SUDAN UNIVERSITY OF SCIENCE AND TECHNOLOGY

COLLEGE OF GRADUATE STUDIES

Synthesis of Some 2-sulphanilamido-1,4-Quinone Derivatives

تخليق بعض مشتقات 2- سلفونيل اميدو-1،4- كينون

A Thesis Submitted in Fulfillment of the Requirements for the Degree of

M.Sc. in Chemistry

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(B.Sc. (Honours). Chemistry)

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August. 2015

بســـم الله الرحـــمن الرحـــــيم

قـــــــال تعالى : (وَما تَكُونُ فِي شَأْنٍ وَما تَتْلُوا مِنْهُ مِنْ قُرْآنٍ وَلا تَعْمَلُونَ مِنْ عَمَلٍ إِلاَّ كُنَّا عَلَيْكُمْ شُهُودًا إِذْ تُفِيضُونَ فِيهِ وَما يَعْزُبُ عَنْ رَبِّكَ مِنْ مِثْقالِ ذَرَّةٍ فِي الأَرْضِ وَلا فِي السَّماءِ وَلا أَصْغَرَ مِنْ ذلِكَ وَلا أَكْبَرَ إِلاَّ فِي كِتابٍ مُبِينٍ) صدق الله العظيم . يونس الاية 61

DEDICATION

I dedicate this work with deep love and respect to my

Parents,

Husband,

Sons,

Daughter,

Brothers and Sisters

ACKNOWLEDGEMENTS

Praise be to Allah the Almighty, the glorious who has bestowed upon us the faculties of thanking, searching and learning. I would like to express my sincere gratitude and great appreciation to my supervisor Prof Ahmed Elsadig Mohammed Saeed, Professor of organic chemistry, Chemistry department -College of Science, Sudan University of Science and Technology for suggesting the idea of this work.

I wish to record my deep gratefulness to Dr. Abubabaker Mohammed Osman, the assistant profosor of organic chemistry, King Khalid University, Faculty of Science, Saudi Arabia and the techniques staff of laboratory, College of Science, University of Sudan of Science and Technology, for their help and facilities kindly provided.My special and deepest thanks Dr. Ahmed Shrif, College of Pharmacy, reseach Centre , King Saud university, Saudi Arabia and. I express my sincere thanks and gratitude to my husband, Khattab Hassan.

Abstract

Ten new 2-sulfonilamido-1, 4-quinone derivatives were prepared in this work with their corresponding intermediates which include five p-aminobenzene sulphonilamido derivatives and two 1,4-quinone derivatives. Synthesis of the titled compounds was accomplished by chlorosulphonation of acetanilide and amination (sulfamethoxzole, 4-aminophenazone, sulfadoxine, sulphonilamide and sulfasulph onilamide) to furnish the p-acetamedobenzene sulphonilamido derivatives, the latter upon acid hydrolysis yielded p-amino benzene sulphonilamido derivatives.

1,4- quinone (1,4-naphthoquinone and 2-methyl-1,4-benzoquinoe were prepared by standard methods of chromic acid oxidation of naphthalene and o-crezol respectively. Coupling of the aminobenzene sulphonil amido derivative with 1,4-quinone moiety furnished the titled product. All synthesized compounds checked their reaction progress by (TLC) techniques. The structures of synthesized compounds were confirmed by some physical properties; (melting point) and spectroscopic analysis like (IR, ^{1}H-NMR, ^{13}C-NMR and MS).Synthetic designing and mechanisms of the reactions of the different groups of compounds were discussed.

الخلاصـــــــــــــــة

تمكنت هذه الدراسة من تحضير عشرة من مركبات2- السلفونيل اميدو4,1 –بارا كينون – متضمنة خمسة من مشتقات بارا امينو بنزين سلفوميل اميدو واثنين من مشتقات 1,4 – با كينون والتي تم تحضيرها باستخدام الاسيتانلايد كمركب اساسي (ابتدائي) حيث تمت معالجته بعملية كلورة المسلفنة. حيث تتفاعل المواد الناتجة مع السلفوناميد لانتاج مركبات الاسيتاميدو والتي تتم اماهتها الحمضية الى مركبات الامين المقابلة. حيث تقترن هذه الامينات مع اثنين من الكينونات المحضرة وفقا للطريقة المعتمدة لاكسدة حمض الكروميك وباستخدام النافثالين والارثو كريزول كمواد اولية لتحضير كل من 1,4- نافثوكينون والميثل بنزوكينون علي التوالي. اقتران هذه المركبات مع بعضها (مركبات البارا امينو بنزين سلفونيل اميدو و 1,4- بارا كينون) تعطي المركبات المستهدفة في هذا البحث. جميع المركبات المحضرة تمت متابعتها باستخدام الية كروماتوغرافيا الطبقة الرقيقة للتصاكد من سريان التفاعل – اما تحديد او التاكد من التركيب البنائي للمركبات المحضرة تم بواسطة بعض التقنيات الفيزيائية مثل نقطة الانصهار والتحليل الطيفي مثل الاشعة تحت الحمراء، الرنين النووي المغنطيسي لانوية ذرات الهيدروجين والكربون وكذلك استخدام طيف الكتلة لتحديد الوزن الجزيئي. تمت مناقشة جميع تصميمات التصبيع وميكانيكيات التفاعل لمختلف المركبات المحضرة.

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List of Abbreviations

hrs	Hours
min	Minutes
Ph	Phenyl group
DMSO	dimethylsulfoxide
IR	Infrared Spectroscopy
1H-NMR	Proton nuclear magnetic resonance
Me	Methyl group
MeOH	Methanol
EtOH	Ethanol
cm	Centimeter
g	gram
ml	Millimeter
c	Centigrade
M	Molar
st	Stretching
vib	Vibration
temp	Temperature
recy	Recrystalization
solv	Solvent
mp	Melting point
TLC	Thin layer chromatography
arom	Aromatic
s	singlet
d	doublet
m	multiplied
Ar	Aryl group
δ	Chemical shift

Chapter One

1.1Definition of quinones

Quinones are one of class of aromatic diketones in which the carbon atoms of carbonyl groups are part of the ring structure (Solomon and Feyhte.,2000),or any member of a class of acyclic organic compounds comprising a six membered unsaturated ring to which two oxygen atoms are bonded as carbonyl groups (Bratinnica.2007). This structure plays an important rote in theories and chemical structure of colour, since quinones occur as plant pigments in bacteria, fungi, and certain higher plants. Animals containing quinones obtain them from plants they eat. Quinones are not true aromatic compounds because upon examine the benzenoid structure they are to be regard as α,β-unsaturated conjugated cyclic ketones. They are generally colored due to conjugation in IR region they absorb carbonyl stretching between 1690-1600cm^{-1} which is similar to that of α,β-unsaturated ketones (Finar.1975).

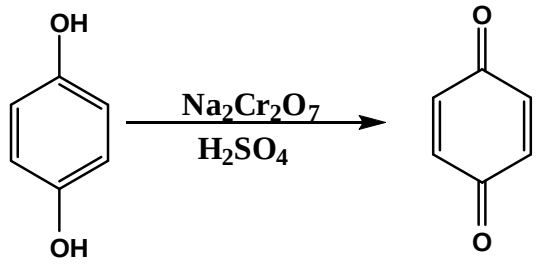
They are readily converted to dihydric phenols on reduction and these dihydric phenols on oxidation give back the quinones. This reduction of quinones is sufficiently rapid and reversible and provides an oxidation-reduction system which gives reproducible electrode potential in an electrolytic cell. In fact quinoride structure has been very helpfull in the correlation of colour and chemical constitution (Ksteart. *et al*.,1998). K_1 and K_2 vitamins are naphthaquinones which are found in blood and are responsible for proper blood clotting reaction.

1.2 Nomenclature of quinones

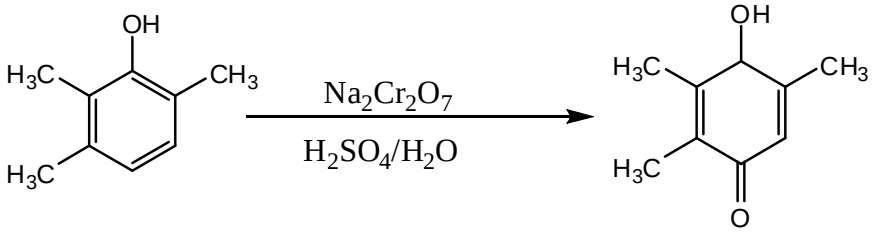
The name of quinones is derived from of corresponding aromatic hydrocarbons, benzoquinone from benzene, naphthaquinone from naphthalene and so on (Loudon.1988). As *o*- and *p*-quinones according to

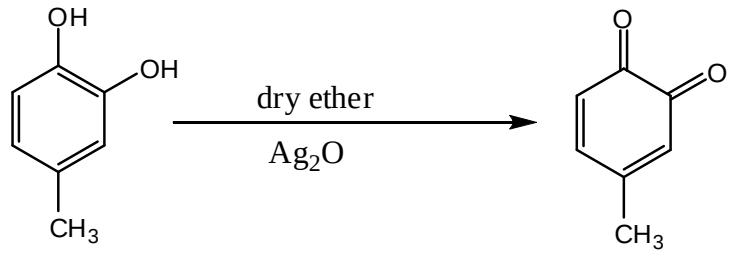
the position of the two carbonyl oxygen there is no *m*-quinone is known presumably because it is impossible to arrange two carbonyl carbon at *m*-position in a ring having two double bonds conforming to valancy requirement in poly nuclear quinones the carbonyl group may be present in different rings (Ksteart. *et al*.,1998).

Tertiary alcohols are not readily oxidized, one expected phenols to resist oxidation. Yet it is found that phenols oxidized to quinones.



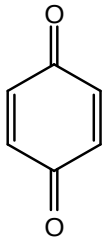
hydroquinone ***p*- benzoquinone**



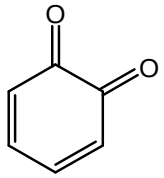


p-hydroxy phenols (hydroquinone) and *o*-hydroxy phenols (catechols) and phenols with an unsaturated position *para* to the hydroxy group are oxidized to quinones although the term quinones is sometimes used as a

common name of *para* benzoquinone it is generic name for any compound containing either of the following structural units

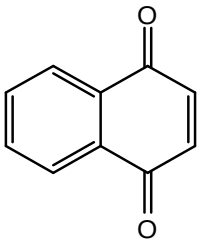


p-quinone



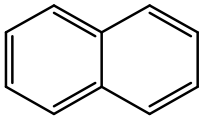
o-quinone

If the quinone oxygen have 1,4(para) relationship, the quinone is called para-quinone and if the oxygen are in 1,2 (*ortho*) arrangement the quinone is called an ortho quinone the following compounds are typical of quinones.

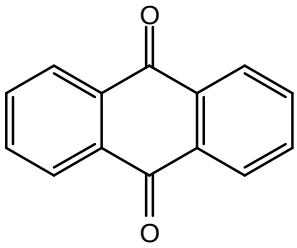


1,4 naphthaquinone

derived from

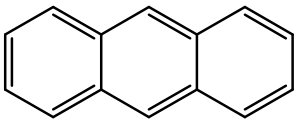


naphthalene



anthracene-9,10-dione

derived from

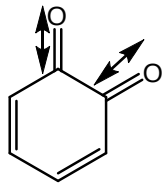


anthracene

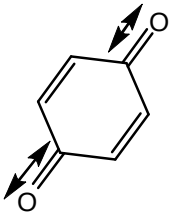
1.3 Stability of quinones

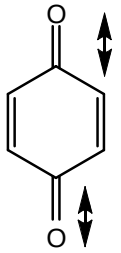
Ortho quinones particularly ortho-benzoquinones are considerably less stable than the isomeric *para*-quinones. One reason for this difference is that, in ortho-quinones the C=O dipoles are nearly aligned and therefore

are pulsive destabilizing interaction. In *p*-quinones these dipoles are further part.



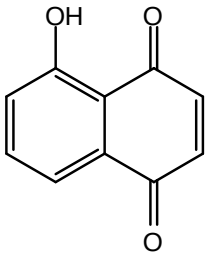
ortho-quinones
bond dipoles nearly
aligand



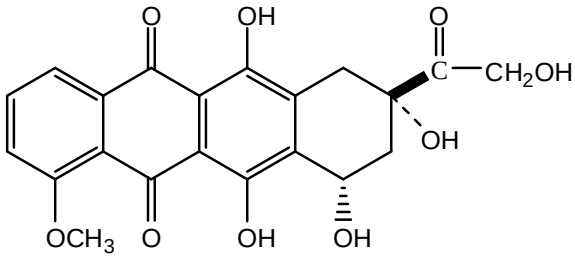


para-quinones
bond dipoles further
part

A number of quinones occur in nature, Juglone occurs in walnut shells, dexorubbien (adriamycin), isolated from amicrorganism is an important antitumor drug

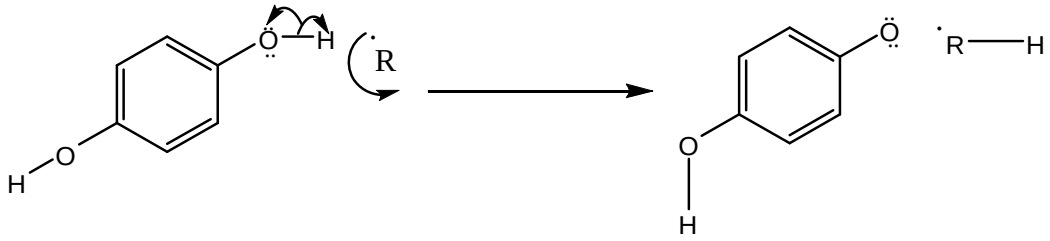


Juglone



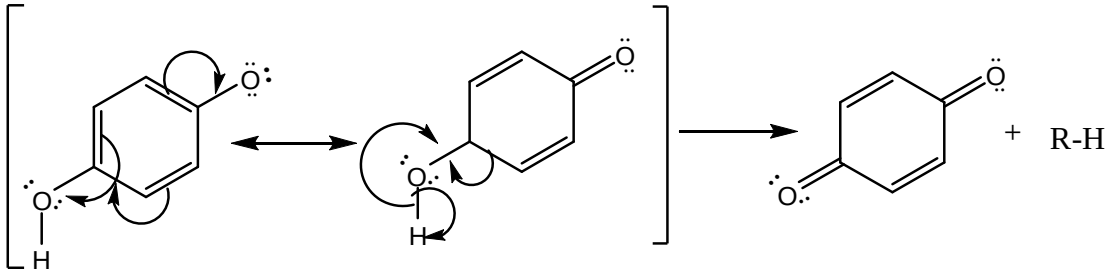
Doxerubici - Adriamycin

The oxidation of phenols by air (O_2) to colored quinones - containing products is responsible for the darking that is observed when some phenols are stored for long periods of time. The oxidation of hydroquinones and its derivatives to the corresponding *p*-benzoquinones can also be carried out reversibly in an electrochemical cell. Oxidation potentials of number of phenols with respect to standard electrodes are well known. The oxidation of phenols has several practical applications, for example, hydroquinones and ortho-phenols can be used as inhibitors of free radicals chain reactions. Many free radicals abstract from hydroquinones to form every stable radicals called a semi quinones.



semi quinone

These radicals were resonance stabilized a second free radicals can react with the quinones to complete its oxidation to quinone.



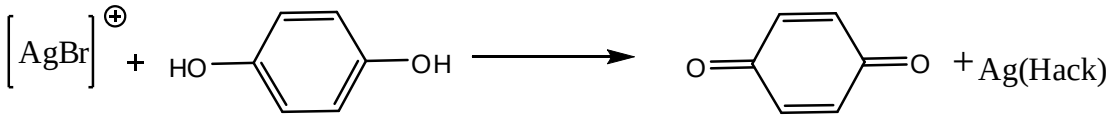
Hydroquinones thus terminates free radicals chain reaction by intercepting free radicals intermints $R^{\bullet}$ and reducing them to R-H. The oxidation of hydroquinone lies at heart of the photographic process. When photographic film is exposed to light, grains of silver bromide in the photographic emulsion on the film absorb light and are activated sensitized (Wade.1974).

$$AgBr + light \longrightarrow [AgBr]^{+}$$

sensitized silver bromide

Because silver bromide is trapped in the photographic emulsion, it is immobile. Thus sensitized silver bromide molecules provides, a faithful record of the position on the film that have been struck by light. Now a sensitized silver bromide is a much better oxidized agent than silver bromide that has not been light when exposed films treated by solution of

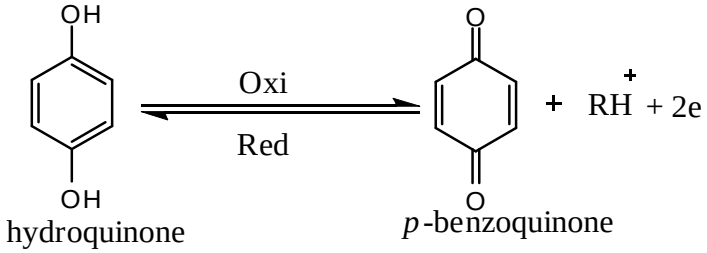
hydroquinone (a common photographic developer) [AgBr] oxidizing the hydroquinone (which is subsequently washed away) and the silver (I) is reduced to finally divided silver metal which remain trapped in the photographic emulsion.

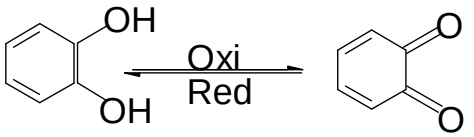


Because inactivated AgBr oxidized hydroquinone much more slowly silver metals form only where light has impinged the film. This precipitated silver is the black of a black and white negative (Loudon 1997).

1.4 Preparation of quinones

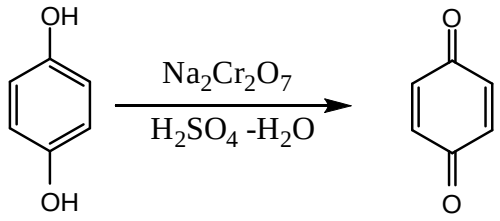
Quinones are oxidized form of aromatic diols and are unsaturated rings. Methods for synthesis of quinones vary with their structure. Benzoquinone is prepared by oxidation of aromatic hydrocarbons witch are oxidized directly to form quinones, ortho quinones are usually prepared from ortho disubstituted derivatives of the corresponding aromatic system. Oxidation and the corresponding hydroquinones oxidation-reduction couples that give reproducible electrode potentials.



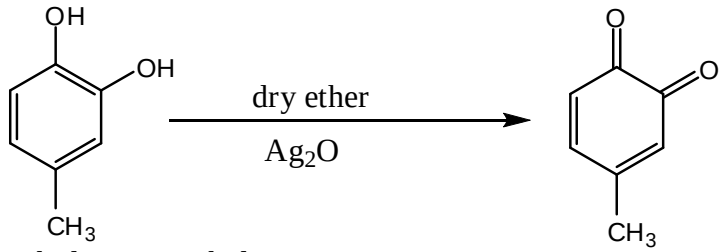


Catechol ***o*-quinone**

The oxidation potential of many quinones have been measured by potentionmetric titration of the hydroquinones of known oxidation potential. Electron withdrawing substitents such as NO_2, CN, SO_2Ar, CO_2H cause the oxidation potential making quinones more powerful oxidant. Electron donor substituent such as -$NHCH_3$, -NH_2, -$NH(CH_3)_2$, -OH, -OH_3, -$NHCOCH_3$, -C_6H_5 and –$OCOCH_3$ lower the potential since reduction of quinone involves hydrogenations, the quinone-hydroquinone system is used as indicator electrode for measurement of the hydrogen-ion activities of water solution. The system is known as quinohydrone electrode because hydroquinone and quinone combine to form a molecular compound called quinohydrone, the molecular complex has characteristic black color (Hendrictson *et al*.,1970). Phenols are more easily oxidized than alcohols and a large number of in organic oxidizing agents have been used for this purpose. The phenol oxidations that more most used by organic chemist are those involving derivatives of 1,2 benzene diol (pyrecete-cat) and 1,4 benzene diol (hydroquinone) oxidation of these compounds called quinones.



