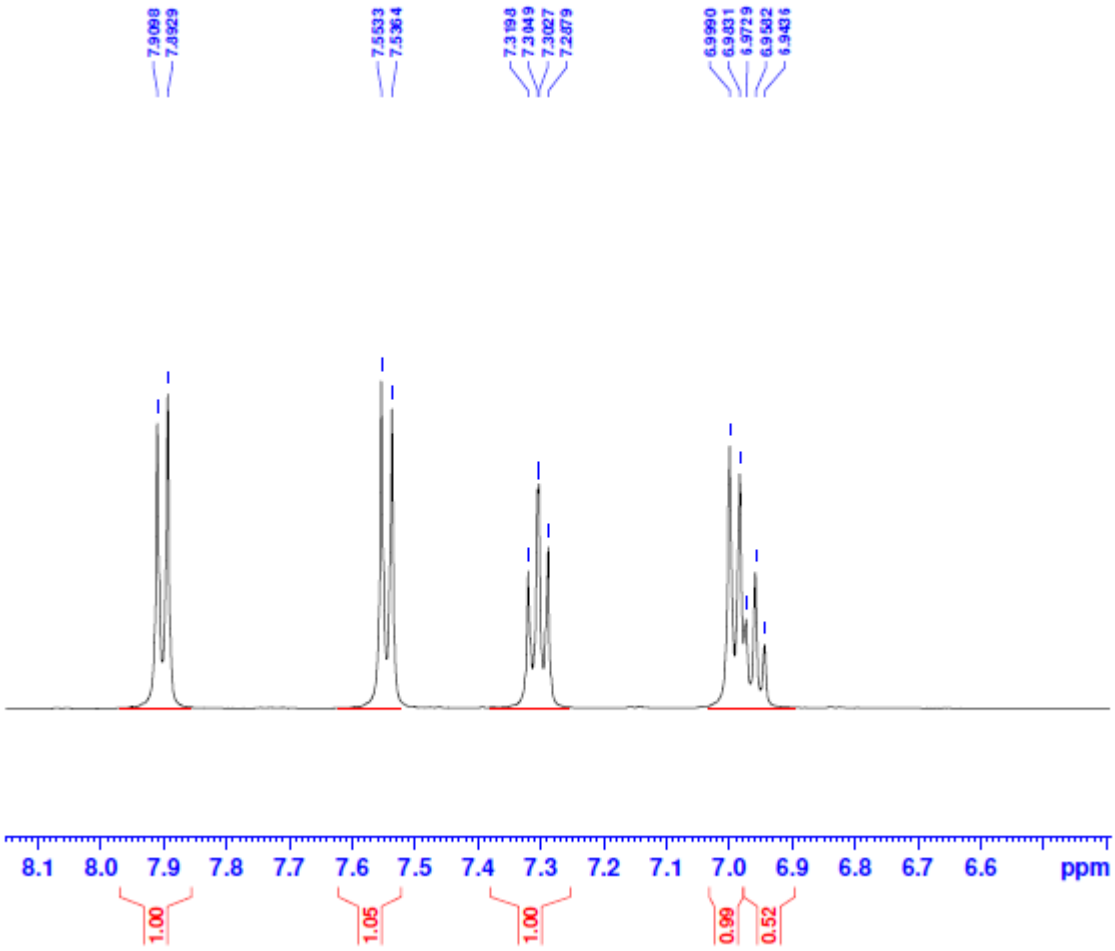



**Expansion of aliphatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 3-aminobenzoate**

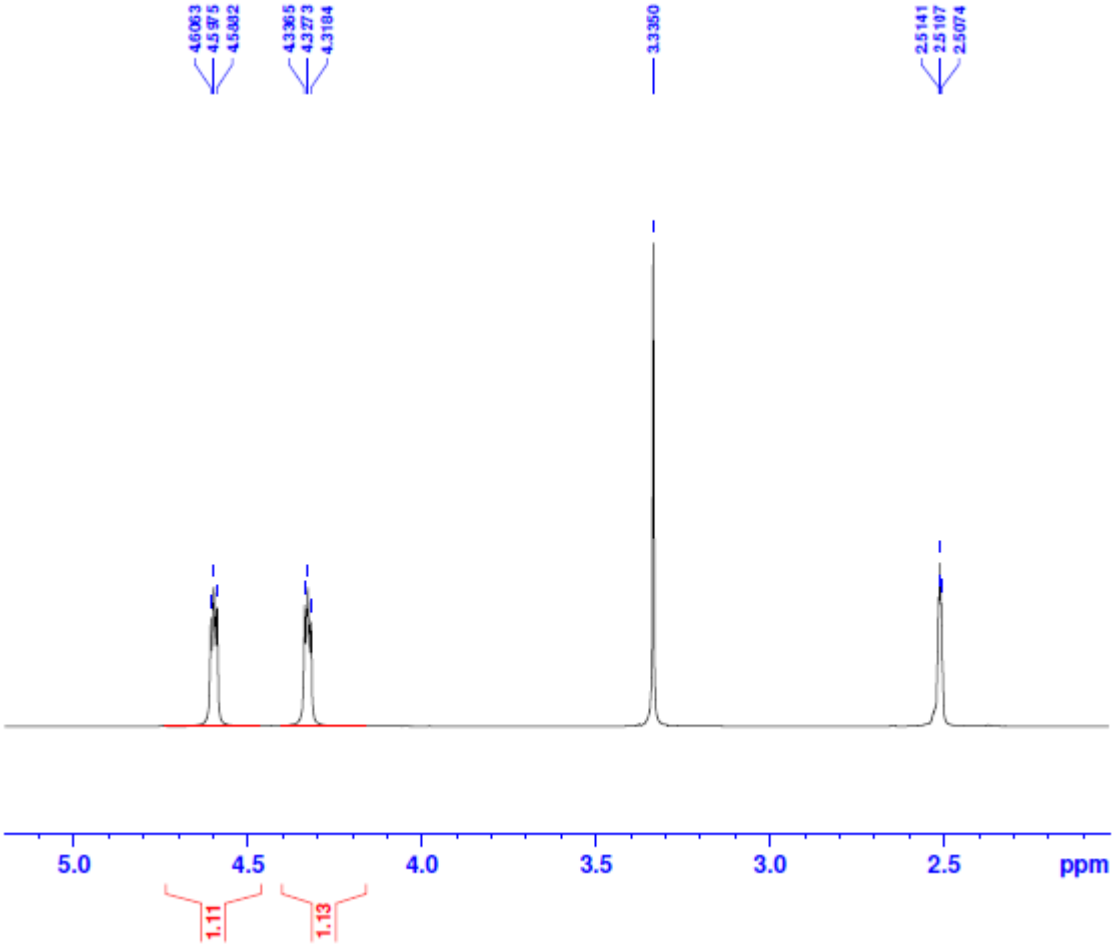
## B11 2-phenoxyethyl 4-tertbutylbenzoate