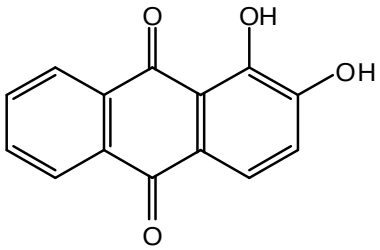
hydroquinone *p*-benzoquinone



4-methyl pyrocetrchol
4-methy-1,2 benzene diol

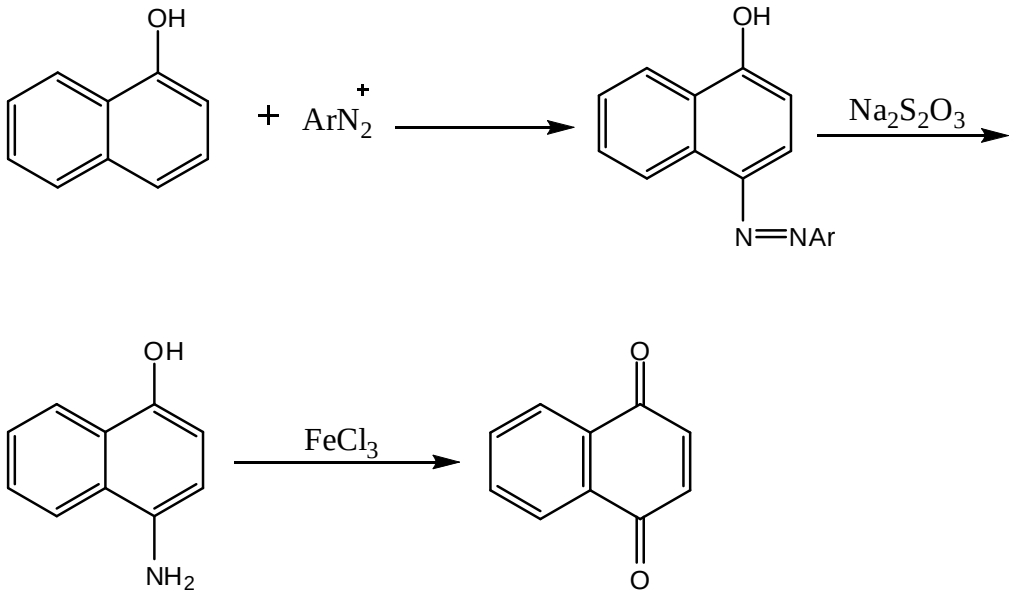
4-methy-1,2 benzoquinone

Alizarin is a red pigment extracted from the roots of the madder plants, its preparation is from anthracene.

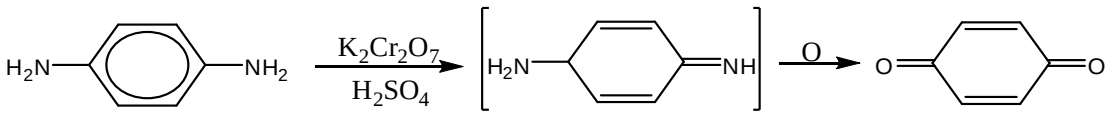


Alizarin

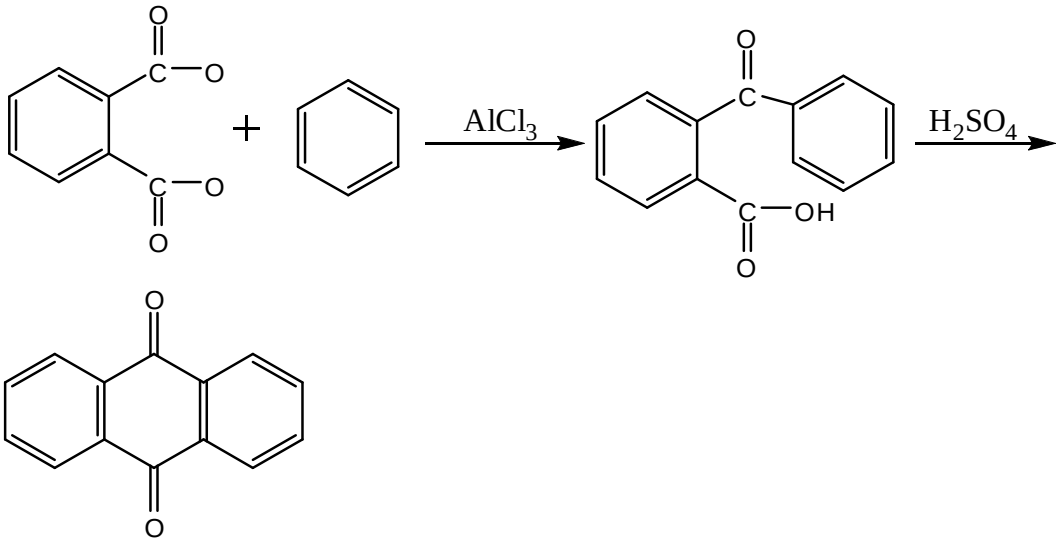
Quinones are also obtainable other way, by oxidation of o-and p-amino phenols and in many cases are direct oxidation monohydric phenols and aromatic amines. Indeed the most practicable method of preparing p-benzoquinone itself is by the oxidation of aniline. The ready oxidation of p-amnophenols to quinone permits one to prepared quinone and thus hydroquinones from simpler phenols by diazonium coupling to give an azo compound and reduction of the aza compound and oxidation of the amine formed for example (Ressman.1977).



Oxidation of *p*-phenylene diamine with potassium dichromate and sulfuric acid yields the following compound (Ksteart. *et al*., 1998).

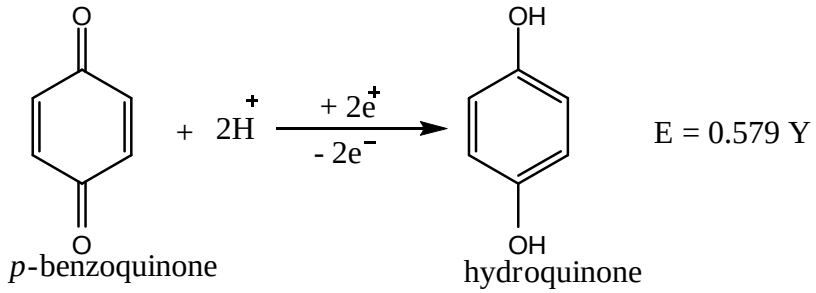


By treating benzene with phthalic anhydride in the presence of anhydrous aluminum chloride give *o*-benzoyl benzoic acid which losses water on treatment with sulfuric acid (Degerin.1957).

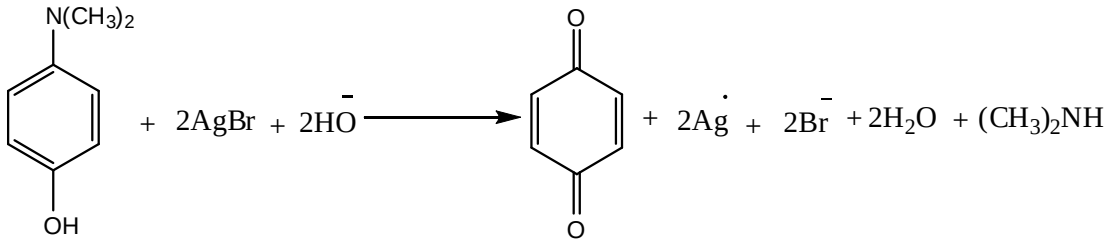


1.5 Chemistry of quinones

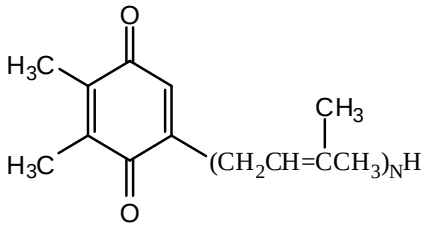
Quinones-hydroquinones pair forms an oxidation-reduction system of chemical and electrochemical interest. The pair readily interconverts with a reduction potential which has been used as standard electrochemical cells.



A part of chemistry of photographic development involve is quinone and hydroquinone and related *p*-aminophenols are oxidized to *p*-benzoquinone by photoactivated silver bromide, the reduced silver metal leaves the black image of system hyposulfite (hypo)(Wade 1974).

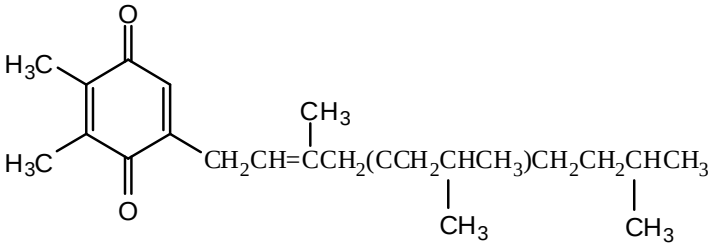


Plast quinone is synthesized by plant and appears to play a role in electron transfer during photosynthetic process. Along terpenoid side chain is connected to the quinone group.

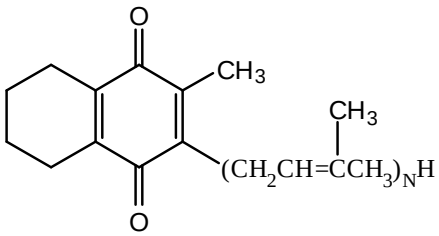


plast quinone

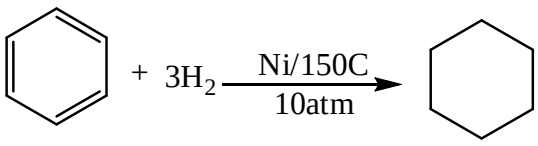
Vitamins K_1 and K_2 are naphthaquinone with terpenoid side chain. They are broadly distributed in plants and believed to be essential for coagulation in blood animals.



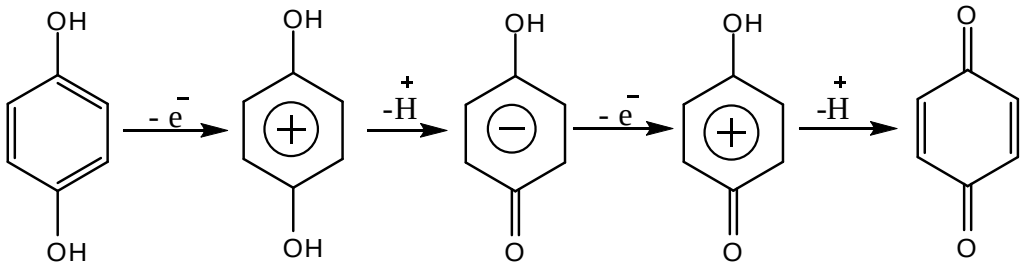
vitamin K_1



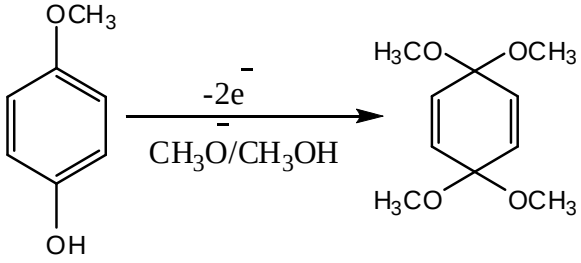
The benzene ring is relativity resistant to most reduction techniques. Catalytic hydrogenation can be accomplished, but elevated temperature and pressure are normally required. Reduction generally proceeds all the way to cyclohexene.



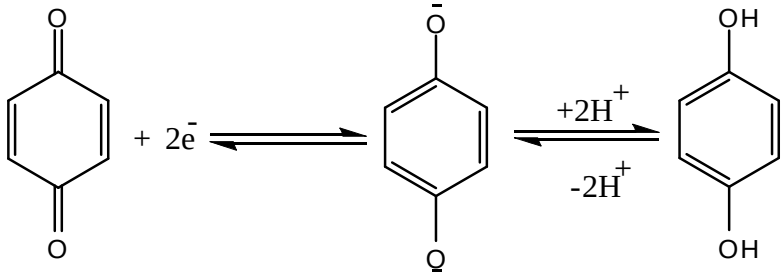
Phenolic compound leads to radical cations that are stabilized by the oxygen atom, the products are quinones and their analogous.



An interesting application of this electrochemical oxidation is conversion of hydroquinone dimethyl ether to the diketal of quinones (Pine *et al.*, 1980)



1.6 Reactions of quinones



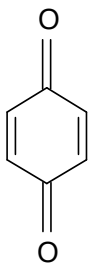
From the formula of quinones it shows us that quinones are unsaturated cyclic di ketone. It has all the reactions expected of such compounds, the

reaction above shows us how it is possible to add two electrons to quinone converting from an unsaturated diketone into addition of adihydric phenol. Oxidation is loss of electrons and reduction, is gain of electrons in equilibrium of this kind the oxidizing or reducing power of the solution can be measured by inserting an electrode unattacked by the solution, a solution of the mixture of quinones and quinol can form system.

$$C_6H_4(OH)_2 \rightleftharpoons C_6H_4O_2 + 2H^+ + 2e^-$$

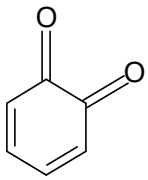
The electrode potential of the system would be as followed

$$E = E1 - \frac{2RT}{2F} \ln \frac{a_Q \, a_H^{2+}}{q_a H_2}$$

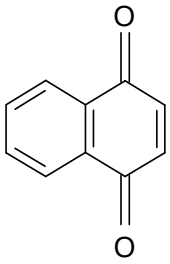


G_o = 0.699 volt in H_2O

0.715 volt in EtOH



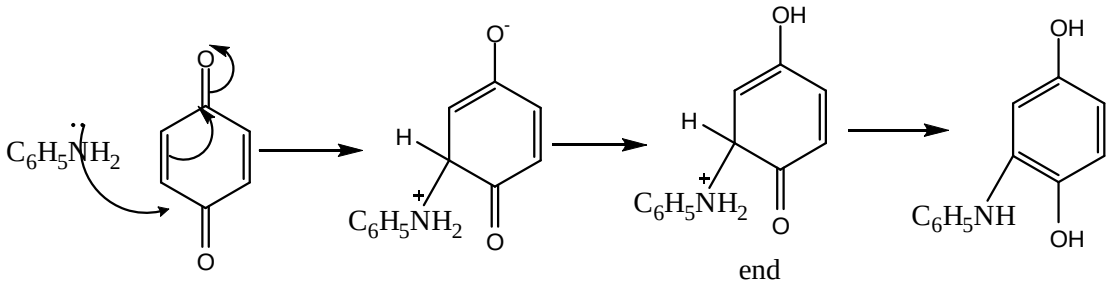
G_o=0.792 volt In H_2O



G_o=0.47 volt in H_2O

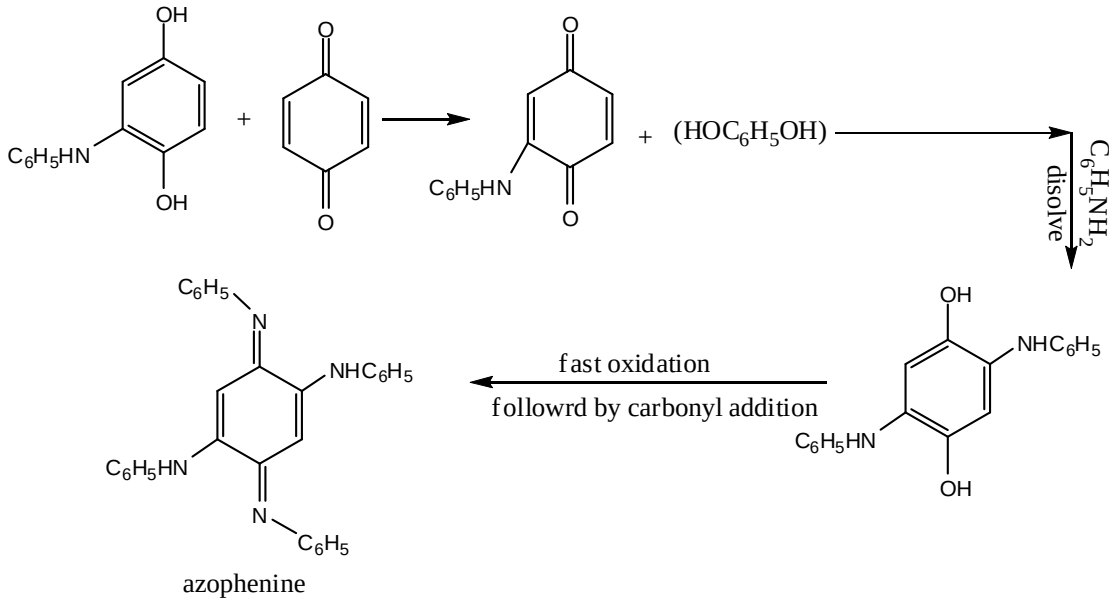
0.484 volt in EtOH

o.benzoquinone has higher electrode potential than *p*.benzoquinone suggesting that the o.quinonoid system is of higher energy and less stable than the *p*.quinonoid. Phenyl hydrazine behaves as a reducing agent and oxidized by quinones but substituted phenyl hydrazine will react with carbonyl group in the normal manner, in general, strong nucleophiles tend to addition conjugated fashion for example aniline



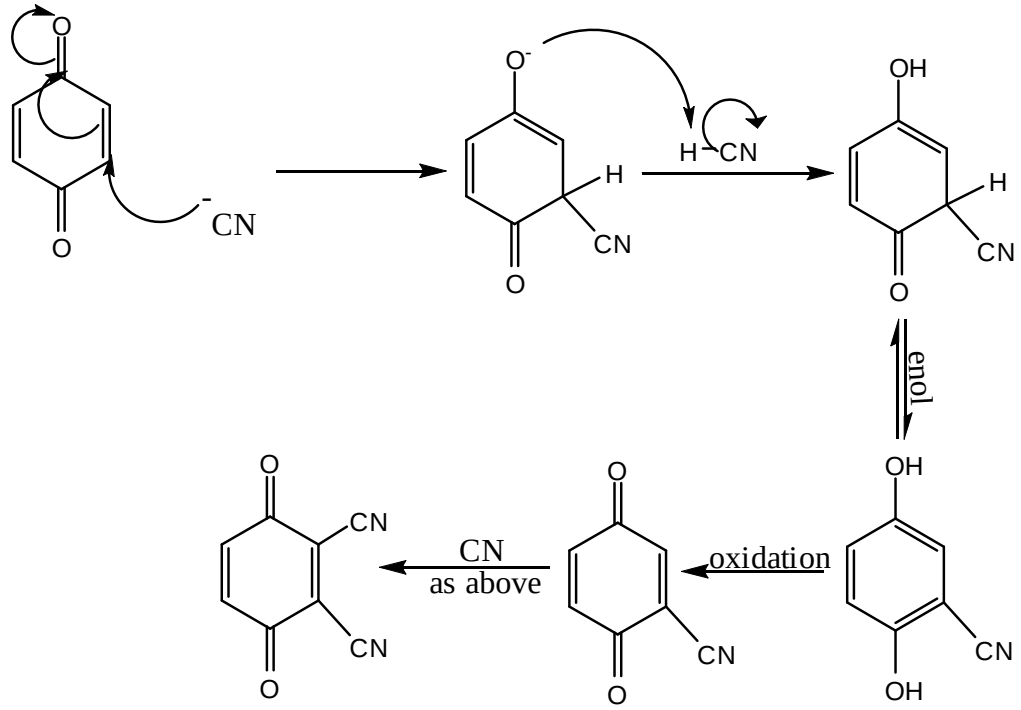
end

The electron donor group lowers the electrode potential so that in presence often in excess of quinone the aniline quinoquinol will be oxidized. The resulting anilinequinone will then react further with more aniline.