**[1]H-NMR spectrum of 2-phenoxyethyl 4-tertbutylbenzoate**



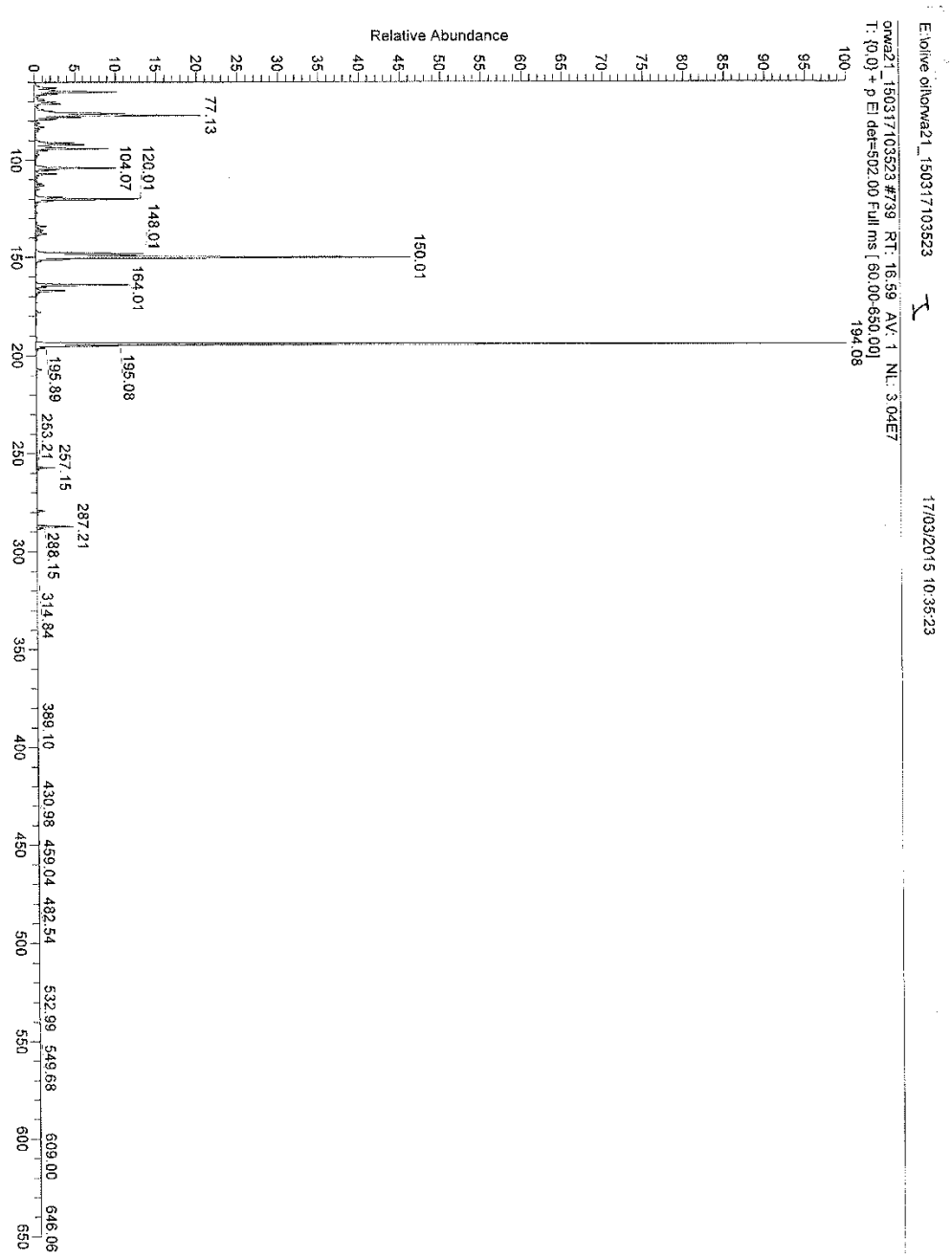

**Expansion of aromatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 4-tertbutylbenzoate**




**Expansion of aliphatic region of $^{1}$H-NMR spectrum of 2-phenoxyethyl 4-tertbutylbenzoate**

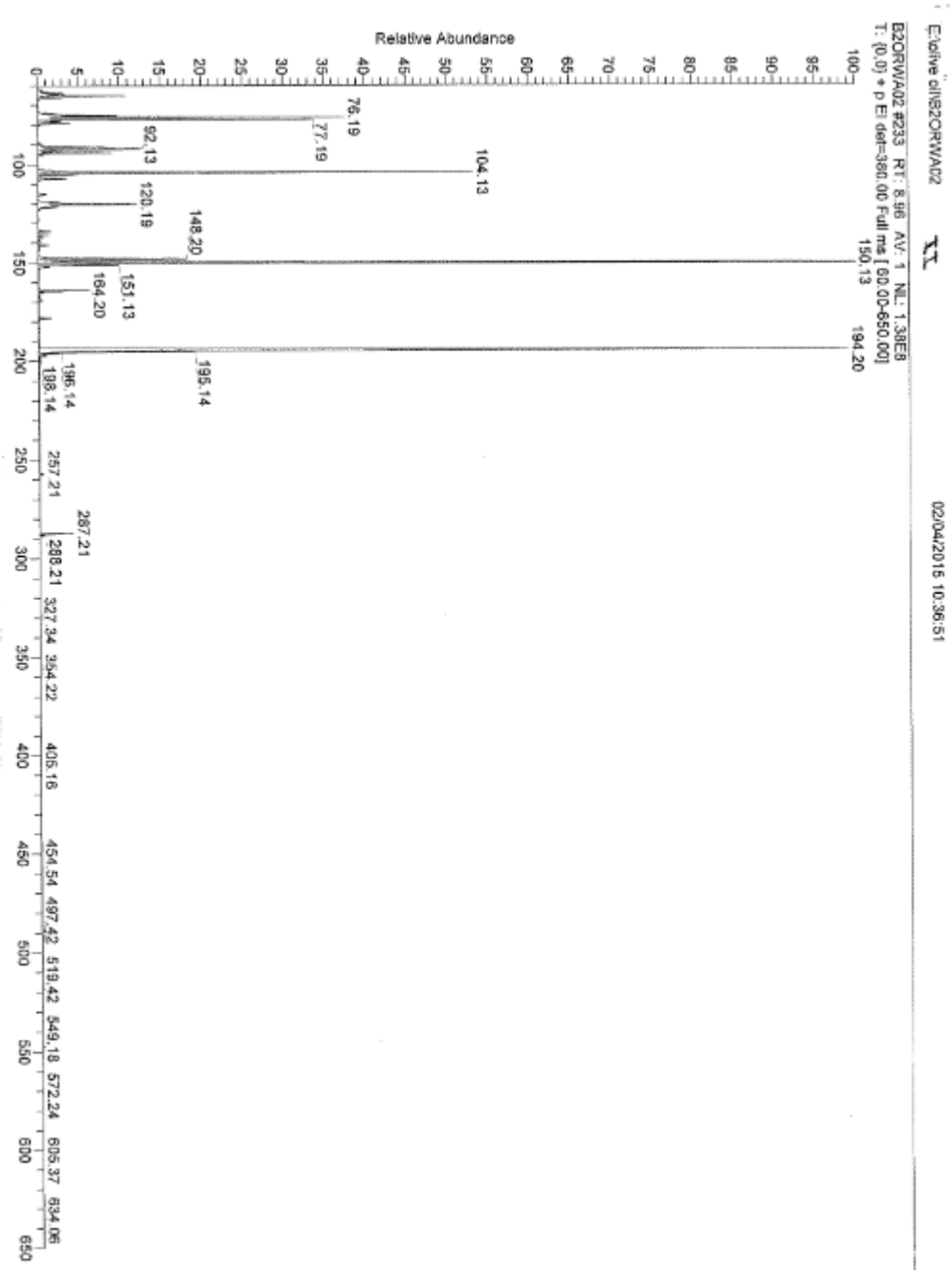
## AppendixIII: Mass Spectroscopy

## C1 2-phenoxyethyl 2-nitrobenzoate



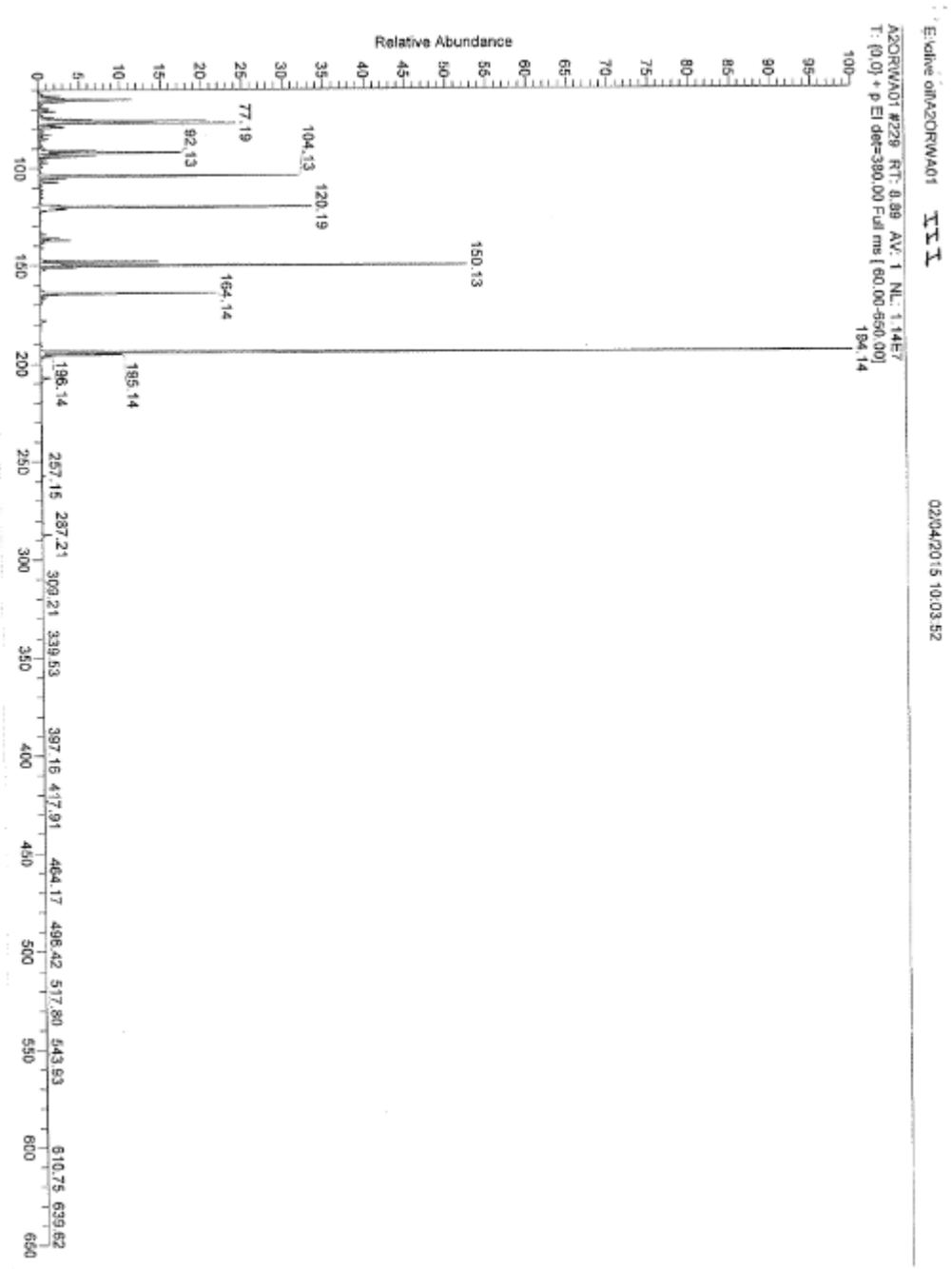

**MS spectrum of 2-phenoxyethyl 2-nitrobenzoate**

## C2 2-phenoxyethyl 3-nitrobenzoate



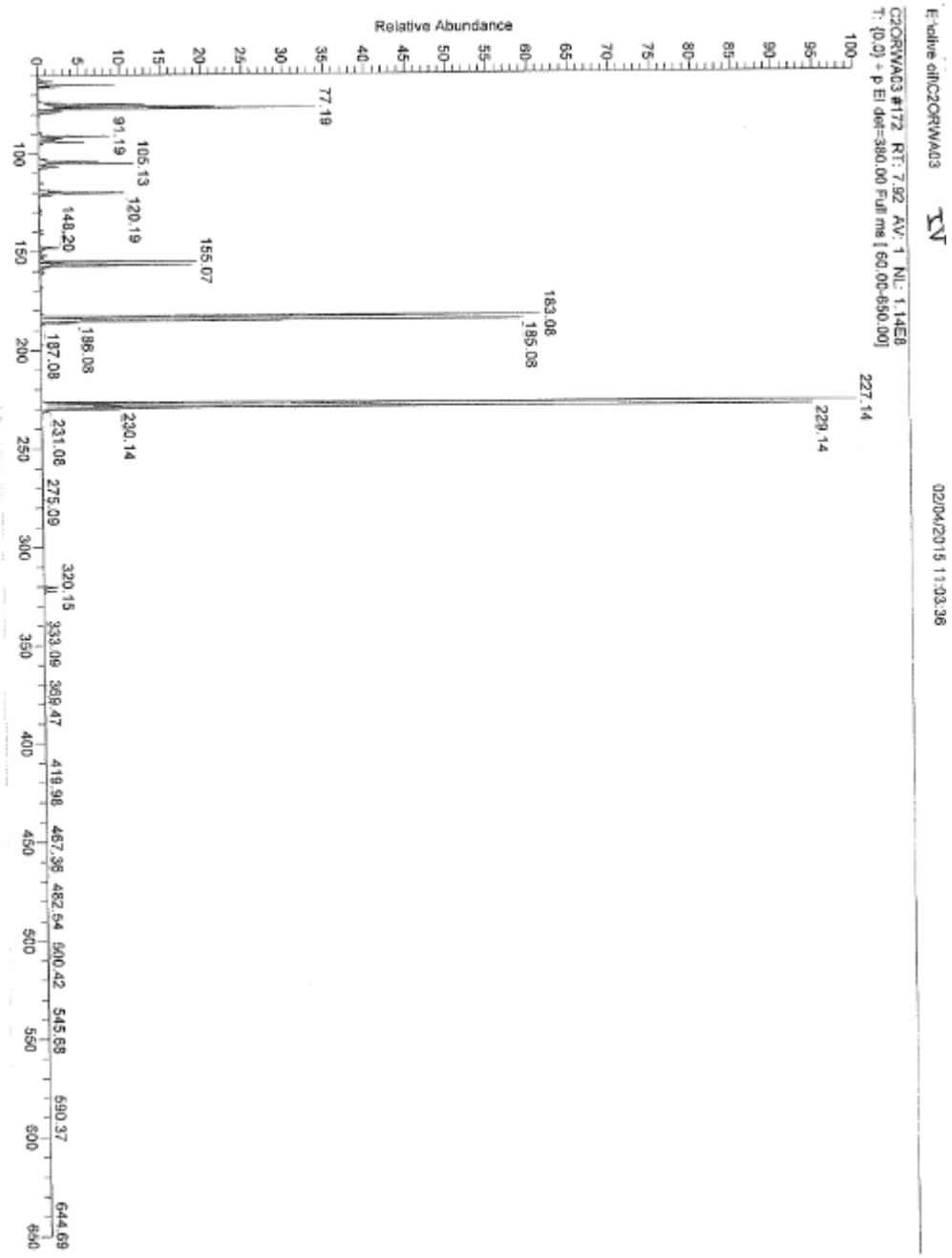