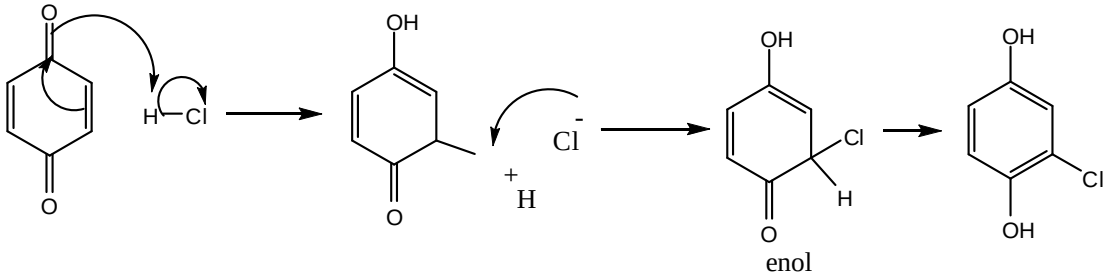


azophenine

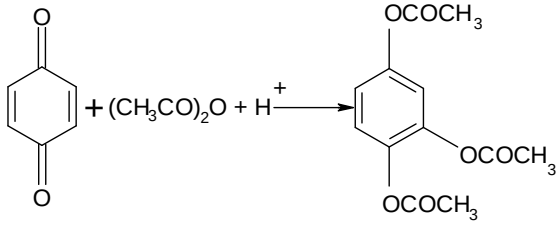
This conjugate addition of nucleophilies to the olefenic carbon atom of quinones is a very general reaction .A good example is addition of cyanide as illustrated



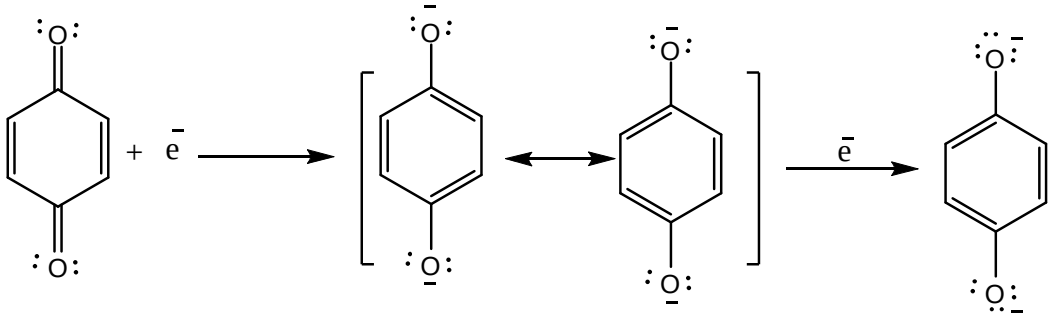
Electrophiles as well as nucleophilies add to an isolated carbonyl double bond, so acid will add electrophilically to quinones, usually in a conjugate fashion for example, the addition of hydrogen chloride yields 2-chloroquinol.



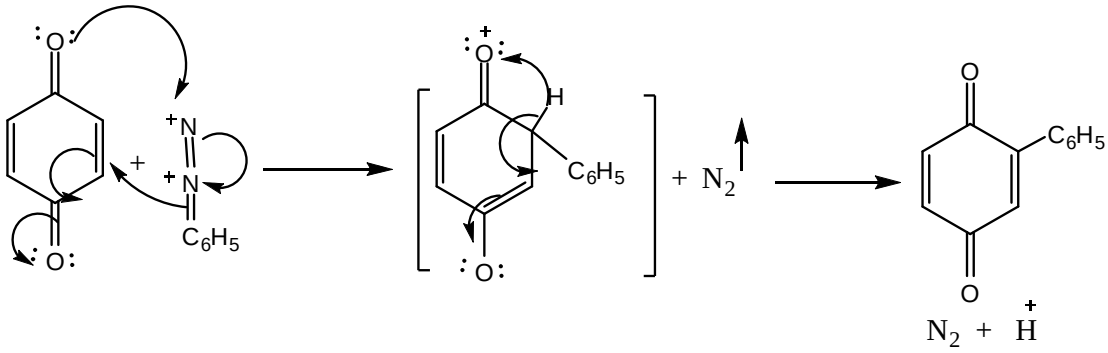
A similar reaction occurs with acetic anhydride and strong acid



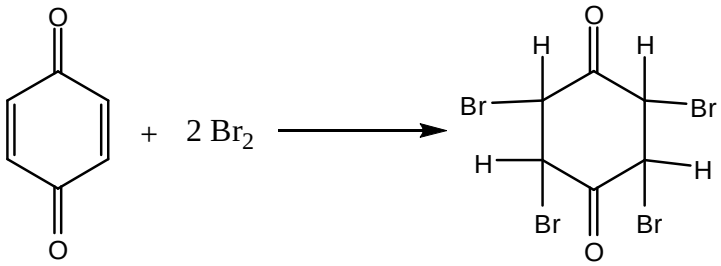
The reduction of quinone is a two-stage process and in many cases the presence of the semiquinone radical ion can be established.



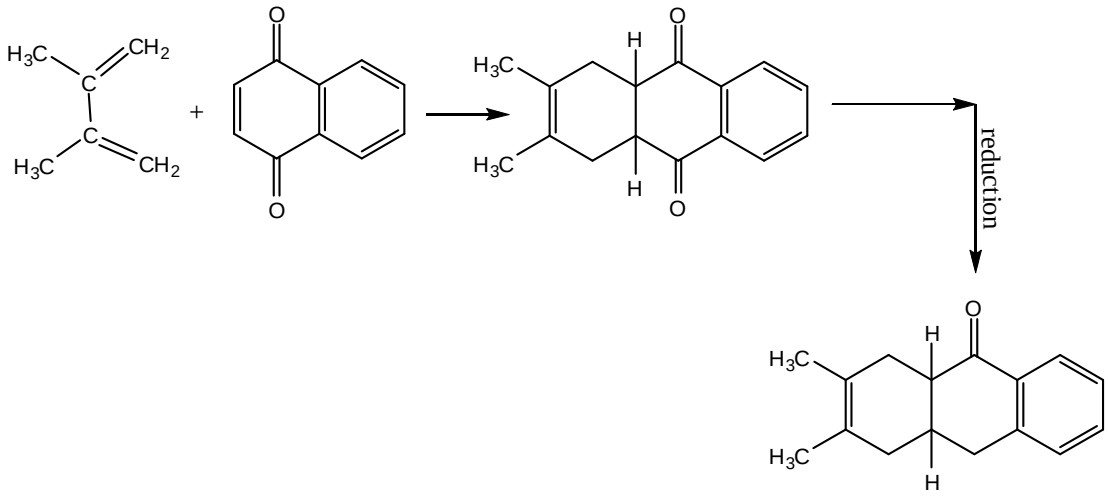
In some reactions this one electron transfer can be important; for example when quinone is treated with diazonium salt, nitrogen is evolved the overall mechanism of reaction is possibly as follows:



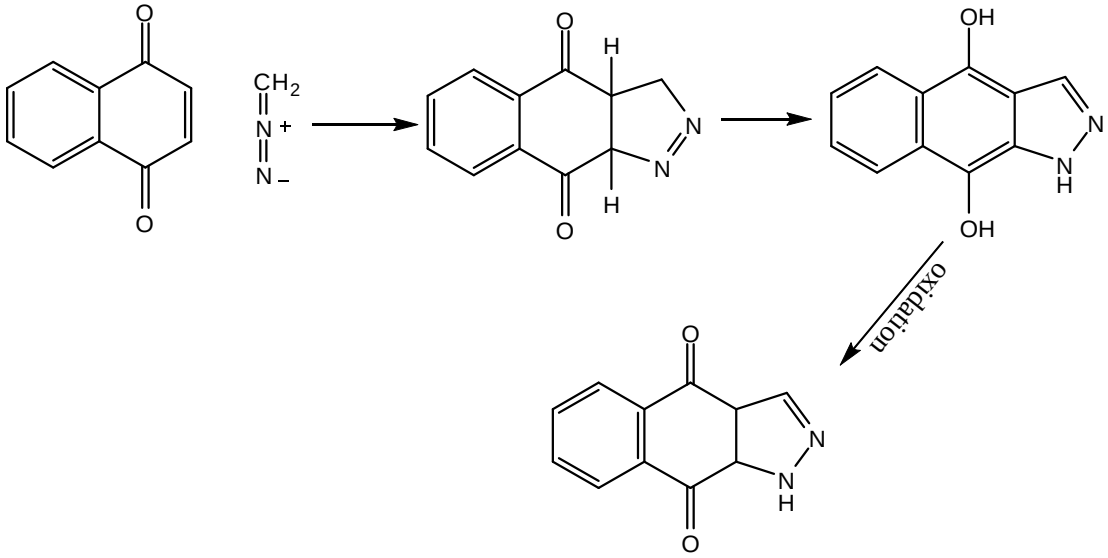
Direct addition to the carbon-carbon double bond can occur in special case, for example, bromine reacts with quinone to give the saturated tetrabromodiketone.

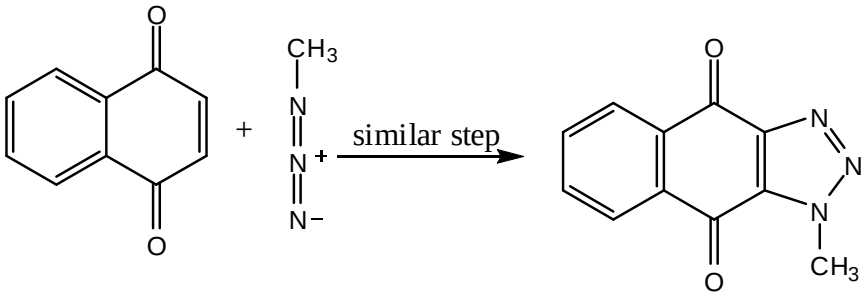


In diels Alder reactions the ethylenic double bond in quinone has two adjacent carbonyl bonds and it undergoes the reaction very readily, acting as adinophile (Tedder and Nechvatal.1967).



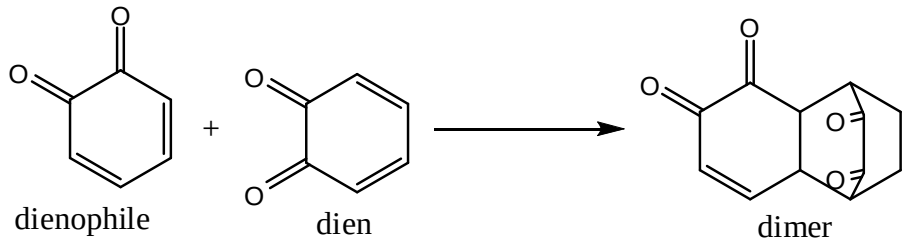
The carbon – carbon double bond in quinones undergoes this electrodic addition quite generally and not only will dienes add but also other such as reagents adiazomethane and methylazide (Geissman.1977).





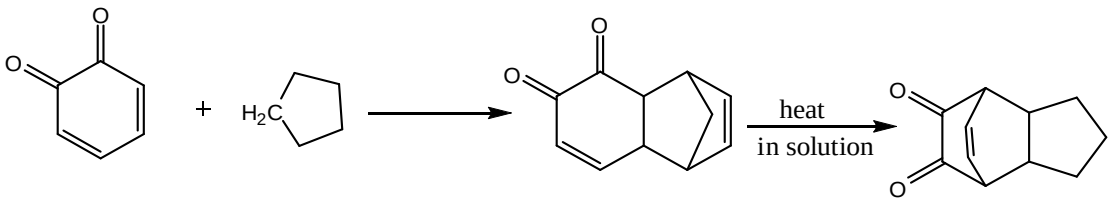
o-benzoquinone has much higher electrod potential than p-benzoquinone it also much more reactive although it can be prepared enstalline if

decomposed with a half and a hour of its preparation. In solution it undergoes Diels-Alder reaction with itself as a diene and dienophile.

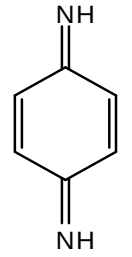


dienophile dien dimer

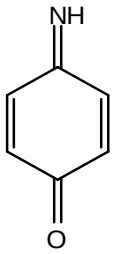
With acydopentadiene or cyclohexadiene o-benzoquinone behaves as adienophile although the alternative adduct is formed on heating



we can risualize a nitrogen analogue of quinone in which the oxygen atom is replaced by an nitrogen such compounds are known as quinone imines (Tamson.1997), (Kstewari *et al*., 1998).



quinone di-imine

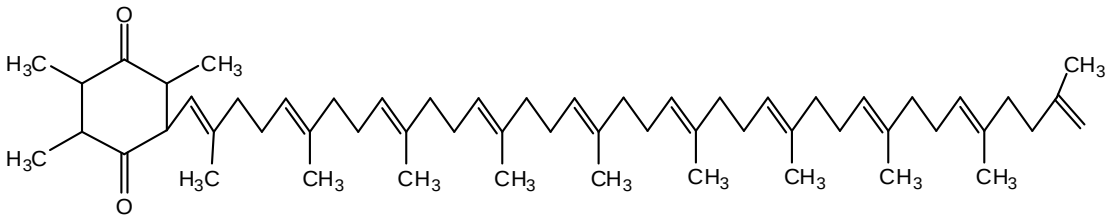


quinone imine

1.7 Antibacterial and antifungal activities of quinones

Quinones of many kinds are important compounds both, because of their wide-spread occurrence in nature as the products of plants and animals metabolism and because of their use in medicine especially as electro carriers(Martius.1961),(Green *et al*., 19965),(Redfearn and Burgas.1966).

The largest number of quinones are obtained synthetically among them 2-hydroxy-3-alkyl-1,4-naphthoquinones which are active against malaria parasite (Fieser and Leffler.1948) and 2-methyl-1,4;naphthaquinone is a clinically useful (vitamin K1) which in used combat certain diseases characterized by reduced clotting power to the blood. A group of quinones typed by the one shown below but differing in the length of the chain of five carbon atoms units are widely distributed in living cells in which they play important roles in metabolism/ probably by electron transfer involving reversible quinone interconversion.



Conzime Q10

Other derivaties are active against bacteria and fungi and marine organism, in many of which they are responsible for yellow orange and red color.Geissman.1977),(Holmes *et al*., 1964).

1.8 Aim and Objectives:

p.quinone α,β-unsaturated diketones are one of the most important naturally occurring or synthetic group of compounds through their incorporation in different biological processes. On the other hand different classes of sulfonamides of process various types of biological activities. The present work aimed at make use of the richness of the quinonoid unit on witch selected and design sulfonamide can be allowed to couple to the required p.quinones. One of the aim of this study is to prepare some derivative of p.quinone, different p.quinone structures have been used in this study and a selected amines which satisfied certain structural requirement where considered. The synthetic procedures mechanetic explanation and retrosynthetic analysis of the target amino-p-quinones form one of the objectives of this study. The chromatoghraphic behavior especially Thin Layer Chromatography (TLC) of the p-quinones and their amines coupled products have been investigated and compared.

The study may highlight upon certain vibrational and electronic spectral patterns of quinones. Deep insight into benzenoid and quinoid rings spectral properties could be summarized from this work.

Chapter two

2. Materials and Methods

2.1 Materials

2.1.1Chemicals

Chrlorosulphonic acid, acetaanalide, sulfamethoxzyle,4-aminophenzone, sulfadioxine,sulphonylamide,sulfasufonylamide,sulfadoxine,o.cresol, naphthalene, potassium dichromate, sodium hydroxide, hydrochloric acid, sodium hydrosulfyte, amoniumchloride, ammonia solution,nitric acid, sulfuricacid,ethanol,methanol,acetone,diethylether,chloroform,dimethylsulfoxide, ethyl acetate, n-butanol. All GPR, were obtained for BDH, England.

2.1.2 Thin layer chromatography

Thin layer chromatography was carried out using silica gel 60 GF254 pre- coated plates (250µ) over aluminum plate (Mereck) with different solvent system.

2.2 Instruments

2.2.1 Infra red spectroscopy (IR)

Infra red spectral data were recorded as KBr film disc using IR instrument model Perkin Elmer (1000), (USA)

2.2.2 Nuclear magnetic resonance (^{1}H-NMR, ^{13}C-NMR) spectroscopy

The proton nuclear magnetic resonance spectral data were obtained with NMR instrument model (Bruker, Germany) 500, 133 Hz.

2.2.3 Mass spectroscopy (MS)

MS. used in this work is ISQ Single Quadrupole MS.Perkin Elmer(USA).

2.2.5 General Equipments

Magnetic stirrer, hotplate, (ST 15 OSA, BIBBI sterilin LTD, UK), melting point apparatus (SMP 10, PIPPY sturat scientific, UK), sensitive balance (ADA 210 LE, ADAM EQUIPMENT Co.LTD JAPAN), thermometer (Gallen Kam. England), all glassware was of pyrex type.

2.3 Synthetic methods

2.3.1 Synthesis of *p*-acetomedobenzenesulfonylchloride (II)

To 15.0 c m^3 of chlorosulphonic acid in dry flask in ice bath (cold water) was added gradually in small portions 7 grams of acetanilide with stirring, the mixture was heated on water bath for one hour to complete the reaction, the clear solution was powered into 300gm of crushed ice, the product filtered and air dried.

2.3.2 Synthesis of *p*-acetomedobenzenesulfonamide (III,V,VII,IX,XI)

To (1.77g) 10mmole (1.77g) of the required amine dissolved in (20mmole) (0.8 g) sodium hydroxide in 100ml water in flask was added p.acetmedo benzene sulphonylchloride. The reaction mixture was stirred

for two hours at 60 $^{\circ}$ **C**. The solution was filtered, cooled to room temperature and acidified with dilute hydrochloric acid.

2.3.3 Synthesis of *p*.aminobenzene sulphonylamide (IV,VI,VIII, X and XII)

To one gram *p*.acetomedobenzene sulphon amide derivatives in 100ml round bottomed flask was added 20ml of dilute hydrochloric acid (1:1). The mixture was heated under reflux directly in hot plate and stirring for two hours. The clear solution was filtered while hot and cooled to room temperature. Sodium hydroxide was added to adjust the pH to 4.5. The product filtered, washed and recrystallized.

2.3.4 Synthesis of 1,4-quinone derivatives

2.3.4.1Synthesis of 1,4-naphthaquinone

On 500ml round bottomed flask with three-necked 20g (0.2mol) of pure chromium trioxide was added to 25ml of 80% acetic acid, the flask was surrounded by ice and put in a magnetic stirrer and thermometer to read temperature. Solution of pure naphthalene in 100 ml of glacial acetic acid was added over a period of 2-3 hours while the temperature maintains 10-5 ^{o}C. The stirring was continued overnight in room temperature; the dark green solution was left for three days and stirred occasionally. The mixture was poured into 1litre of water; the crude product was collected by filtration and washed by 30ml of water, dried and recrystallized from 63ml of petroleum ether (Babula *et al*., 2007).