**MS spectrum of 2-phenoxyethyl 3-nitrobenzoate**

# C3 2-phenoxyethyl 4-nitrobenzoate



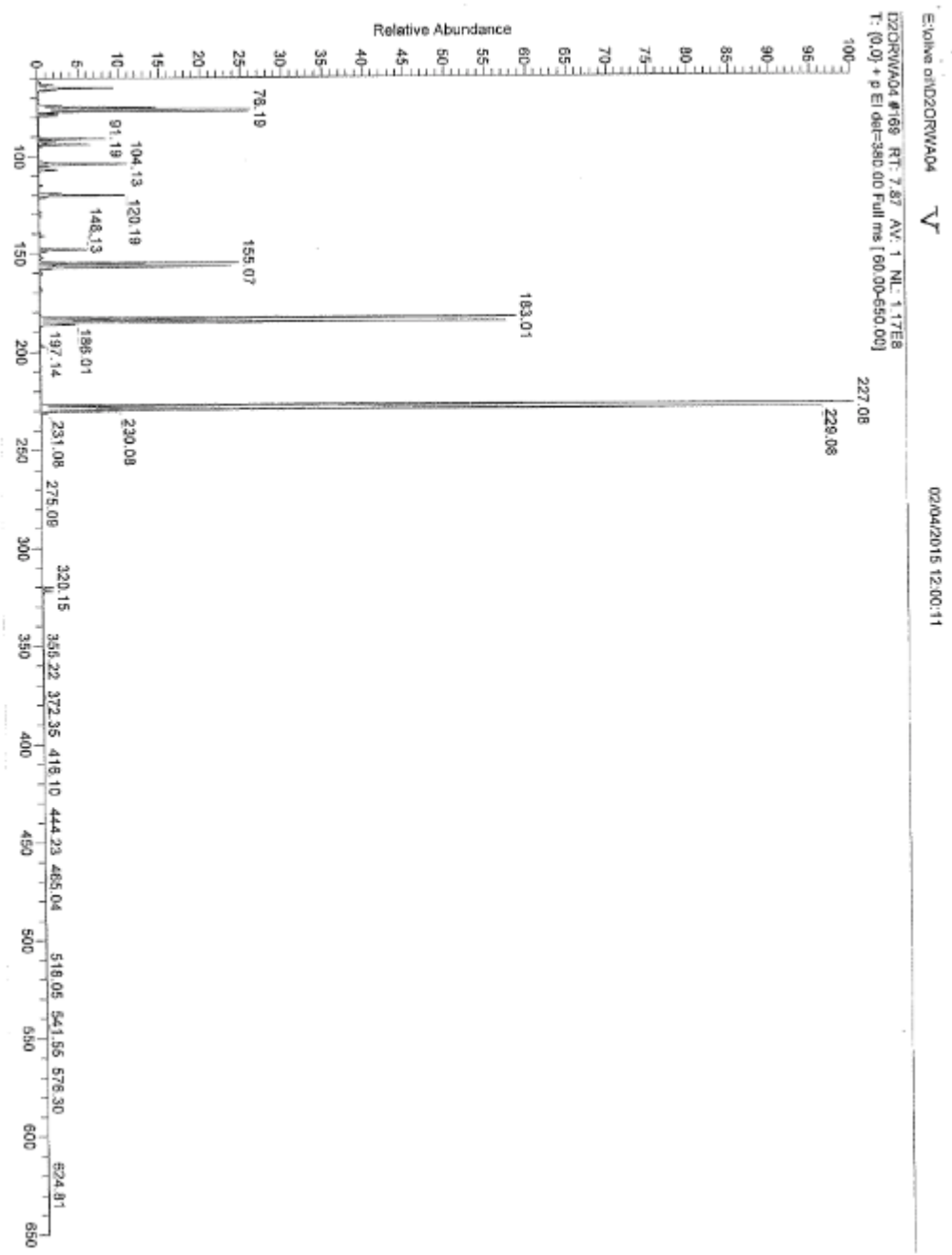

**Ms spectum of 2-phenoxyethyl 4-nitrobenzoate**

# C4 2-phenoxyethyl 2-bromobenzoate



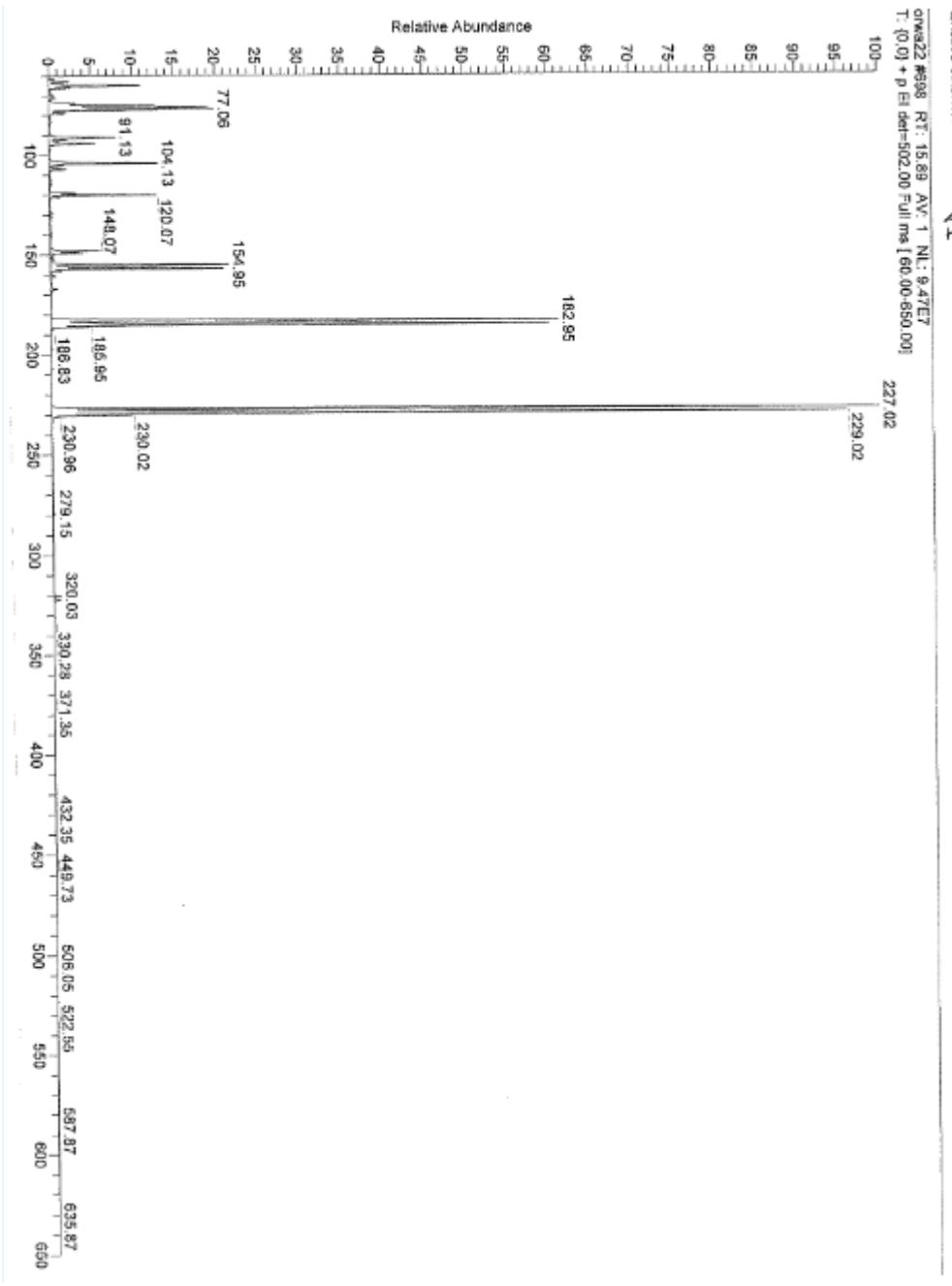

**MS spectrum of 2-phenoxyethyl 2-bromobenzoate**

# C5 2-phenoxyethyl 3-bromobenzoate



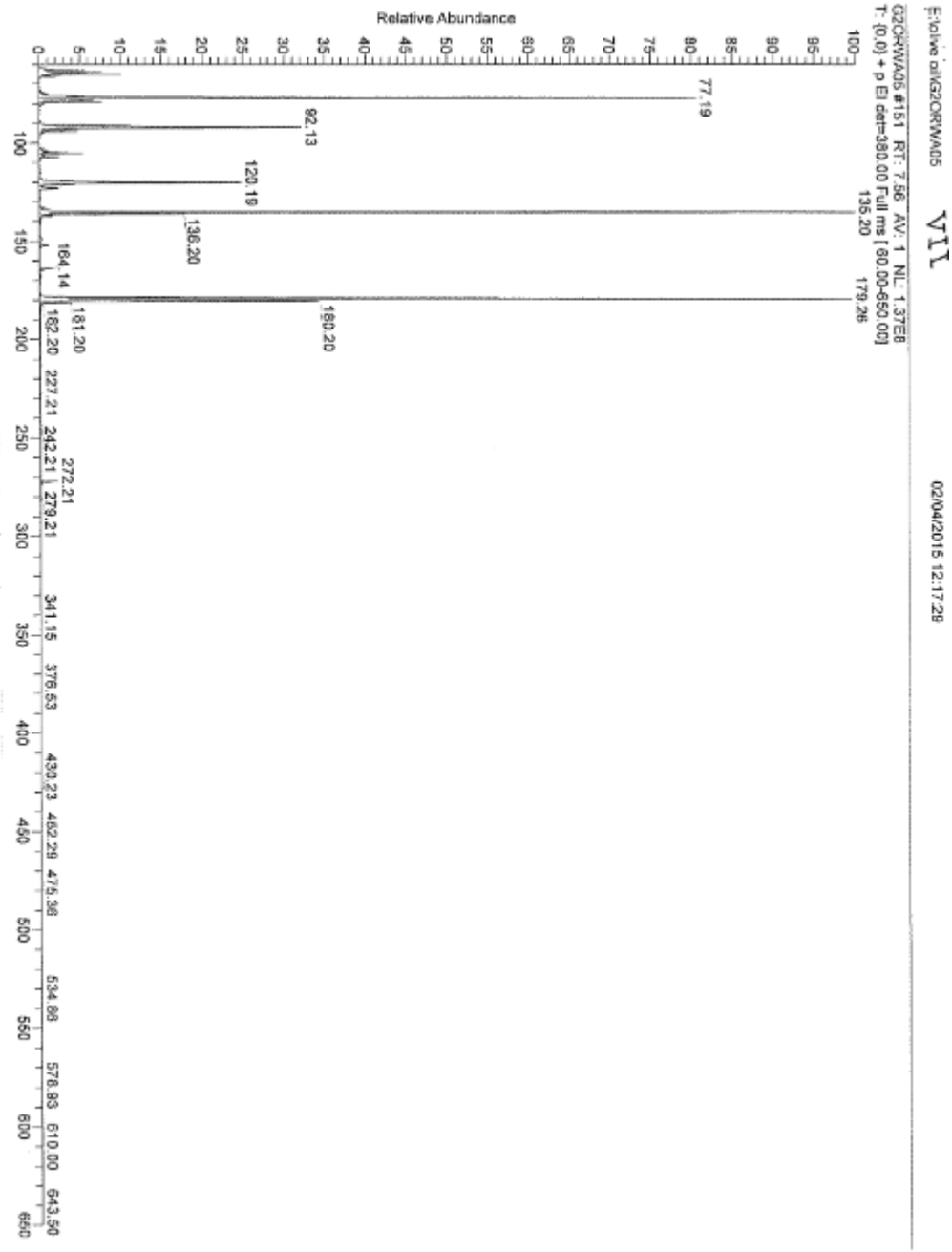

**MS spectrum of 2-phenoxyethyl 3-bromobenzoate**

## C6 2-phenoxyethyl 4-bromobenzoate



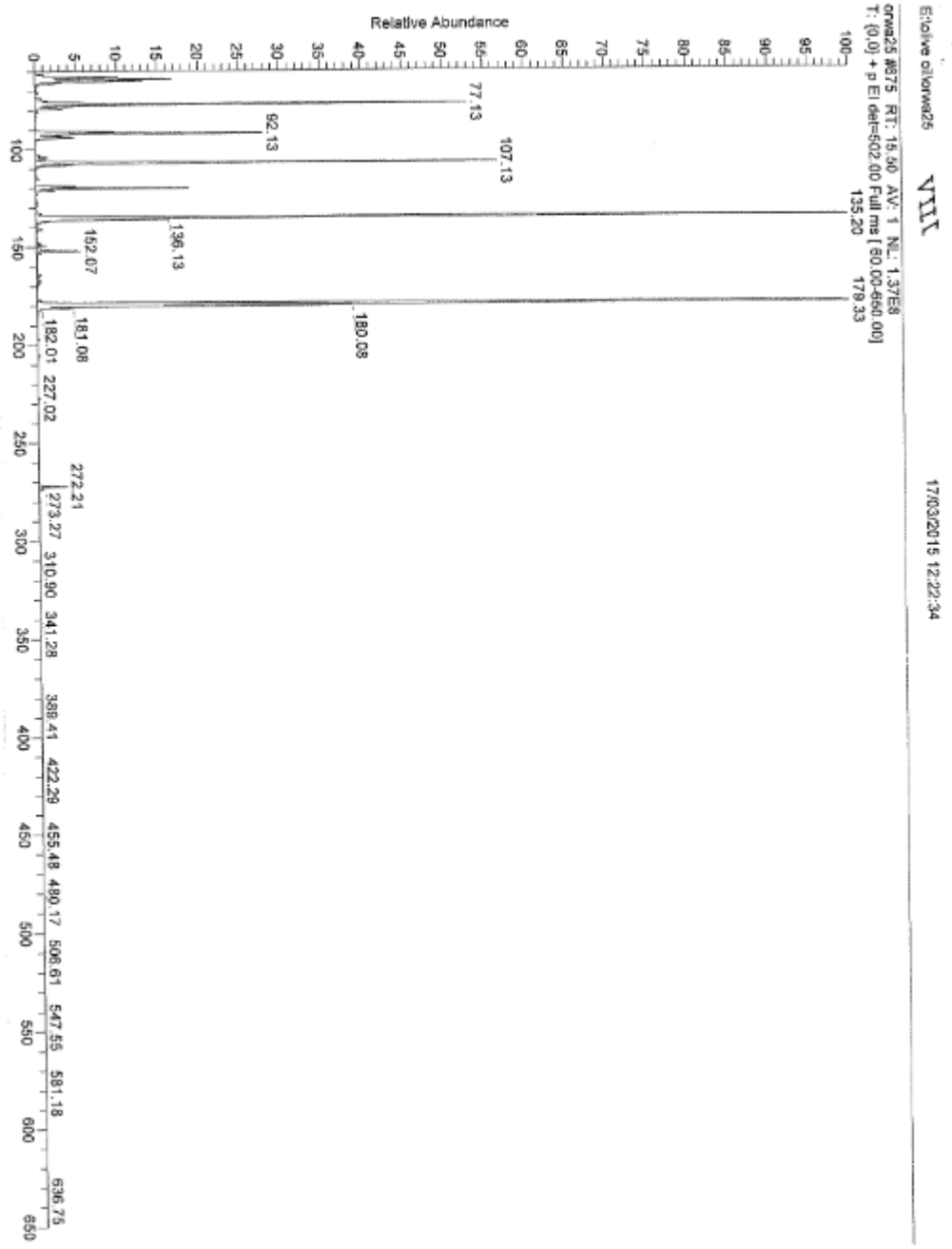