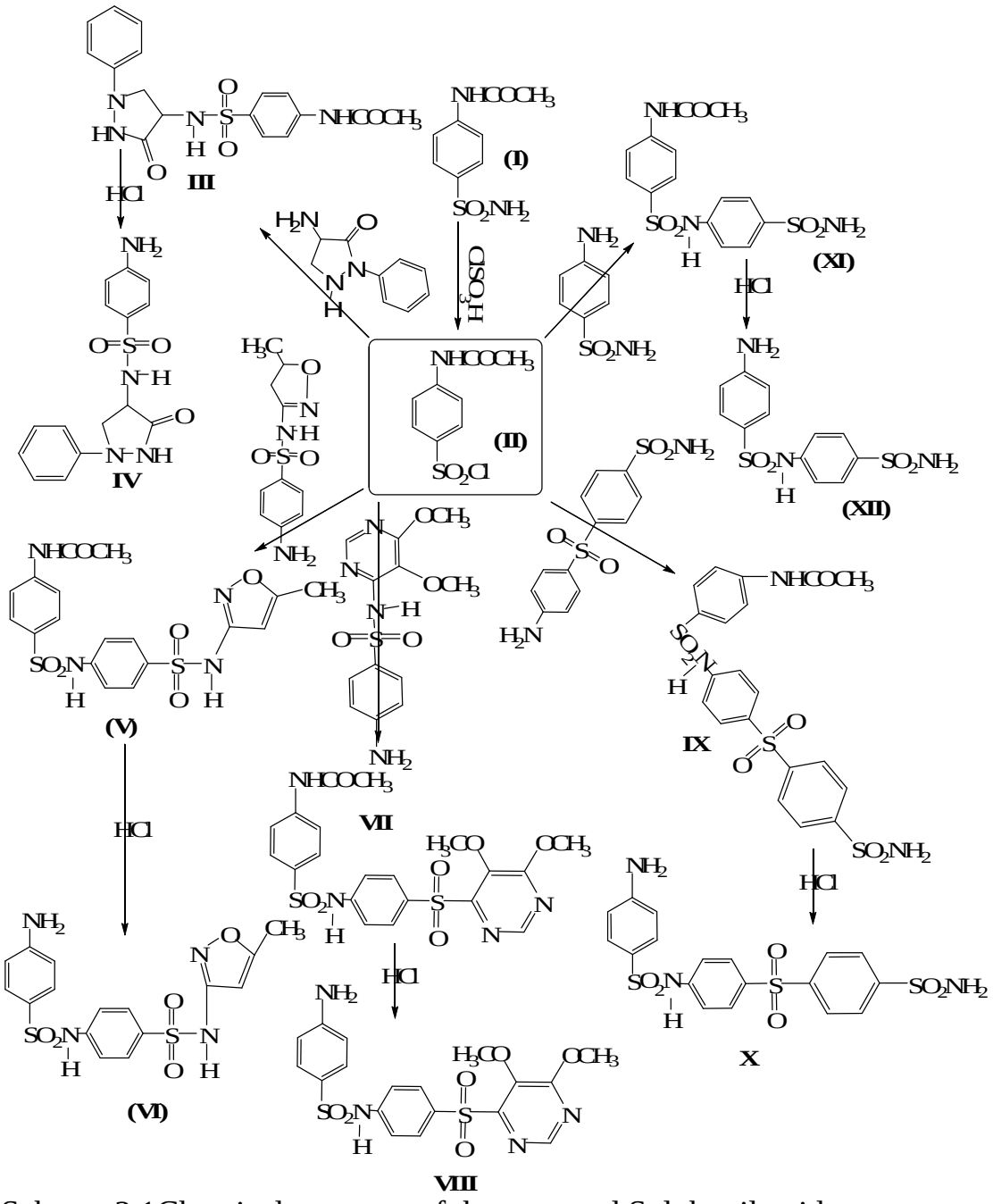
2.3.4.2 Synthesis of 2-methylbenzoquinone

In 500ml beaker was placed 32gm (0.33mol) *o*.cresol in 90ml of 60% acetic acid and the beaker was cold until the temperature below 5 $^{\circ}$**C** in ice. A solution of 42g of chromium trioxide in 70ml water on 30ml of

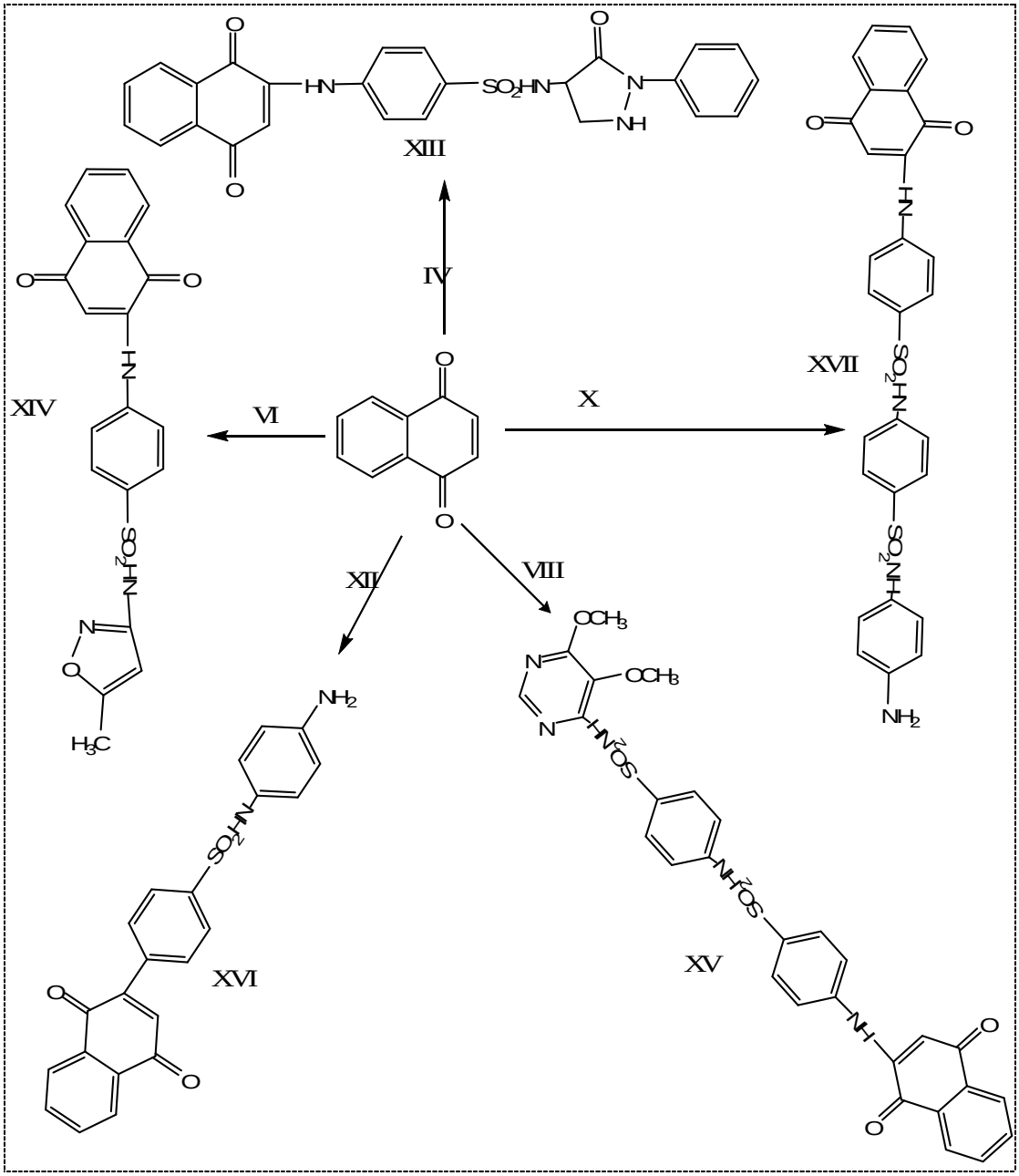
glacial acetic acid was added in period about two hours and the temperature below 10 $^{\circ}$**C.** The mixture was filtered at once and washed 10ml portions of ice –cold water several time and dried (Anees Pangal *et al.*, 2013).

2.3.4.3 General synthesis of 2-sulfonamido-1,4- quinone

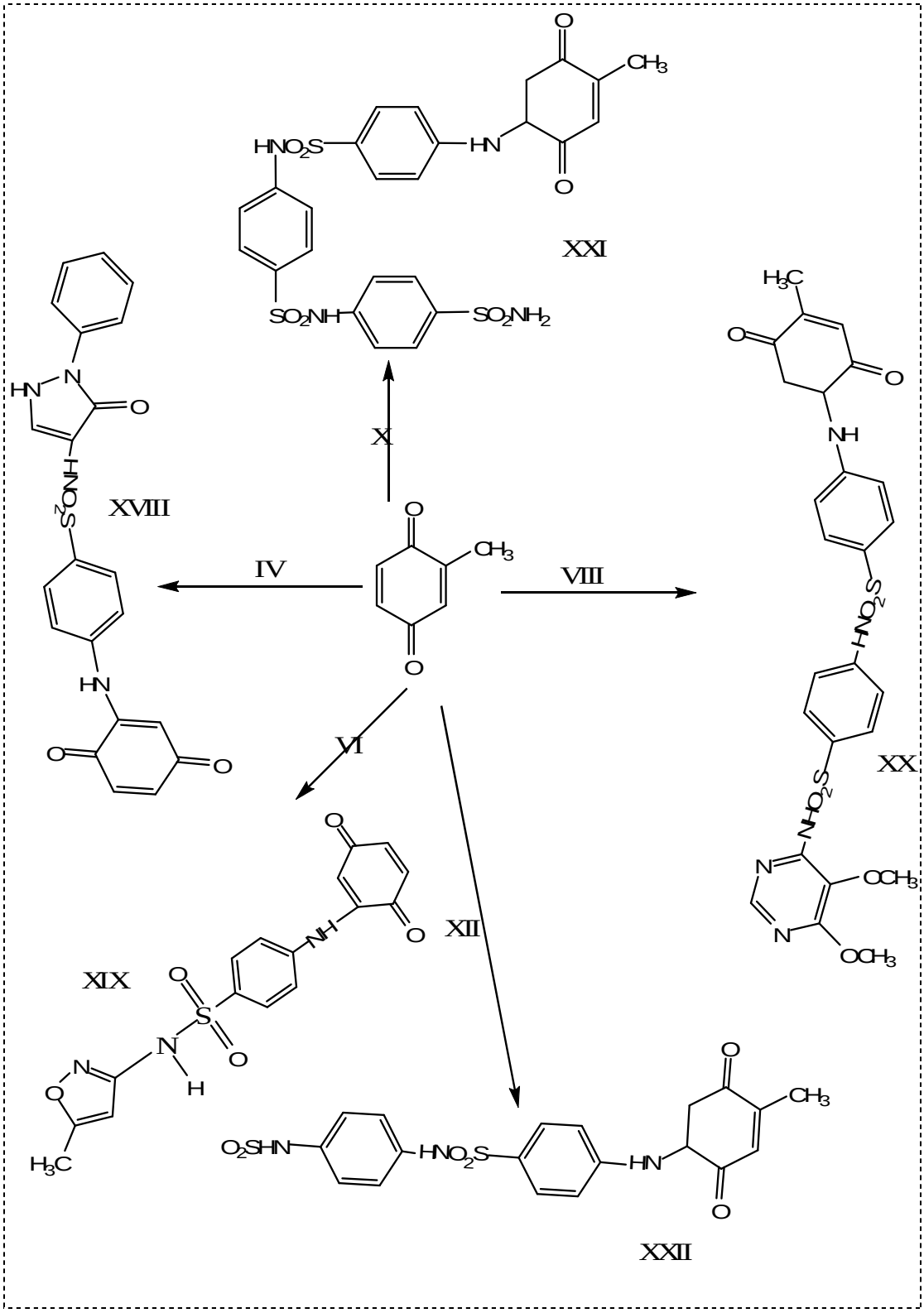
In 50ml quickfit round bottom flask was placed 0.002mol of the required 1,4-quinone in 20ml of 95% ethanol, 1ml of glacial acetic acid and 1ml of water, the mixture was stirred at room temperature, 0.001mol of the required sulphonamide in 10ml of 95% ethanol and 0.1gm of anhydrous sodium acetate was added over a period of five minutes. The reaction mixture was refluxed under stirring for three hours. The precipitate was filtered and washed by addition of 3-5ml cold water, the product was air dried and recrystallized (Ravichandiran *et al*., 2012).



Scheme 2.1Chemical structure of the prepared Sulphonilamide derivatives. (III-XII).



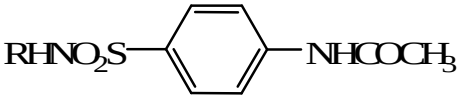
Scheme 2.2 Coupling of naphthoquinone and sulfonamide (XIII-XVII).



Scheme 2.3 Coupling of o-methylbenzooquinone and sulfonamide (XVIII-XII).

Table 2. 1: Chemical names of synthesized compounds

Table 2.1.1: Chemical names of p.acetamidobenzene sulfonylamides



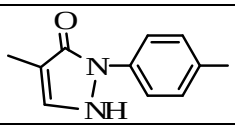
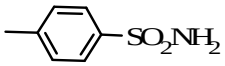
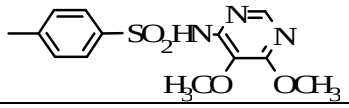
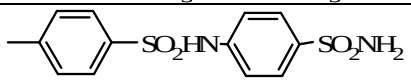
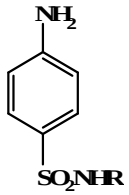
Comp. No	R	Chemical names
III		N-(4-(N-(5-oxo-1-phenylpyrazolidin-4-yl)sulfamoyl)phenyl)acetamide
V		N-(4-(4-(5-methylisoxazole-3-sulfonamido)phenylsulfonamido)phenyl)acetamide
XI		N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)acetamide
VII		N-(4-(N-(4-(N-(5,6-dimethoxypyrimidin-4-yl)sulfamoyl)phenyl)sulfamoyl)phenyl)acetamide
IX		N-(4-(N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)sulfamoyl)phenyl)acetamide

Table 2.1.2: Chemical names of p.aminobenzene sulphonylamide



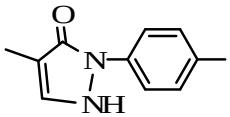
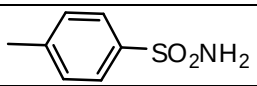
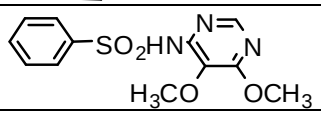
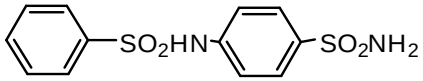
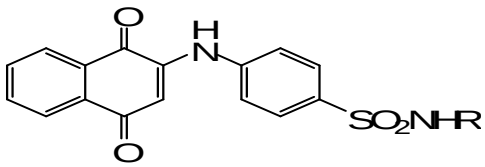
Comp. No	R	Chemical names
IV		4-amino-N-(5-oxo-1-phenylpyrazolidin-4-yl)benzenesulfonamide
VI		4-amino-N-(4-(N-(5-methylisoxazol-3-yl)sulfamoyl)phenyl)benzenesulfonamide
XII		4-amino-N-(4-sulfamoylphenyl)benzenesulfonamide
VIII		4-amino-N-(4-(N-(5,6-dimethoxypyrimidin-4-yl)sulfamoyl)phenyl)benzenesulfonamide
X		4-amino-N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)benzenesulfonamide

Table 2.1. 3: Chemical names of coupling compounds with naphthaquinone



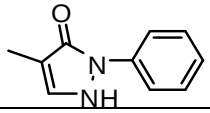
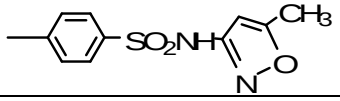
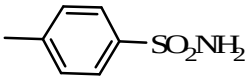
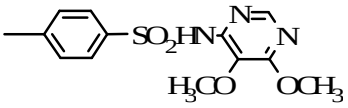
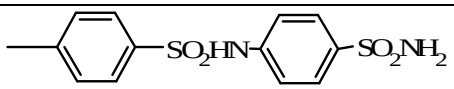
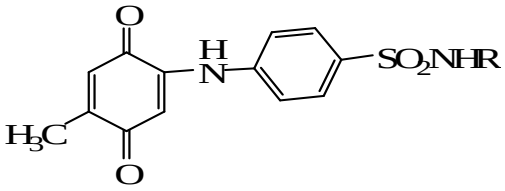
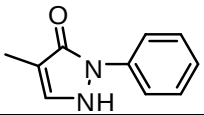
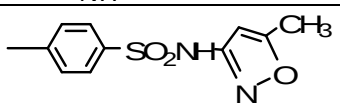
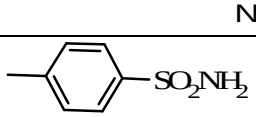
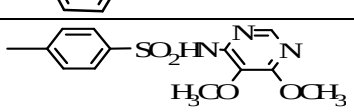
Comp. No	R	Chemical names
XIII		4-(1,4-dioxo-1,4-dihydronaphthalen-2-ylamino)-N-(5-oxo-1-phenylpyrazolidin-4-yl)benzenesulfonamide
XIV		4-(1,4-dioxo-1,4-dihydronaphthalen-2-ylamino)-N-(5-methylisoxazol-3-yl)benzenesulfonamide
XVI		N-(4-aminophenyl)-4-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)benzenesulfonamide
XV		N-(5,6-dimethoxypyrimidin-4-yl)-4-(4-(1,4-dioxo-1,4-dihydronaphthalen-2-ylamino)phenylsulfonamido)benzenesulfonamide
XVI		N-(4-aminophenyl)-4-(4-(1,4-dioxo-1,4-dihydronaphthalen-2- ylamino) phenylsulfonamido)benzenesulfonamide

Table 2.1. 4: Chemical names of coupling compounds with 2-.methylbenzylquinone



Comp. No	R	Chemical names
XVIII		4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) benzenesulfonamide
XIX		4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(5-methylisoxazol-3- yl) sulfamoyl)phenyl)benzenesulfonamide
XXII		4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-sulfamoylphenyl)benzenesulfonamide
XX		N-(5,6-dimethoxypyrimidin-4-yl)-4-(4-(4-methyl-3,6-dioxocyclohexa-1,4- dienylamino) phenylsulfonamido)benzenesulfonamide

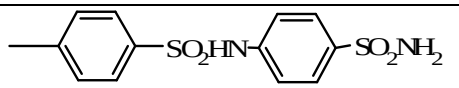
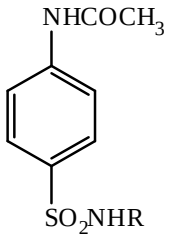
XXI		4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)benzenesulfonamide

Table 2.2.Reaction conditions of synthesized compounds

Table 2.2.1.Reaction conditions of p-acetamedobenzenesulfonyl derivatives



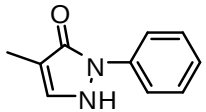
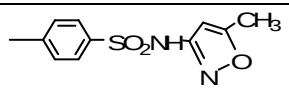
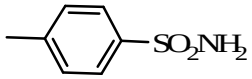
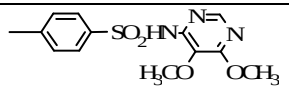
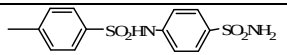
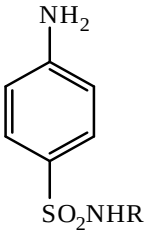
Comp. No	R	Re. Time	Temp	Recy.solv	Yeild %	m.p	Mo.Ph.sol	R_f
III		3hurs	60°C	EtOH	70%	276	Chloroform:MeOH	0.7
V		3hurs	60°C	EtOH	79%	141	Chloroform:MeOH	0.71
XI		3hurs	60°C	EtOH	73%	153-155	Chloroform:MeOH	0.61
VII		3hurs	60°C	EtOH	80%	195	Chloroform:MeOH	0.92
IX		3hurs	60°C	EtOH	79%	172	Chloroform:MeOH	0.82

Table 2.2.2.Reaction conditions of p-aminobenzenesulfonyl derivatives



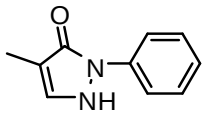
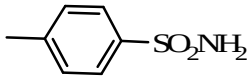
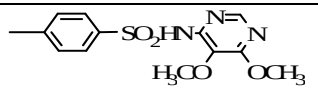
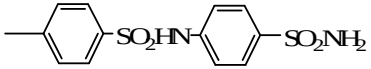
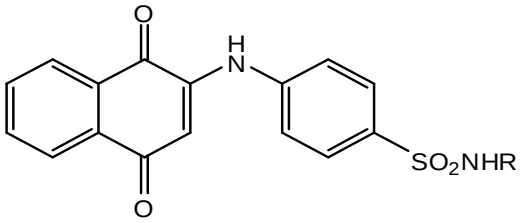
Comp. No	R	Re. Time	Temp	Recy. solv	Yeild %	m.p	Mo.Ph.sol	R_f
IV		2hurs	45°C	EtOH	65%	238-242	Chloroform:MeOH	0.6
VI		2hurs	45°C	EtOH	77%	220	Chloroform:MeOH	0.67
XII		2hurs	45°C	EtOH	79%	167- 169	Chloroform:MeOH	0.61
VIII		2hurs	45°C	EtOH	79%	142	Chloroform:MeOH	0.62
X		2hurs	45°C	EtOH	75%	175- 179	Chloroform:MeOH	0.73

Table 2.2.3.Reaction conditions of naphthoquinone derivatives



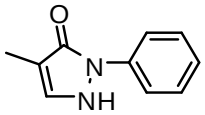
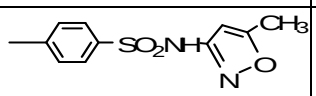
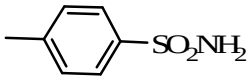
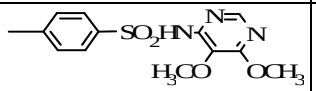
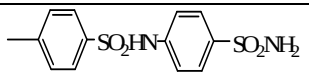
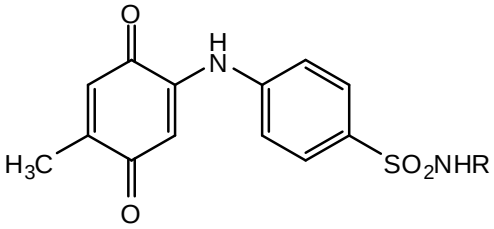
Comp. N	R	Re. Time	Temp	Recy.solv	Yeild %	m.p	Mo.Ph.sol	R_f
XIII		24hurs	room	p.ether	71%	293-295	Chloroform:MeOH	0.6
XIV		24hurs	room	p.ether	80%	285	Chloroform:MeOH	0.75
XVII		24hurs	room	p.ether	72%	273- 277	Chloroform:MeOH	0.65
XV		24hurs	room	p.ether	72%	265-267	Chloroform:MeOH	0.78
XVI		24hurs	room	p.ether	70%	289- 290	Chloroform:MeOH	0.60

Table 2.2.4.Reaction conditions of methylbenzoquinone derivatives



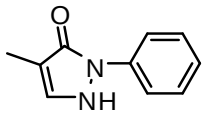
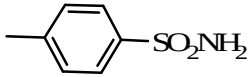
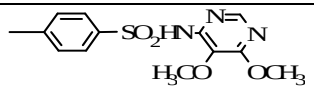
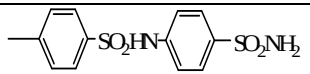
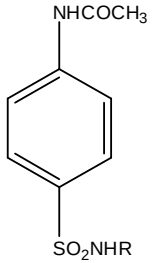
Comp. No	R	Re. Time	Temp	Recy.solv	Yeld %	m.p	Mo.b.sol	R_f
XVIII		24hurs	room	ligroin	60%	292	toluene	0.62
XIX		24hurs	room	ligroin	69%	235	toluene	0.65
XXII		24 hurs	room	ligroin	72%	215- 220	toluene	0.60
XX		24hurs	room	ligroin	65%	249-250	toluene	0.75
XXI		24 hurs	room	ligroin	73%	255	toluene	0.65

Table 2.3 Infrared spectrum

Table 2.3.1 Infrared spectrum bands of synthesized compounds



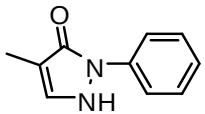
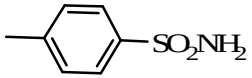
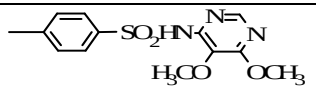
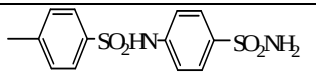
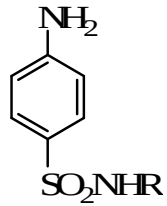
Comp. No	R	SO_2 st–vib	C=O st–ib	C=C arom	C –H. st	CH arom	N – H st-vib	Other NH, SO_2NH
III		1369 -1153	1697	1587,1534,1496	2990	3036	3479,3415,3243	840 p
V		1367,1332,1155	1672	1618,1596, 1469	2990	3040	3413,3379,3299	833 p, 1092 C-O
XI		1372, 1155	1685	1591,1533,1502	2936	3049	3502,3412, 3331,3277	834 p
VII		1320,1159	1674	1586,1534,1453	2942	3040	3469,3414,3236	840 p
IX		1397,1326	1676	1591,1566,1533	2990	3049	3460,3400,3236	840 p

Table 2.3.2 Infrared spectrum for *p*-aminobenzenesulphnilamide compounds



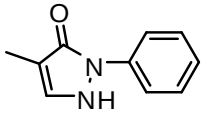
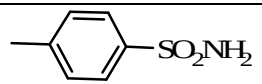
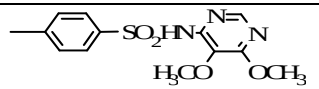
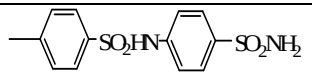
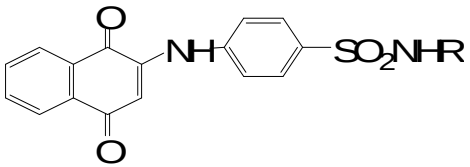
Comp. No	R	N – H st-vib	N –H bend	SO_2	N – H st-vib for SO_2NH	C=C	other
IV		3502,3464	1610	1363,1148	3330	1595,1496	3209 (N-H), 2980 (C-H) 1630 (C=O) 872 P
VI		3478,338	1634	1385,1321,1189 .1150	3234,3210	1597 ,1461	2990 (C-H), 1090 (C-O), 895 P
XII		3592,3449	1629	1327,1144	3364	1591, 1464	823 P
VIII		3474,3415	1618	1320,1154	3234	1592, 1448	2935 (C-H), 834 P
X		3600,3592	1618	1325,1119	3233	1591, 1488,	840 P

Table 2.3.3 Infrared spectrum for coupling compounds with naphthoquinone



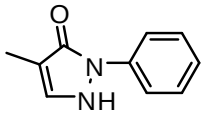
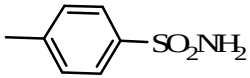
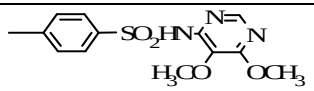
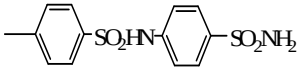
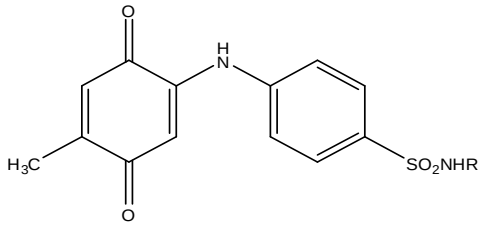
Comp. NO	R	C=O	N – H	SO_2	C=C
XIII		1675, 1625,1666	3801,3280	1360,1157	1589,1521
XIV		1676,1616,1589	3307,3180	1332,1294,1271	1527,1510,1480
XVII		1674,1620	3286,3270	1321,1155	1585,1515,1404
XV		1664,1589	3434,3278	1296,1159	1448,1332
XVI		1676,1625	3371,3284,3200	1330,1155	1583,1539

Table 2.3.4 Infrared spectrum for coupling compounds with 2-methylbenzoquinone



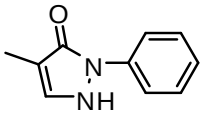
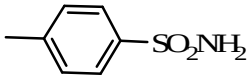
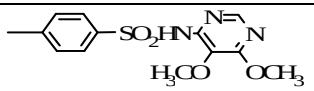
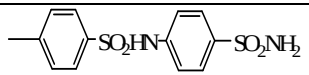
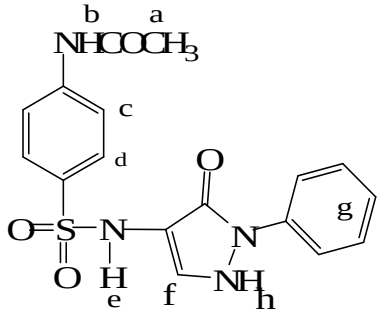
Compd NO	R	C=O	N – H	SO_2	C=C	other
XVIII		1652	3386, 2921, 2360	1119	1595, 1481	877 p
XIX		1652	3419	1191	1600, 1467	
XXII		1652, 1710	3409, 2993, 2360	1190,1116, 1041	1600, 1483	676 p
XX		1652	3382	1191,1155	1593,1483, 1448	823p, 2923 CH
XXI		1652	3438, 2921	1190, 1118	1602, 1482	873p

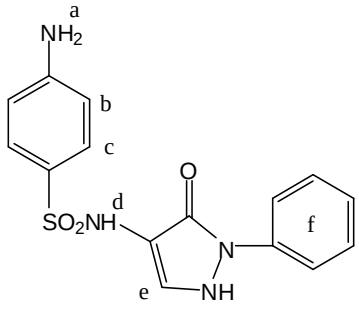
Table 2.4 proton nuclear magnetic resonance spectrum bands of synthesized compounds (^{1}H –NMR)

Table 2.4.1 (^{1}H–NMR) spectrum bands of *p*-acetamidobenzenesulfonyl-4-amino phenazone



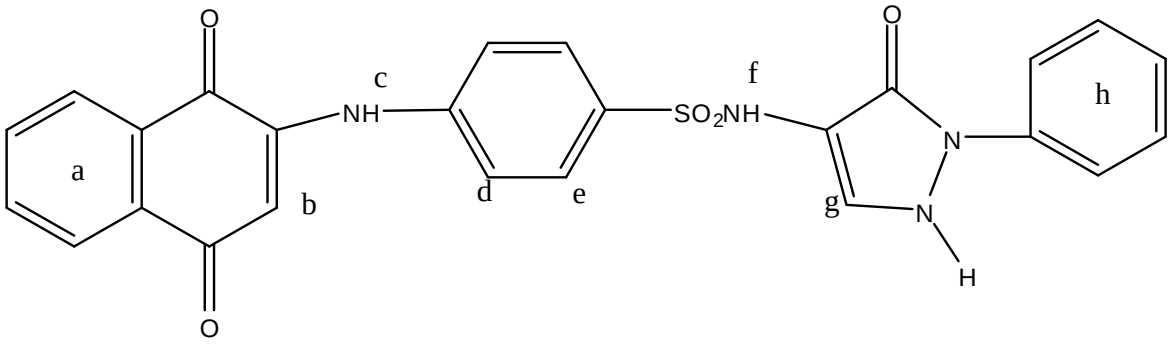
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
III DMSO-d6	a, 1.93(3, s); b, 5.88(1, s); c, 6.5(2, d, J = 2.0 Hz); d, 7.2(2,d, J = 3.0 Hz); e, 8.67(1, s); f, 7.30(1. s); g, 7.41 – 7.47(5, m)

Table 2.4.2 (H^1 – NMR) spectrum bands of *p*-aminobenzenesulfonyl-4-amino phenazone



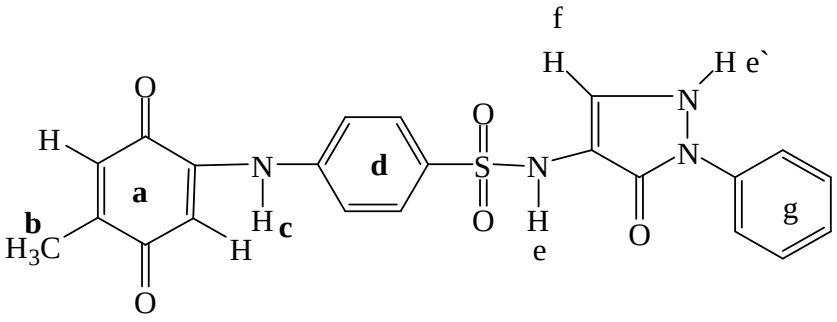
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
IV DMSO-d6	a, 2.00(2, s); b, 7.24(2, d, J = 3.0 Hz); c, 7.45(2, d, J = 2 Hz); d, 10.29(1, s); e, 9.08(1, s); f, 7.44 – 7.46 (5, m).

Table 2.4.3 (^{1}H – NMR) spectrum bands of coupling of Naphthoquinone and p-aminobenzenesulfonyl-4-aminophenazone.



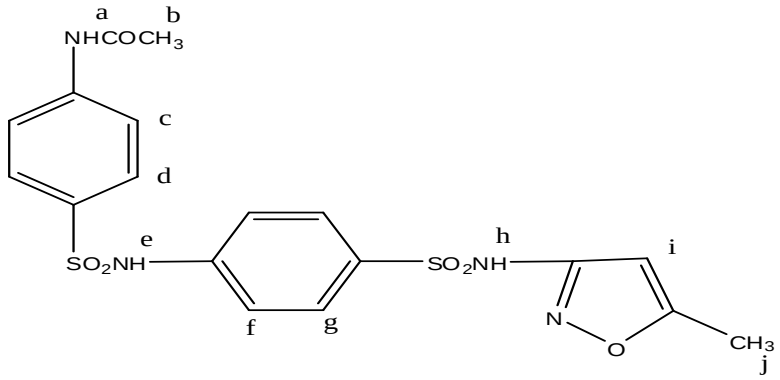
Compd No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XIII DMSO-d6	a, 7.25 – 7.32 (5m); b, 7.45 (1,s); c, 9.407 (1,s); d, 7.81(2,d, J = 3Hz); e, 7.91 (2,d, J = 4Hz); f, 9.21 (1,s); g, 8.08 (1,s); h, 7.92 – 7.98 (5, m)

Table 2.4.4 (^{1}H–NMR) spectrum bands of coupling of p-aminobenzenesulfonyl-4-aminophenazone and methylbenzoquinone .



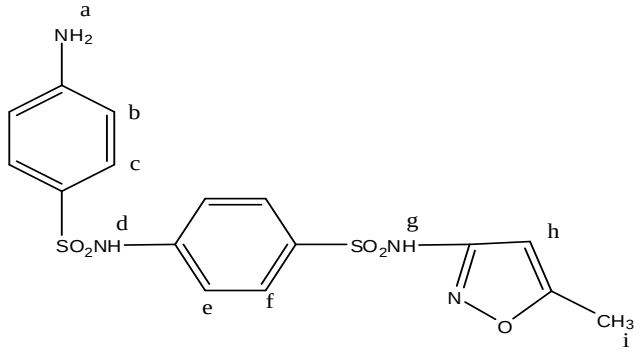
Compd No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XVIII DMSO-d6	a, 6.87 , 7.32 (2s); b, 2.80 (3,s); c, 4.20 (1,s); d, 6.47-.7.62(4,m,); e, 2.01 (2,s); f, 5.44 (1,s); g, 6.90-7.65 (5,m).

Table 2.4.5(^{1}H–NMR) spectrum bands of *p*-acetamidobezenesulfonyl sulfamethoxazole



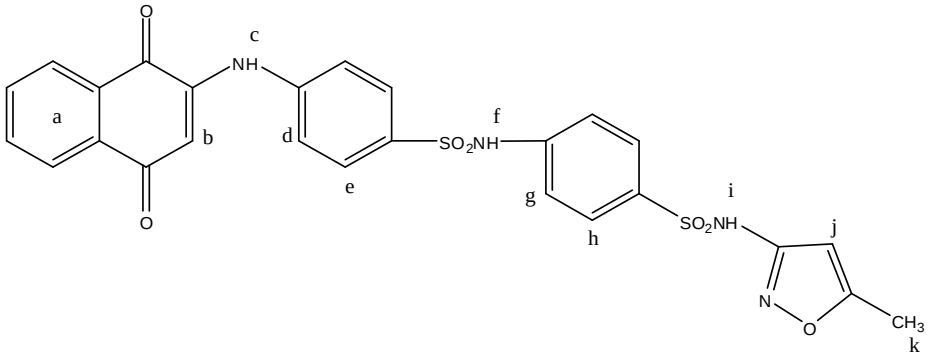
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
V DMSO-d6	a, 10.03 (1,s); b, 2.06 (3,s); c, 6.08 (2,d, J = 3.0 Hz); d, 7.25 (2,d, J= 3 Hz); e, 10.89 (1,s); f, 7.47 (2,d, J = 3.0 Hz); g, 7.75 (2,d, J = 4 Hz); h, 11.77 (1,s), I, 7.70 (1,s); j, 2.28 (3,s)

Table:2.4.6(^{1}H–NMR) spectrum bands of *p*-aminobezenesulfonyl sulfamethoxazole



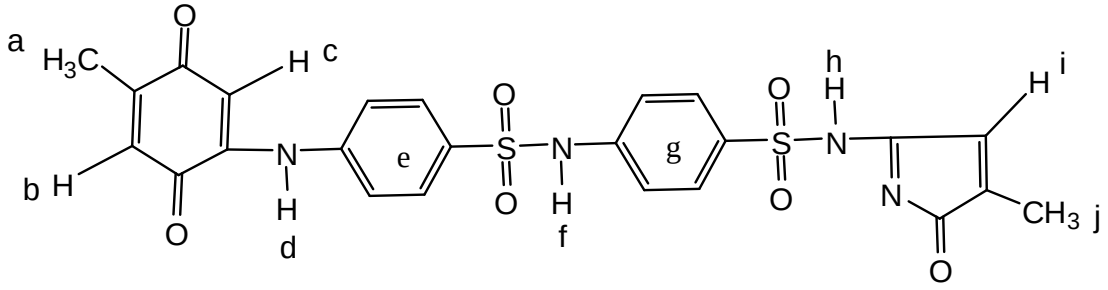
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
VI DMSO-d6	a, 2.28 (2,s); b, 6.05 (2,d, J = 2 Hz); c, 6.56(2,d, J = 3 Hz); d, 11.24 (1,s); e, 7.21 (2,d, J = 2 Hz); f, 7.47 (2,d, J = 4 Hz); g, 10.58 (1,s); h, 7.69 (1,s); i, 3.36 (3,s).

Table 2.4.7 (^{1}H–NMR) spectrum bands of Coupling of naphthaquinone and *p*-aminobezenesulfonyl sulfamethoxazole.



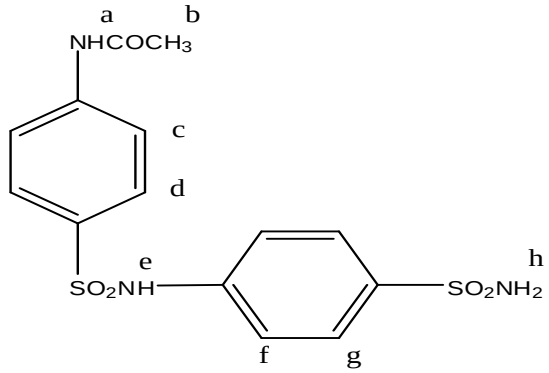
Compd No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XIV DMSO-d6	a, 7.80 – 7.85 (5,m); b, 7.24 (1,s); c, 11.29 (1,s); d, 6.08 (2,d, J = 3Hz); e, 7.2 (2,d, J = 4 Hz); f, 11.04 (1,s); g, 7.27 (2,d, J = 4 Hz); h, 7.59 (2,d, J= 3 Hz); i, 9.5 (1,s); j, 7.70 (1,s); k, 3,29 (3,s).

Table 2.4.8 (^{1}H–NMR) spectrum bands of Coupling of *p*-aminobezenesulfonyl and naphthoquinone.



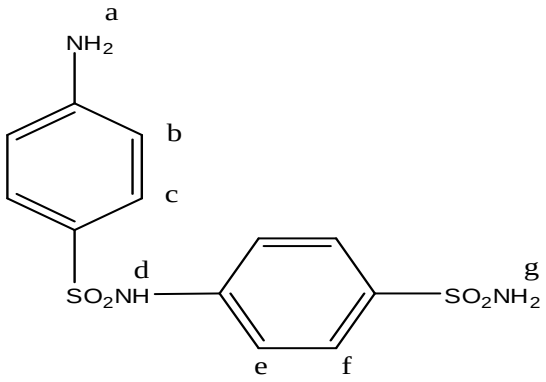
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XIX DMSO-d6	a, 2.50 (3,s); b, 6.69 (1,s); c, 6.25 (1,s); d, 5.4 (1,s); e, 6.47 – 7.70 (4,m,); f, 7.8 (1,s); g, 6.91-7.49 (4,m); h, 2..06 (1,s,); i, 5.44 (1,s); j, 2.54(3,s).

Table 2.4.9 (^{1}H– NMR) spectrum bands of *p*-acetamedobezenesulfonyl sulfonyl amide



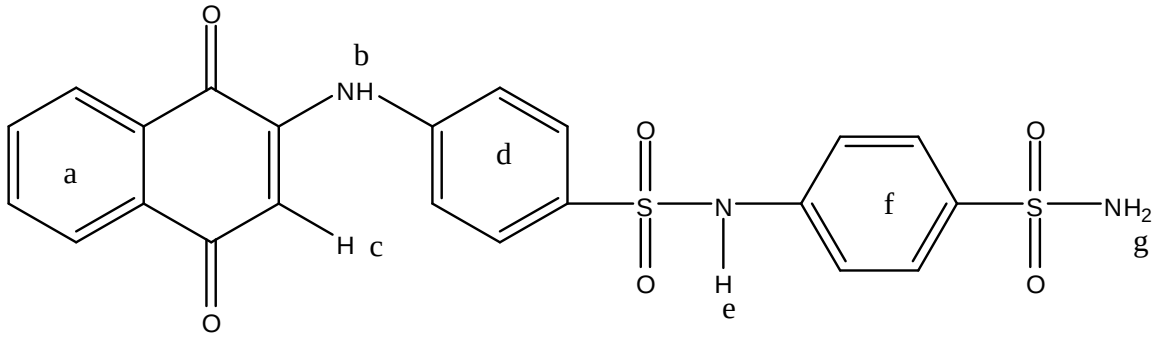
Compd No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XI DMSO-d6	a, 2.05 (3,s); b, 10.30 (1,s); c, 7.19 (2,d, J = 3 Hz); d, 7.66 (2,d, J = 4 Hz); e, 10.70 (1,s); f, 7.72 (2,d, J = 4 Hz); g, 7.77 (2,d, J = 4.5 Hz); h, 3.37 (2,s).