**MS spectrum of 2-phenoxyethyl 4-bromobenzoate**

## C7 2-phenoxyethyl 2-methoxybenzoate



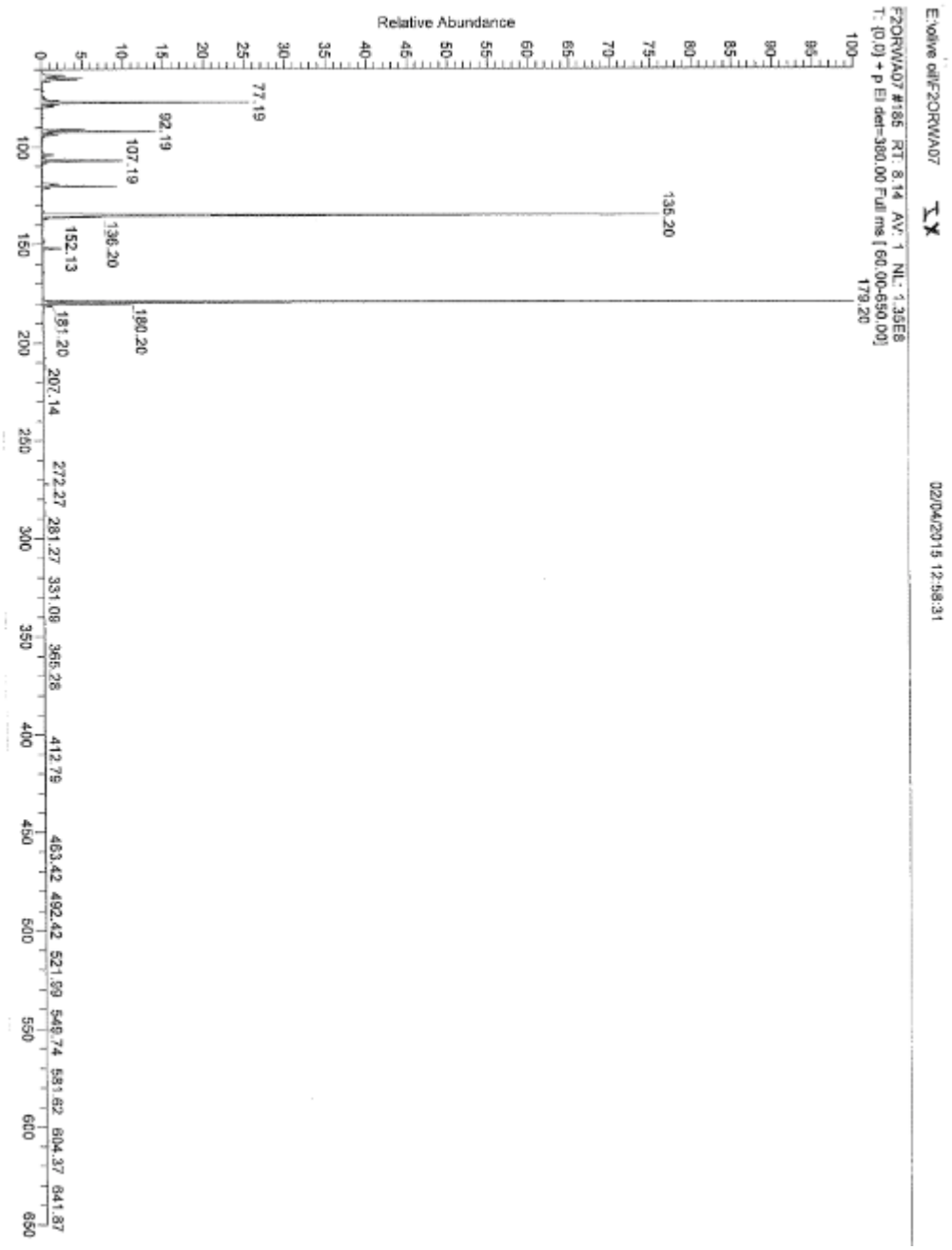

**MS spectrum of 2-phenoxyethyl 2-methoxybenzoate**

## C8 2-phenoxyethyl 3-methoxybenzoate



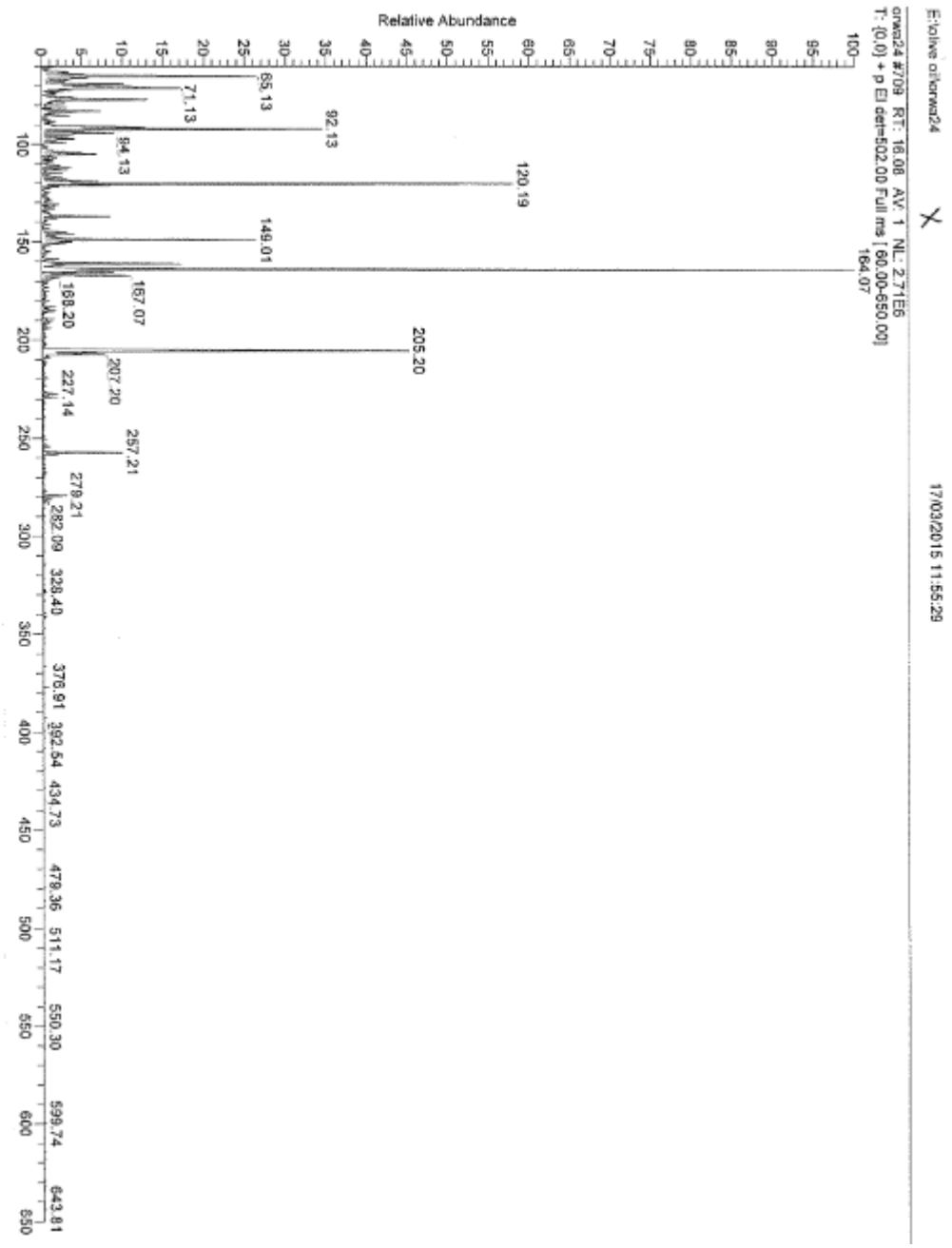

**MS spectrum of 2-phenoxyethyl 3-methoxybenzoate**

## C9 2-phenoxyethyl 4-methoxybenzoate



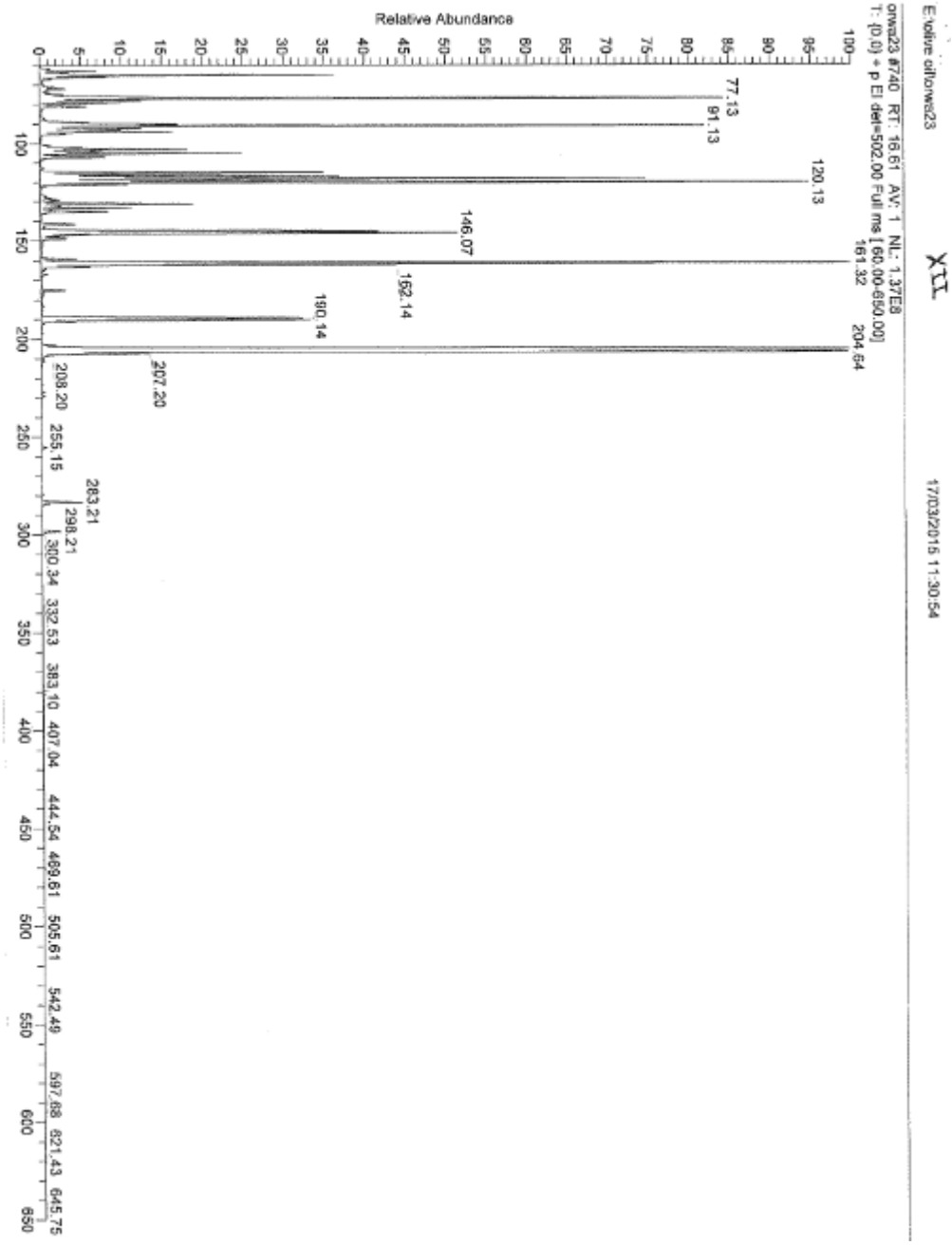

**MS spectrum of 2-phenoxyethyl 4-methoxybenzoate**

## C10 2-phenoxyethyl 3-aminobenzoate



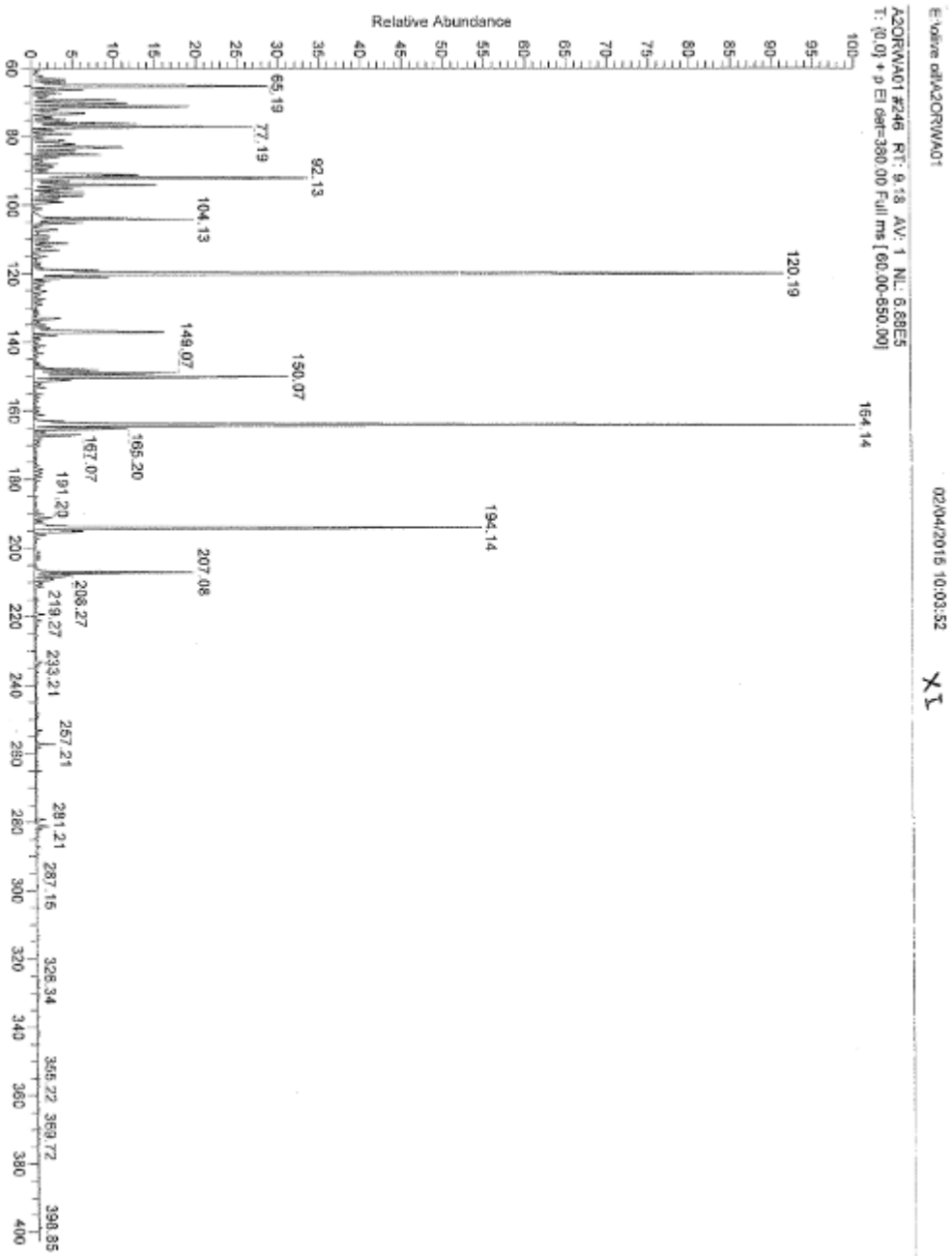