Table 2.4.10 (^{1}H – NMR) spectrum bands of *p*-aminobezenesulfonyl sulfonyl amide



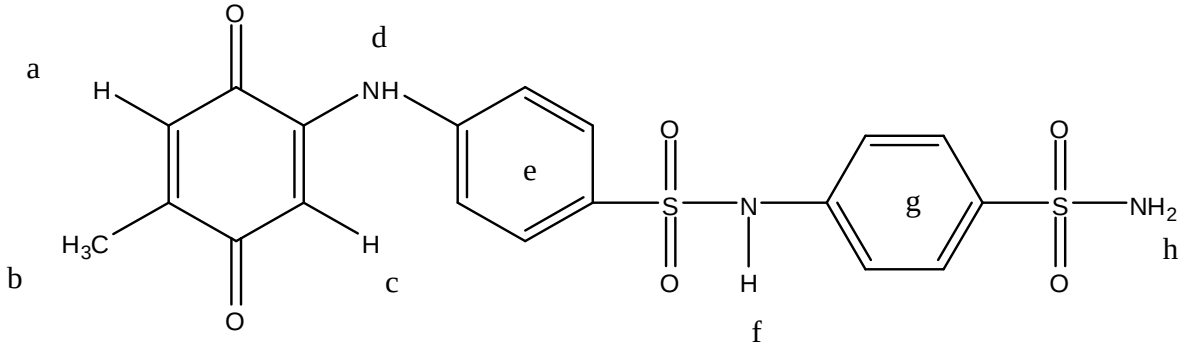
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XII DMSO -d6	a, 2.50 (2,s); b, 6.02 (2,d, J = 3 Hz); c, 7.17 (2,d, J = 4 Hz); d, 10.41 (1,s); e, 7.45 (2,d, J = 3 Hz); f, 7.66 (2,d, J = 3 Hz); g, 3.35 (2,s).

Table 2.4.11: (^{1}H – NMR) spectrum bands of *p*-acetamedobezenesulfonyl sulfonyl amide and naphthoquinone



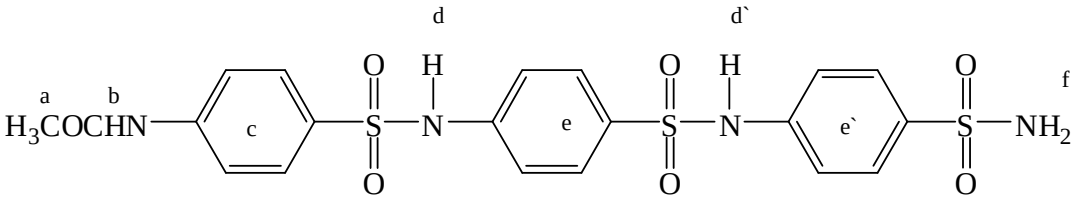
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XVII DMSO-d6	a, 7.60 – 7.98 (4,m); b, 3.35 (1,s); c, 7.34 (1,s); d, 6.32-7. 60 (4,m,); e, 9.42 (1s,); f, 7.37-7.59 (4m,), g, 7.58 (2,s).

Table 2.4.12: (^{1}H–NMR) spectrum bands of *p*-aminobezenesulfonyl sulfonyl amide and methylbenzoquinone.



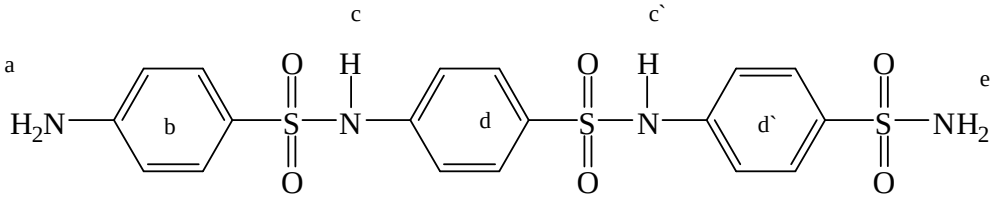
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XXII DMSO-d6	a, 6.72 (1,s) , b,2.48 (3,s); c, 6.35 (1,s); d, 4.05 (1,s); e, 6.72-7.64 (4m); f, 7.97 (1,s); g, 6.91-7. (4,m); h, 7.18 (1,s.

Table 2.4.13 (^{1}H–NMR) spectrum bands of *p*-acetamedobezenesulfonyl sulfa sulfonyl amide.



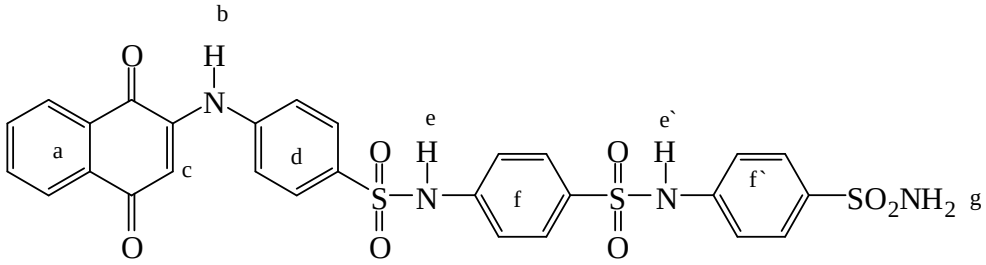
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
IX DMSO-d6	a, 2.05 (3,s) , b,10.3 (1,s); c, 7.66 – 7.77 (4,m); d,f, 10.7 (2,s); e,g 7.1-7.68 (8m); h, 7.24 (2,s).

Table 2.4.14 (^{1}H–NMR) spectrum bands of *p*-aminobezenesulfonyl sulfa sulfonyl amide.



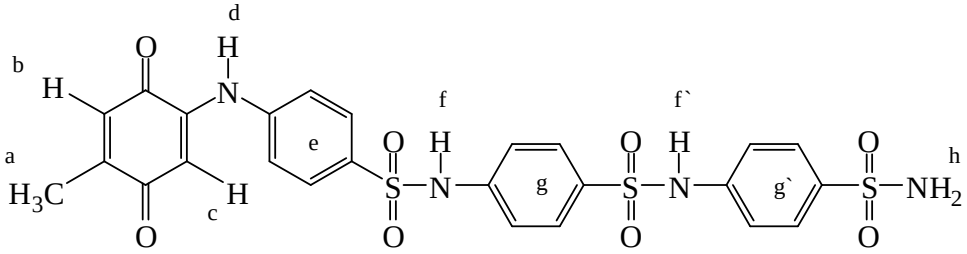
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
X DMSO-d6	a, 10.4 (2,s) , b,7.64-7.66 (4,m); c,c` 10.4 , d,d`, 6.56-7.47 (8,m); e, 7.45 (2,s).

Table 2.4.15 (^{1}H–NMR) spectrum bands of *p*-aminobezenesulfonyl sulfa sulfonyl amide and naphthoquinone.



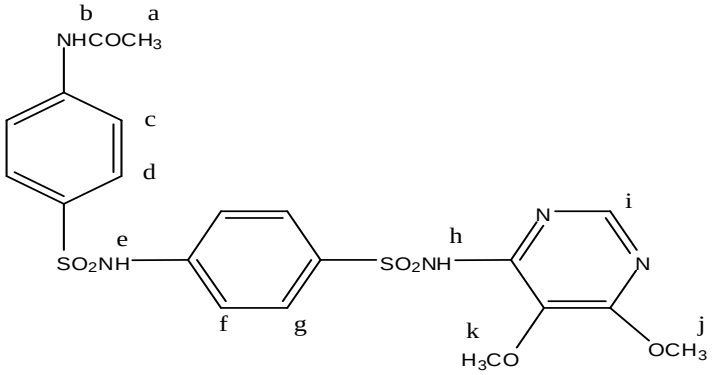
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XVI DMSO-d6	a, 7.69– 7.89 (4,m); b, 3.35 (1,s); c, 6.36 (1,s); d, 7.09-7.60 (4m); e,e` 10. 8 (2,s); f,f` 7.09-7.69 (8,m); g, 7.28 (2,s).

Table 2.4.16 (^{1}H–NMR) spectrum bands of *p*-aminobezenesulfonyl sulfa sulfonyl amide and methylbenzoquinone.



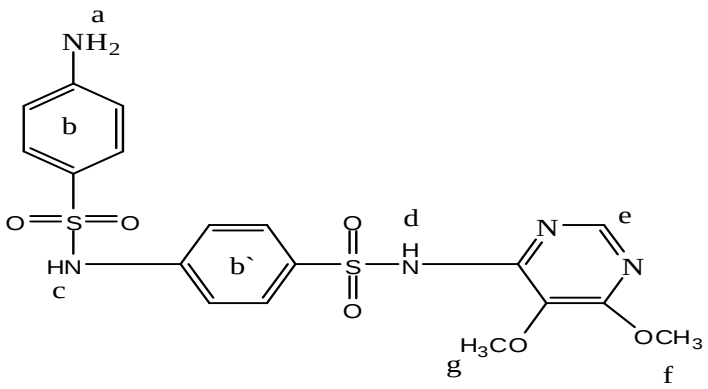
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XXI DMSO-d6	a, 2.44 (3,s); b, 6.75 (1,s); c, 6.24 (1,s); d, 5.4 (1,s); e, 6.47-7.32 (4,m); f,f` 11.71 (2,s); g,g` 6.91-7.32 (8,m), h, 7.32 (2,s).

Table 2.4.17 (^{1}H–NMR) spectrum bands of *p*-acetamidobezenesulfonyl sulfadoxine



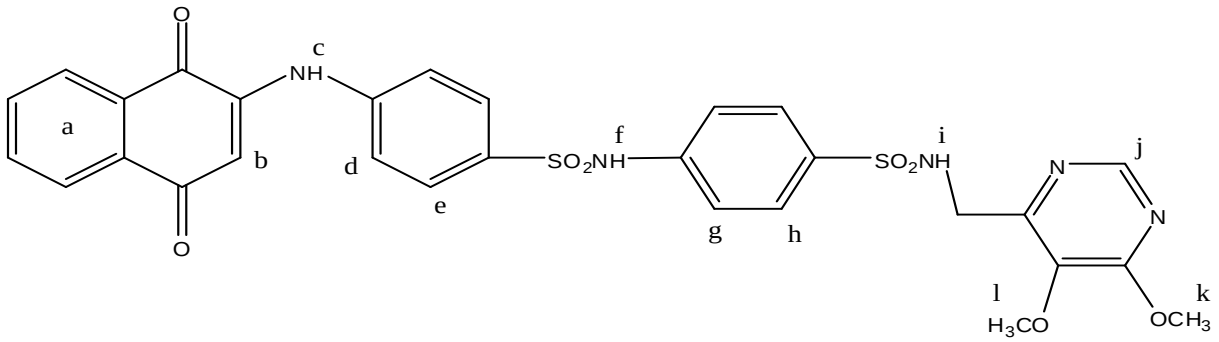
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
VII DMSO -d6	a, 2.06 (2,s); b, 10.34 (1,s); c, 6.59 (2,d, J = 3 Hz); d, 7.25, (2,d, J = 3 Hz); e, 10.55 (1,s); f, 7.65 (2,d, J = 2 Hz); g, 7.67 (2,d, J = 3 Hz); h, 10.83 (1,s); i, 7.97 (1,s); j, 3.66 (3,s); k, 3.68 (3,s).

Table 2.4.18 (^{1}H – NMR) spectrum bands of *p*-aminobezenesulfonyl sulfodoxine



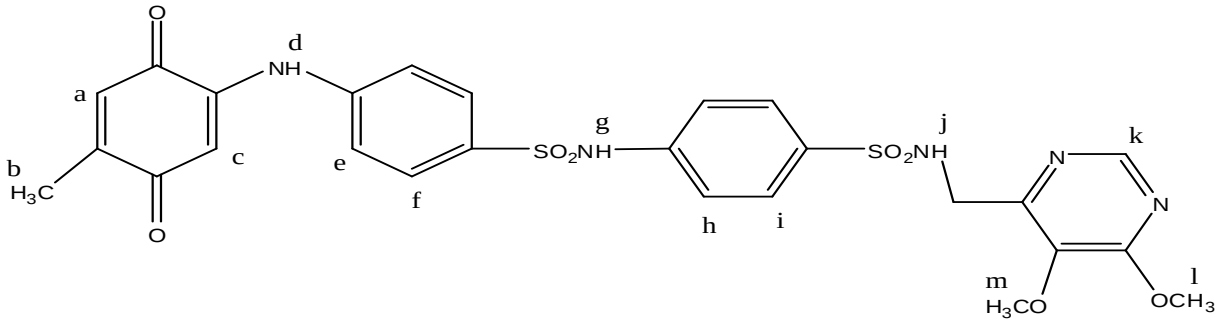
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
VIII DMSO -d6	a, 6. 0 (2,s); b,b` 6.56-7.62 (8,m); c, 10.54 (1,s); d, 10.96 (1,s); e, 8.11 (1,s); f, 3.65 (3,s); g, 3.89 (3,s).

Table 2.4.19 (^{1}H – NMR) spectrum bands of *p*-aminobezenesulfonyl sulfodoxine and naphthoquinone



Compd No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XV DMSO-d6	a, 7.87 – 7.0 (5,m); b, 7.1 (1,s); c, 12.2 (1,s); d, 7.9 (2,d, J = 3 Hz); e, 8.1 (2,d, J = 4 Hz); f, 12.8 (1,s); g, 8.07 (2,d, J = 5Hz); h, 9.41 (2,d, J = 3 Hz); i, 12.5 (1,s); j, 11.8 (1,s); k, 3.28 (3,s); l, 3.65 (3,s).

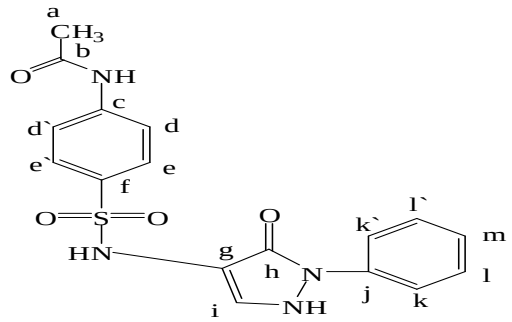
Table 2.4.20 (^{1}H – NMR) spectrum bands of *p*-aminobezenesulfonyl sulfodoxine – and methylbenzoquinone.



Compd No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XX DMSO-d6	a, 7.5 (1,s); b, 2.54 (3,s); c, 7.1 (1,s); d, 10.5 (1,s); e, 8.38 (2,d, J = 3 Hz); f, 8.59 (2,d, J = 4 Hz); g, 9.5 (1,s); h, 9.0 (2,d, J = 2 Hz); i, 9.50 (2,d, J = 3 Hz); j, 11.0 (1,s); k, 8.30 (1,s); l, 3.36 (1,s); m, 4.04 (3,s),

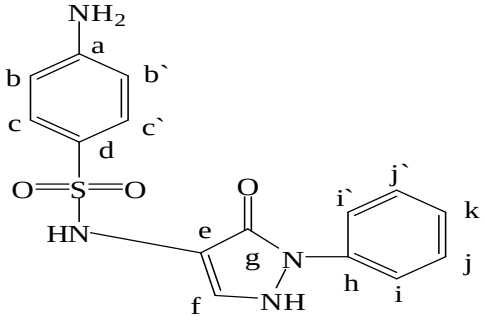
Table 2.5: ^{13}C-nuclear magnetic resonance spectrum bands of synthesized compounds (^{13}C –NMR).

Table 2.5.1 (^{13}C–NMR) spectrum bands of *p*-acetamidobenzenesulfonyl-4-amino phenazone



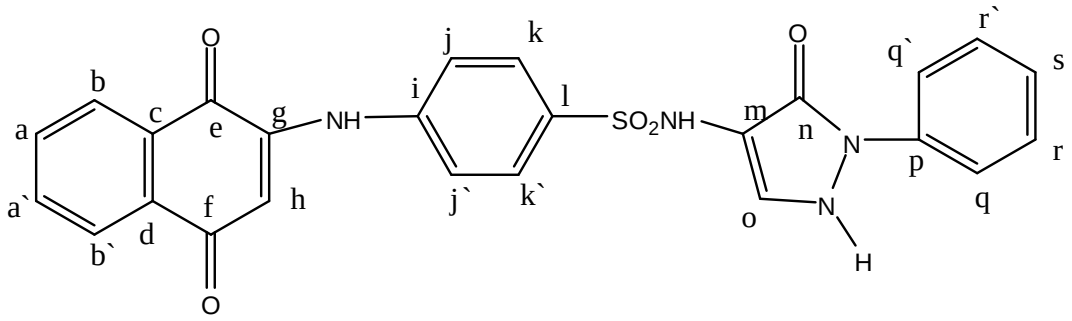
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
III DMSO-d6	a (17.8), b (155.40), c(153.02) , d,d`(106.66), e,e` (129.49), f (135.63), g (124.22), h (162.81), i (126.68), j (135.63), k,k` (112.92), l ,l` (129.25), m (126.78).

Table 2.5.2 (^{13}C–NMR) spectrum bands of *p*-aminobenzenesulfonyl-4-amino phenazone



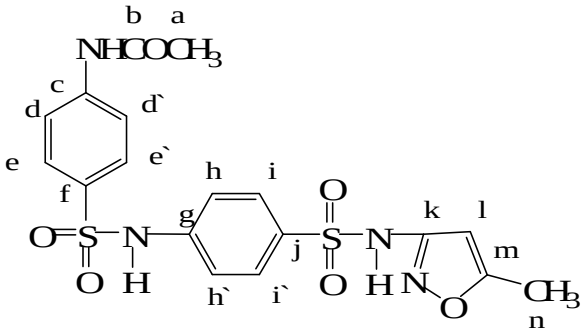
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
IV DMSO-d6	a (155.37), b,b` (112.90), c,c`(129.51) , d, (135.28), e, (126.99), f (124.50), g (162.52), h (135.45), i, i` (118.65), j, j` (128.46), k, (124.22).

Table 2.5.3 (^{13}C – NMR) spectrum bands of coupling of Naphthoquinone and p-aminobenzenesulfonyl-4-aminophenazone.



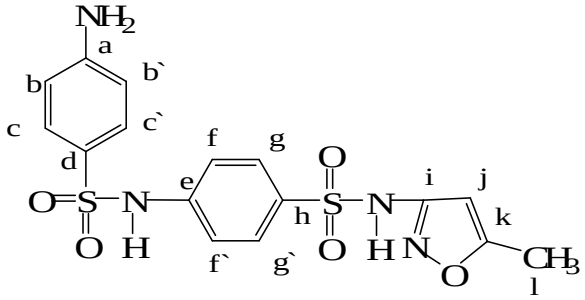
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XIII DMSO-d6	a, a` (135.37), b, b` (126.69), c (130.9), d (133.35), e (181.76), f (183.47), g (155.41), h (105.62), i (145.52), j,j` (104.77), k,k` (133.49), l (129.54), m (124.52), n (162.42), o (122.75), p (125.81), q,q` (122.75), r,r` (128.80), s (125.81).

Table 2.5.4 (^{13}C–NMR) spectrum bands of *p*-acetamidobezenesulfonyl sulfamethoxazole.



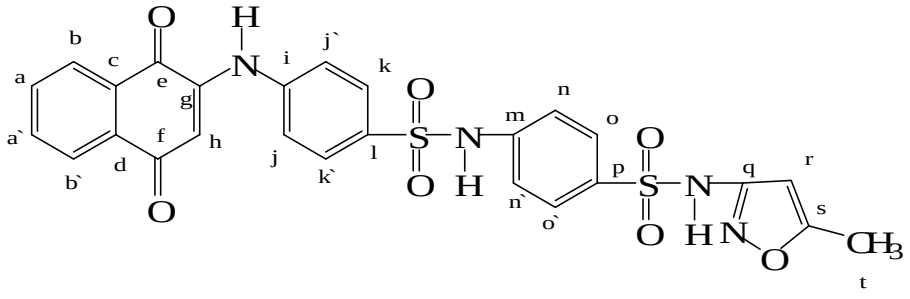
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
V DMSO-d6	a, (12.48), b (170.3), c (128.47), d,d` (119.19), e,e` (129.7), f (129.26), g,g` (153.7), h,h`,(118.7), i,i` (128.83), j (153.73), k,(158.41) l (95.78), , m(158.24), n (12. 4).

Table:2.5.5 (^{13}C–NMR) spectrum bands of *p*-aminobezenesulfonyl sulfamethoxazole



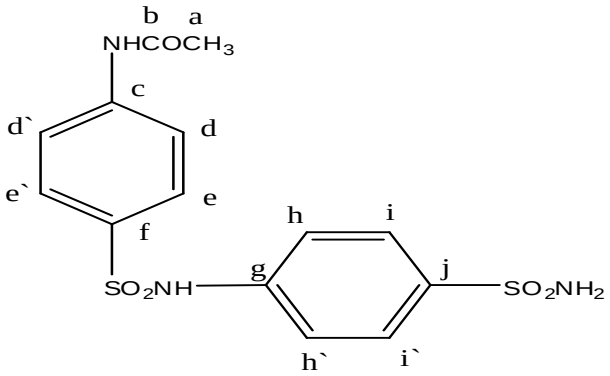
Compd. No	Chemical shift (ppm – δ value) intensity, multiplicity.
VI DMSO-d6	a, (133.34), b,b`(113.21),c,c`(118.16), d, (129.29), e, (143.51), f,f` (153.73), g, g`(124.27), h (153.72), i (153.74), j (95.86), k (170.71), l (12.50).

Table 2.5.6 (^{13}C–NMR) spectrum bands of Coupling of naphthaquinone and *p*-aminobezenesulfonyl sulfamethoxazole.



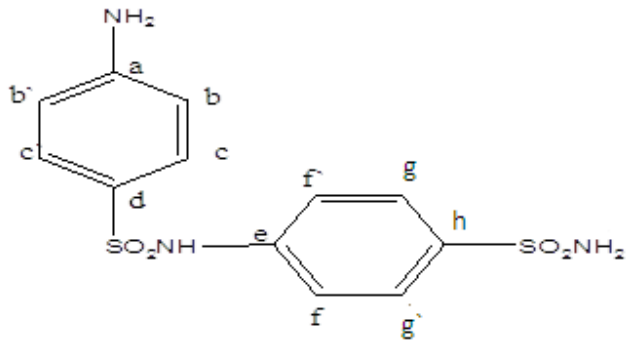
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XIV DMSO-d6	a, a` (135.39), b, b` (126.71), c (128.91), d (128.67), e (181.67), f (183.58), g (157.92), h (105.40), i,(134.43), j,j` (118.77), k,k` (122.94), l (134.43), m (142.29), n,n` (126.7), o,o` (127.17), p (143.55), q,(145.11), r (95.87), s (170.74), t (12.48).

Table 2.5.7 (^{13}C– NMR) spectrum bands of *p*-acetamedobezenesulfonyl sulfonyl amide



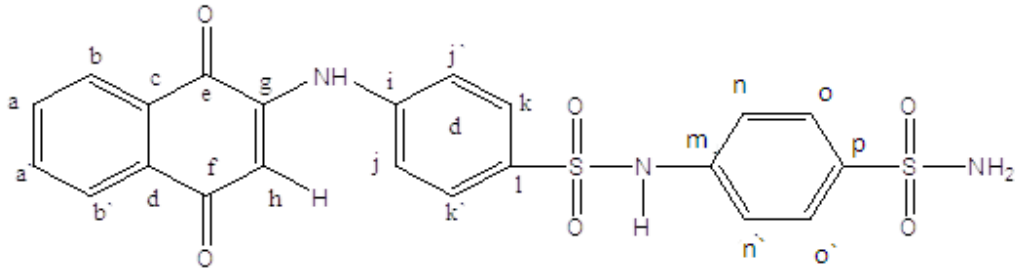
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XI DNSO-d6	a, (24.55), b (169.52), c, (143.88), d,d` (118.90), e,e` (128.48), f (139.23), g (141.47), h,h` (119.20), i,i` (127.54) , j (133.11).

Table 2.5.8 (^{13}C – NMR) spectrum bands of *p*-aminobezenesulfonyl sulfonyl amide



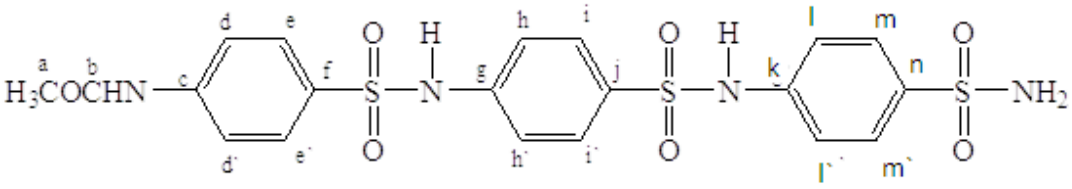
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XII DNSO -d6	a (153.60), b,b` (113.16), c,c` (129.30), d (127.44), e (142.11), f,f` (118.32) , g,g` (124.35), h (138.57).

Table 2.5.9 (^{13}C – NMR) spectrum bands of coupling of sulfonilamide and naphthoquinone



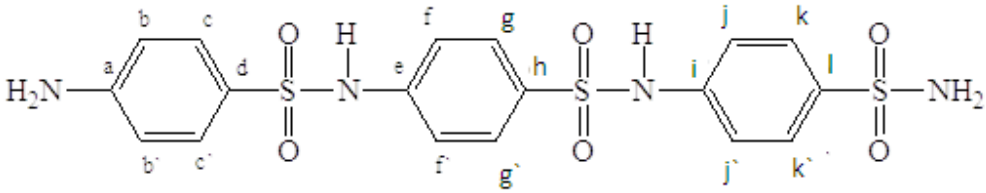
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XVII DMSO-d6	a,a` (135.39), b,b` (126.69), c, (132.86), d, (130.91), e, (183.84), f (181.82), g (141.95), h, (104.39), i, (145.71) , j,j` (123.19), k,k (130.91), l (133.43), m (142.12), n,n` (118.32), o,o` (140.19), p (138.57).

Table 2.5.10 (^{13}C–NMR) spectrum bands of *p*-acetamedobezenesulfonyl sulfa sulfonyl amide.



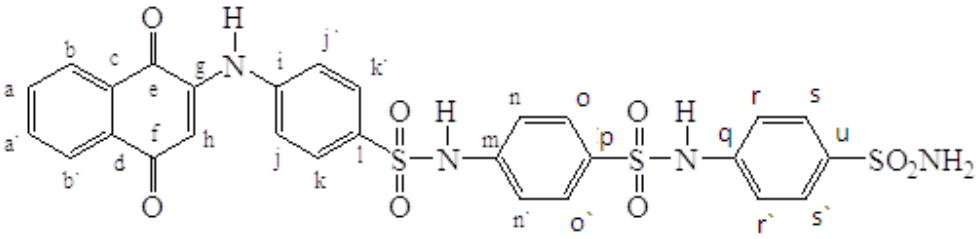
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
IX DMSO-d6	a (24.55), b(169.52), c (143.88), d,d`(118.90), e,e` (128.48), f (139.23), g, (141.47), h,h`(119.20), i,i`,(127.54), j(133.11), k (143.8), l,l`(119.20), m,m`(127.54), n(133.11).

Table 2.5.11 (13C–NMR) spectrum bands of *p*-aminobezenesulfonyl sulfa sulfonyl amide.



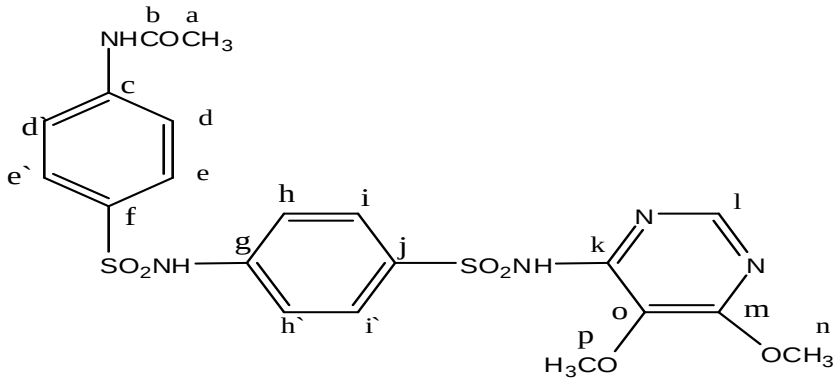
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
X DMSO-d6	a(153.60), b,b`(113.16), c,c`(129.30), d, (127.44), e, (142.11), f,f`(118.32)`,g,g` (113.16), h (124.35), i (138.57), j,j` (118.32), k,k` (124.35), l (127.44).

Table 2.5.12 (13C–NMR) spectrum bands of coupling of *p*-aminobezenesulfonil sulfa sulfonil amide and naphthoquinone.



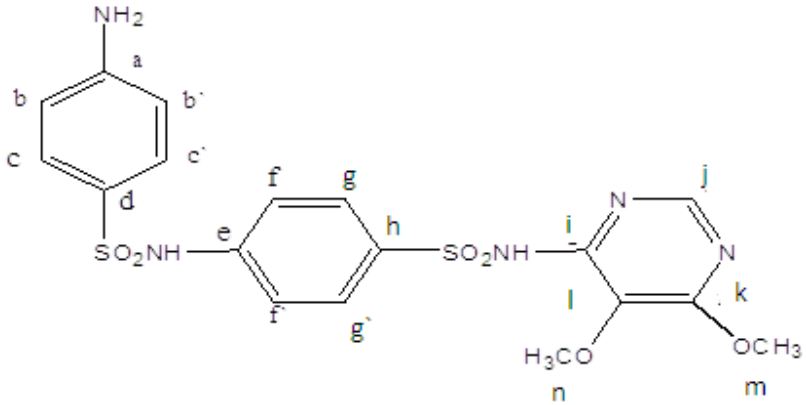
Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
XVI DMSO-d6	a,a` (135.0), b,b`(126.71), c (132.74), d (128.67), e (183.02), f (181.07), g (143.41), h (105.29), i (145.15), j,j` (118.97), k,k` 130.86), l, (127.6),m, (139.38), n,n`(122.96), o,o` (128.69), p (126.33), q (141.35), r.r` (125.81), s,s` (139.33), u (130.38).

Table 2.5.13 (^{13}C–NMR) spectrum bands of *p*-acetamidobezenesulfonyl sulfadoxine



Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
VII DMSO-d6	a(24.54), b(169.53), c (133.05), d,d` (129.49), e,e` (127.29), f (144.00), g (142.53), h,h` (118.39), i,i` (130.24), j (128.48), k (151.22), l (153.3), m(161.83), n (54.4), o (127.86), p (60.64).

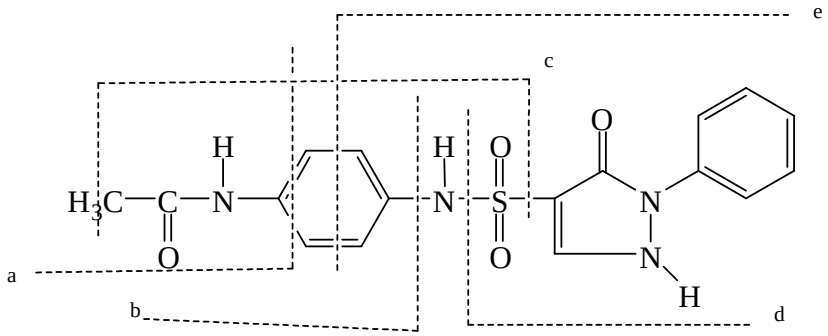
Table 2.5.14 (^{13}C – NMR) spectrum bands of *p*-aminobezenesulfonyl sulfodoxine



Compd. No	chemical shift (ppm – δ value) intensity, multiplicity, J const
VIII DMSO-d6	a (150.99), b,b`(112.64), c,c`, (130.24), d (143.13), e (129.42), f,f` (117.79), g,g` (129.15), h, (127.84), i (), j (153.52), k (126.08), l (129.26), m (54.38), n (59.34).

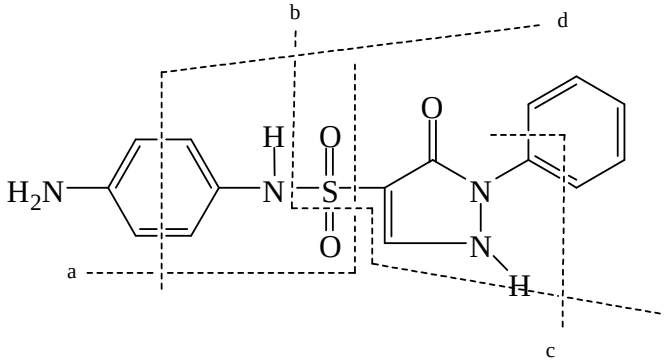
Table 2.6: Mass spectrum bands of synthesized compounds.

Table 2.6.1 Mass spectrum bands of *p*-acetamidobenzenesulfonyl-4-amino phenazone.



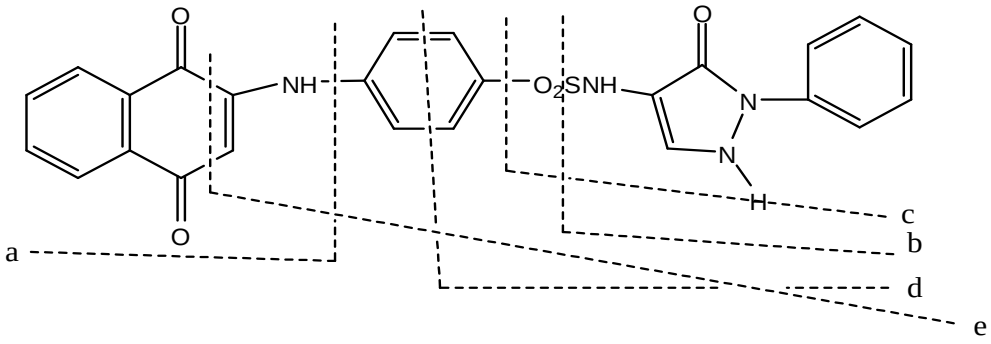
Compd No	m/z (Relative abundance %)
III	a (73) 98%), b (133) (20%), (c (207), (85%),d (221) (18) e (281) 25%.

Table 2.6.2 Mass spectrum bands of *p*-aminobenzenesulfonyl-4-amino phenazone



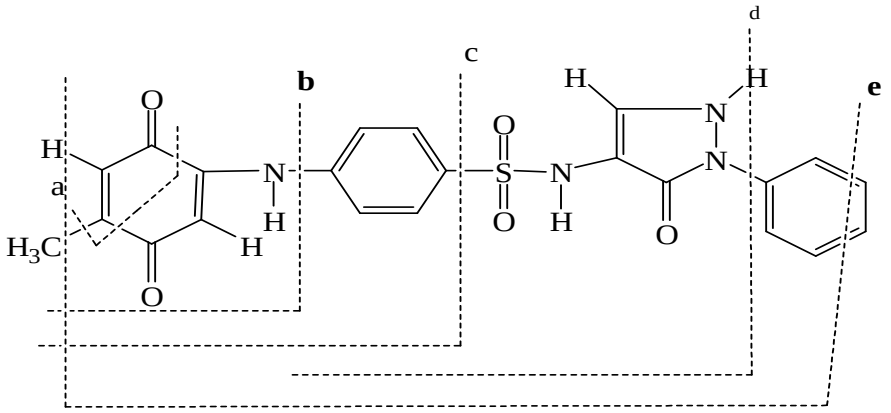
Compd.No	m/z (Relative abundance %)
IV	a (177) (20%), b (207) 98%, c (267) 15%, d (298) 10%.

Table 2.6.3 Mass spectrum bands of coupling of Naphthoquinone and p-aminobenzenesulfonyl-4-aminophenazone.



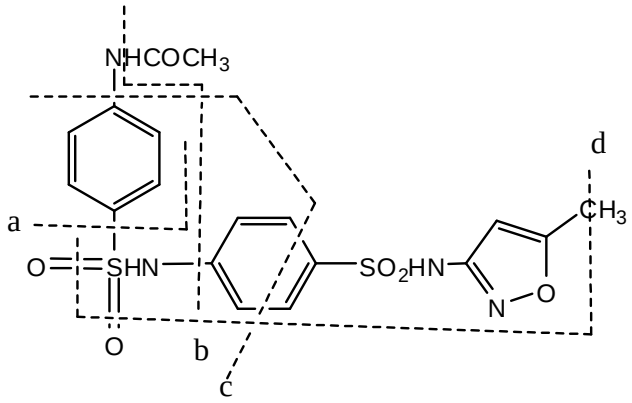
Compd. No	m/z (Relative abundance %)
XIII	a (175) 23%, b (207) 40%, c (235) 23%, d (280) 25%, e (355) 24%.

Table 2.6.4 Mass spectrum bands of coupling of methylbenzoquinone and p-aminobenzenesulfonyl-4-aminophenazone.



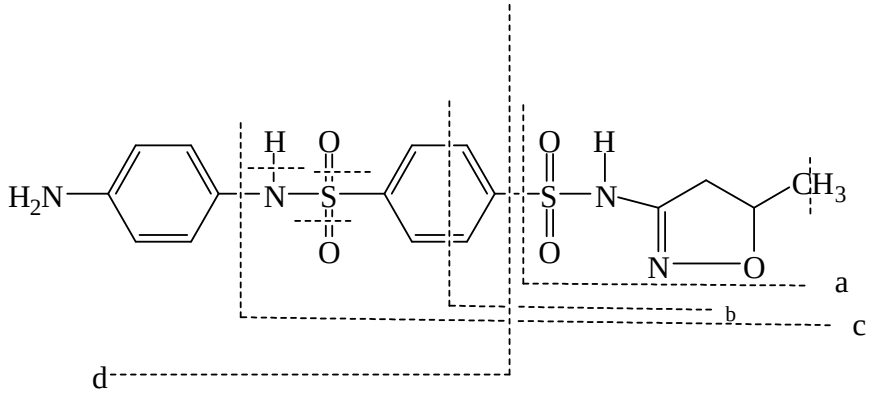
Compd. No	m/z (Relative abundance %)
XVIII	a (56) 100%, b (149) 45% , c (221) 25%, d (355) 25%, e (429) 27%.

Table: 2.6.5 Mass spectrum bands of *p*-acetomedo benzene sulfanyl sulfamethoxazole



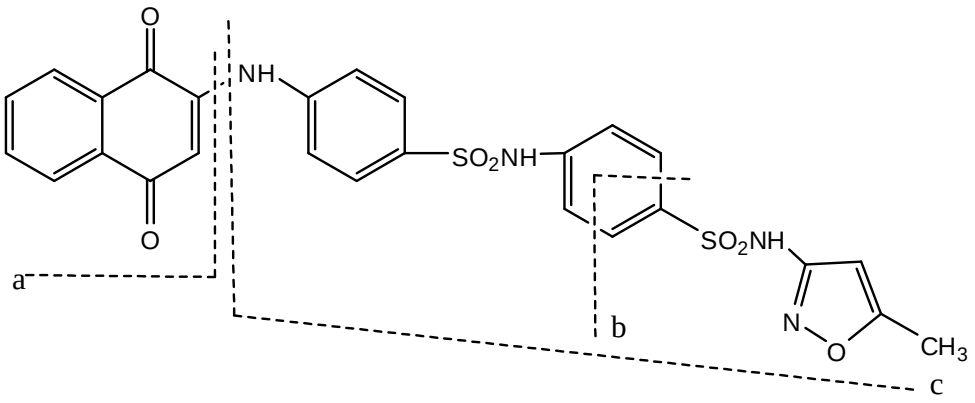
Compd. No	m/z (Relative abundance %)
V	a (135) 20%, b (169) 35%, c (209) 17%, d (281) 17%.