**MS spectrum of 2-phenoxyethyl 3-aminobenzoate**

## C11 2-phenoxyethyl 4-aminobenzoate




**MS spectrum of 2-phenoxyethyl 4-aminobenzoate**

## C12 2-phenoxyethyl 4-tertbutylbenzoate




**MS spectrum of 2-phenoxyethyl 4-tertbutylbenzoate**

جامعة النجاح الوطنية
كلية الدراسات العليا

# تحضير مركبات ايستر أروماتيه من كحول (2–فينوكسي ايثانول) ودراسة بعض أثارها البيولوجية

اعداد

**ندين محمد كامل قلالوة**

اشراف

**د. وحيد الجندي**

**د. عروه حوشية**

قدمت هذه الأطروحة استكمالا لمتطلبات الحصول على درجة الماجستير في الكيمياء بكلية الدراسات العليا في جامعة النجاح الوطنية في نابلس، فلسطين.

2015

# تحضير مركبات ايستر أروماتيه من كحول (2–فينوكسي ايثانول) ودراسة بعض أثارها البيولوجية

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## الملخص

موضوع هذه الرساله هو تحضير اثنا عشر مركبا من المركبات الاروماتيه الاستريه بتفاعل الكحول فينوكسي ايثانول مع االثنا عشر نوعا من الكاربوكسيلك اسيد عبر تفاعلات الاستره وتنقيتها بتقنية ال *Dry coloumn flash chromatography* وجميع هذه المركبات تم دراسة خصائها باستخدام القياسات الفيزيائيه التاليه : ***$^1$H-NMR, MS،IR*** ، **ومن ثم قمنا بدراسة الاثار البيولوجيه متمثله بالفحوص التاليه: *Anti-fungal, anti-oxidant, anti-bacterial***

وقد اظهرت هذه المركبات نتائج مهمه ضد ثلاثة انواع من الفطريات، فعندما استخدمنا الفطر كانيس لاحظنا ان بعض المركبات ثبطت من نمو هذا الفطر بنسبة 100%ا ومن الامثله على تلك المركبات 5,6,7,10,11 على تركيز 1500 ميكروجرام /مل ، والمركب رقم 3 على تركيز 750 ميكروجرام/ مل والمركب رقم 12 على تركيز 375 ميكروجرام / مل.

وعندما استخدمنا الفطر روبيريوم فان المركب رقم 9 قام بتثبيط نمو الفطر بنسبة 100% على تركيز 1500 ميكروجرام / مل والمركبات 5,10,12 على تركيز 750 ميكرجرام /مل.

الفطر الاخير فلاكسوسيوم استخدم مع جميع المركبات ووجد ان الفطر رقم 9 قام بتثبيط نمو هذا الفطر بنسبة 100% على تركيز 1500 اما المركبات 5,10,12 على تركيز 750 ميكروجرام / مل.

وعندما قمنا بفحص مركباتنا ضد الاكسده وجدنا ان المركب رقم 12 له خصائص جيده جدا حيث ان التركيز الذي يثبط نمو الفطر بنسبة 50% هو 22 مقارنة بالاسكوربيك اسيد الذي يمتلك قيمة تساوي 95.

واخيرا قمنا بفحص المركبات ضد ستة انواع من البكتيريا على تركيز 10 ميليجرام /مل مقارنة بالجينتامايسين ولكن لم تظهر مركباتنا اي اثر.