Table:2.6.6: Mass spectrum bands of *p*-aminobezenesulfonyl sulfamethoxazole



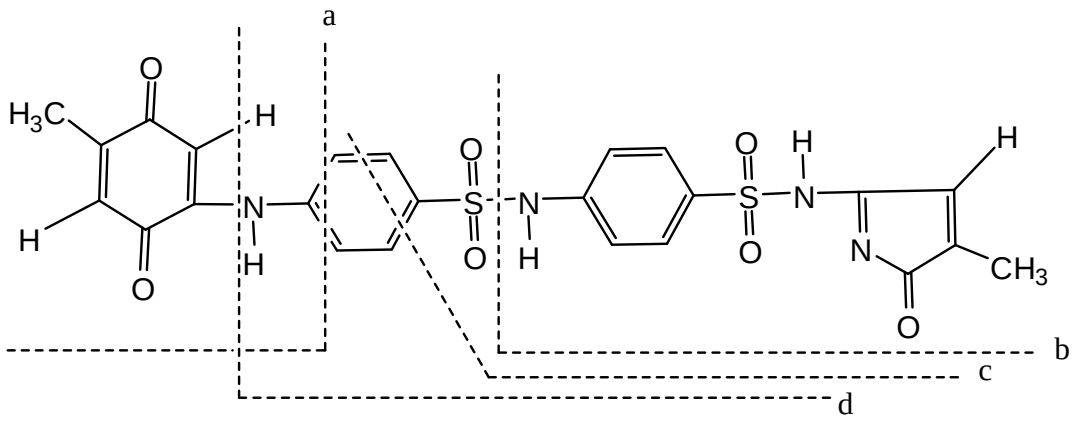
Compd. No	m/z (Relative abundance %)
VI	a (163) 15%, b (207) 85%, c (249) 13%, d (283) 13%.

Table:2.6.7: Mass spectrum bands of coupling of *p*-aminobezenesulfonyl sulfamethoxazole and naphthoquinone.



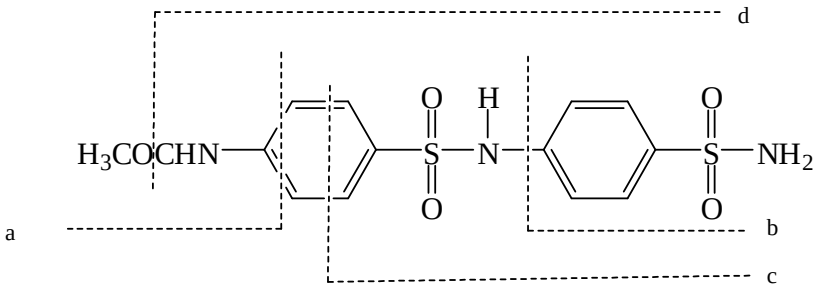
Compd. No	m/z (Relative abundance %)
XIV	a (160) 22% , b (207) 25% , c (271) 20%.

Table:2.6.8: Mass spectrum bands of coupling of *p*-aminobezenesulfonyl sulfamethoxazole and methylbenzoquinone.



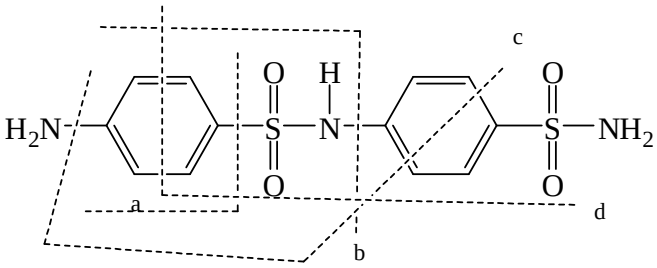
Compd. No	m/z (Relative abundance %)
XIX	a (149) 80%, b (280) 25%, c (355) 23%, d (421) 22%.

Table 2.6.9 Mass spectrum bands of *p*-acetamedobezenesulfonyl sulfonyl amide



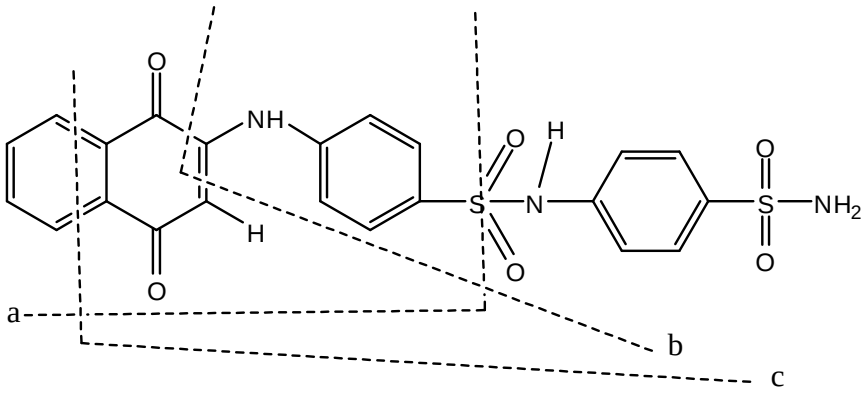
Compd. No	m/z (Relative abundance %)
XI	a (73) 60%, b (156) 25%, c (281) 15%, d (342) 10%.

Table 2.6.10 Mass spectrum bands of *p*-aminobezenesulfonyl sulfonyl amide



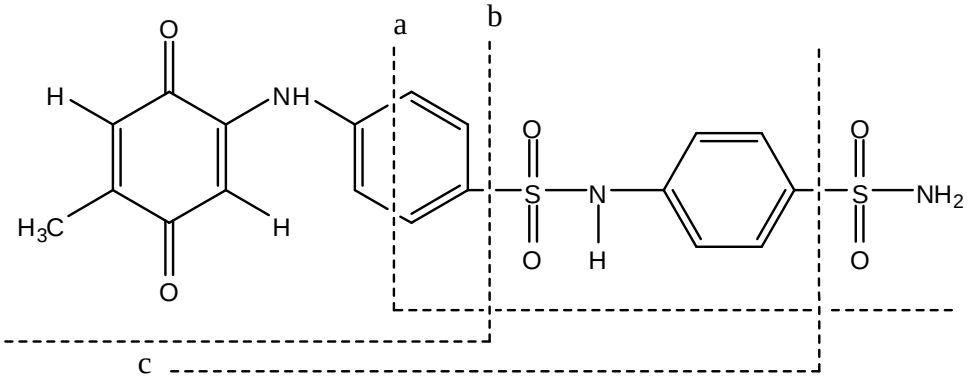
Compd. No	m/z (Relative abundance %)
XII	a (92) 75%, b (173) 20%, c (209) 15%, d (281) 20%.

Table 2.6.11 Mass spectrum bands of coupling of p-aminobezenesulfonyl sulfonyl amide and naphthoquinone.



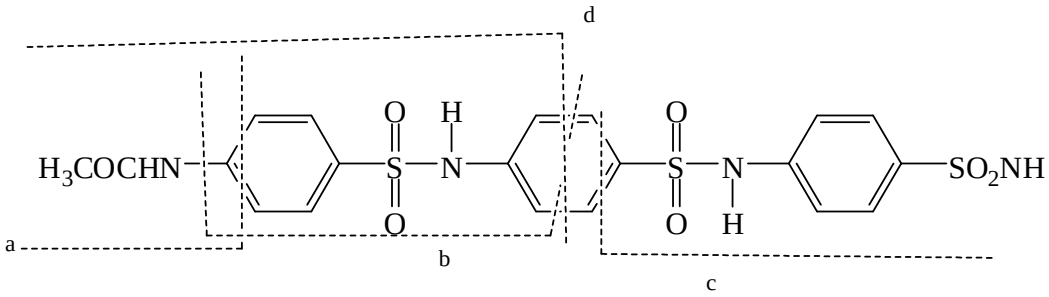
Compd. No	m/z (Relative abundance %)
XVII	a (281) 24%, b (341) 20%, c (429) 20%.

Table 2.6.12 Mass spectrum bands of coupling of *p*-aminobezenesulfonyl sulfonyl amide and methylbenzoquinone.



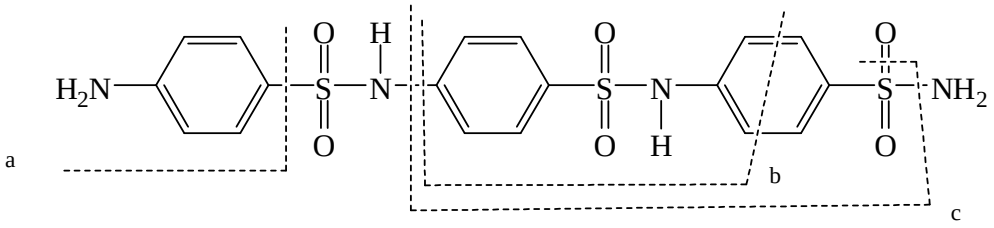
Compd. No	m/z (Relative abundance %)
XXII	a (217)(25%), b (282) 28%, c (375) (22%).

Table 2.6.13 Mass spectrum bands of *p*-acetomrdobezenesulfonyl sulfa sulfonyl amide.



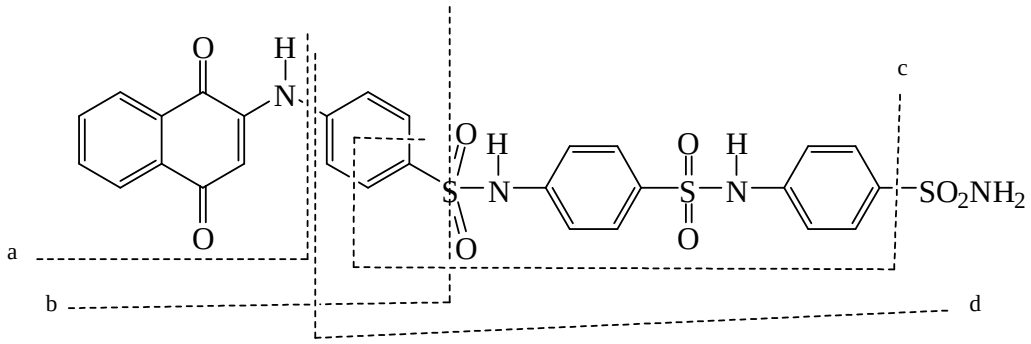
Compd. No	m/z (Relative abundance %)
IX	a (73) 100% , b (207) 95%, c (246) 25%, d (281) 27%.

Table 2.6.14 Mass spectrum bands of *p*-aminobezenesulfonyl sulfa sulfonyl amide.



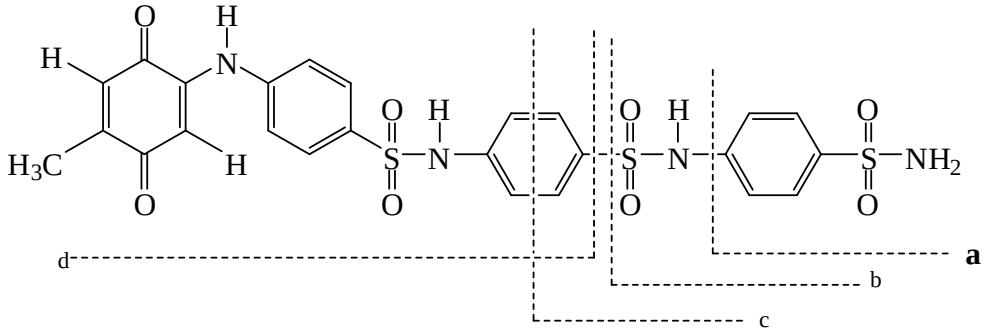
Compd. No	m/z (Relative abundance %)
X	a (92) 80%, b (207) 95%, c (281) 25%.

Table 2.6.15: Mass spectrum bands of coupling of *p*-aminobezenesulfonyl sulfa sulfonyl amide and naphthoquinone.



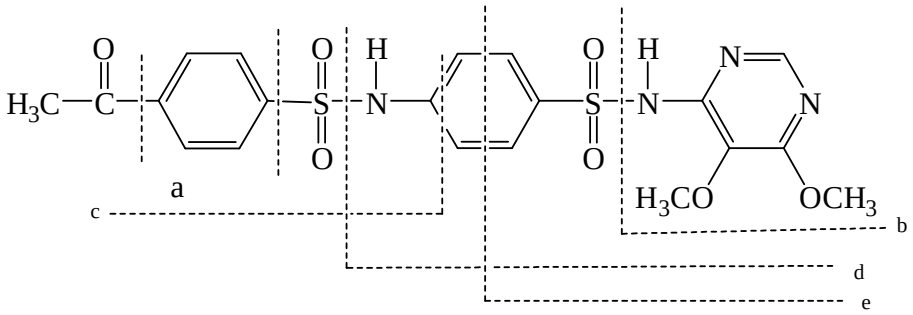
Compd. No	m/z (Relative abundance %)
XVI	a (179) 48% , b (283) 23%, c (341) 25%.

Table 2.6.16: Mass spectrum bands of *p*-aminobezenesulfonyl sulfa sulfonyl amide and methylbenzoquinone.



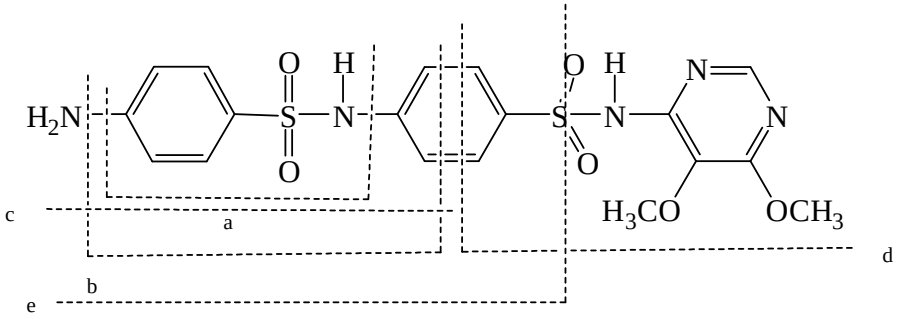
Compd. No	m/z (Relative abundance %)
XXI	a (157) 23%, b (236) 55% , c (281) 65%, d (368) 22%.

Table 2.6.17:Mass spectrum bands of *p*-acetamidobezenesulfonyl sulfadoxine



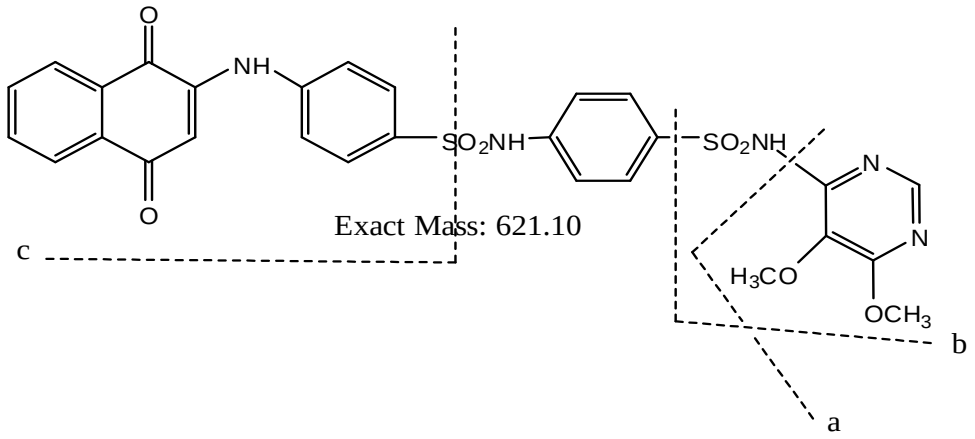
Compd. No	m/z (Relative abundance %)
VII	a (76) 75%, b (230) 25% , c (281) 17%, d (358) 15%.

Table 2.6.18: Mass spectrum bands of *p*-aminobezenesulfonyl sulfodoxine



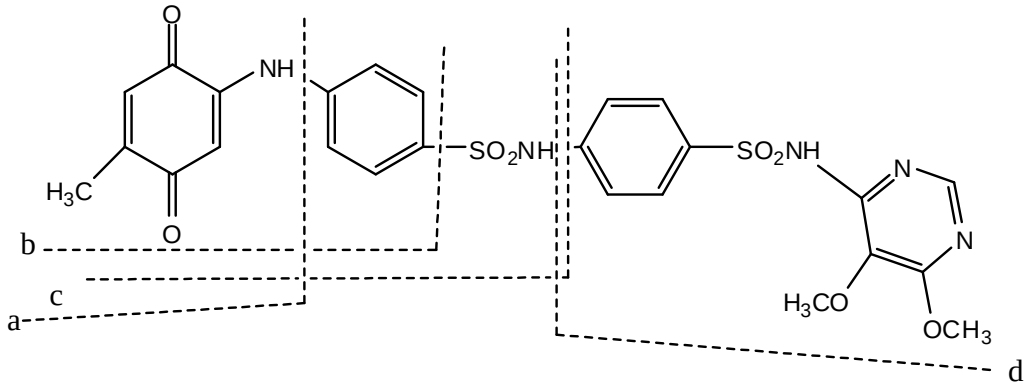
Compd. No	m/z (Relative abundance %)
VIII	a (156) 13%, b (191) 20%, c (245) 30%, d (281) 25%, e (267) 20%.

Table 2.6.19: Mass spectrum bands of coupling of p-aminobezenesulfonyl sulfodoxine and naphthoquinone.



Compd. No	m/z (Relative abundance %)
XV	a (46) 100%, b (139) 23%, c (210) 24%, d (285) 23%.

Table 2.6.20: Mass spectrum bands of coupling of p-aminobezenesulfonyl sulfodoxine and methylbenzoquinone.



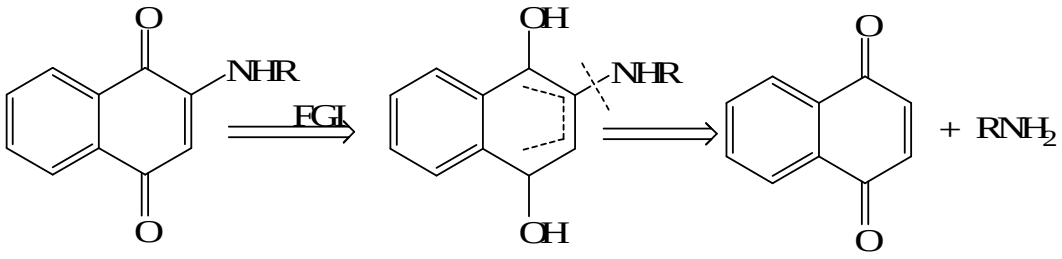
Compd. No	m/z (Relative abundance %)
XX	a, (46) 100%, b (111) 20% , c (221) 15%, d (289) 20%.

3. Results and Discussion

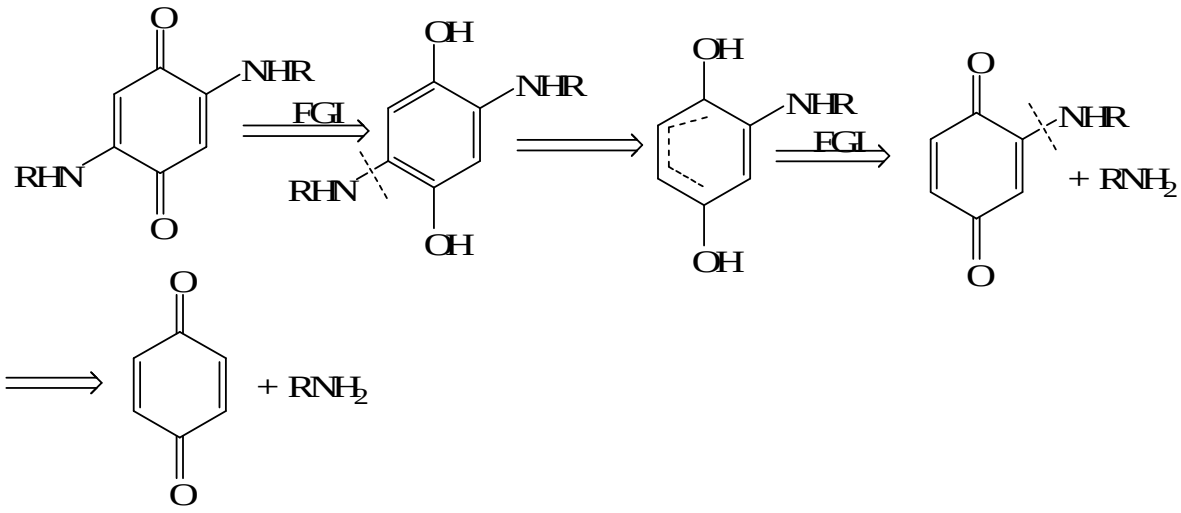
Quinones are non-aromatic conjugated cyclo-hexadienones which are usually colored compounds. The quinone and hydroquinone are performing on oxidation reduction system of chemical and electrochemical interest.

Quinones were reported to poses a wide range of biological activities (Roshdi, *et al*,1979,1977), (Take, et al.,1985).

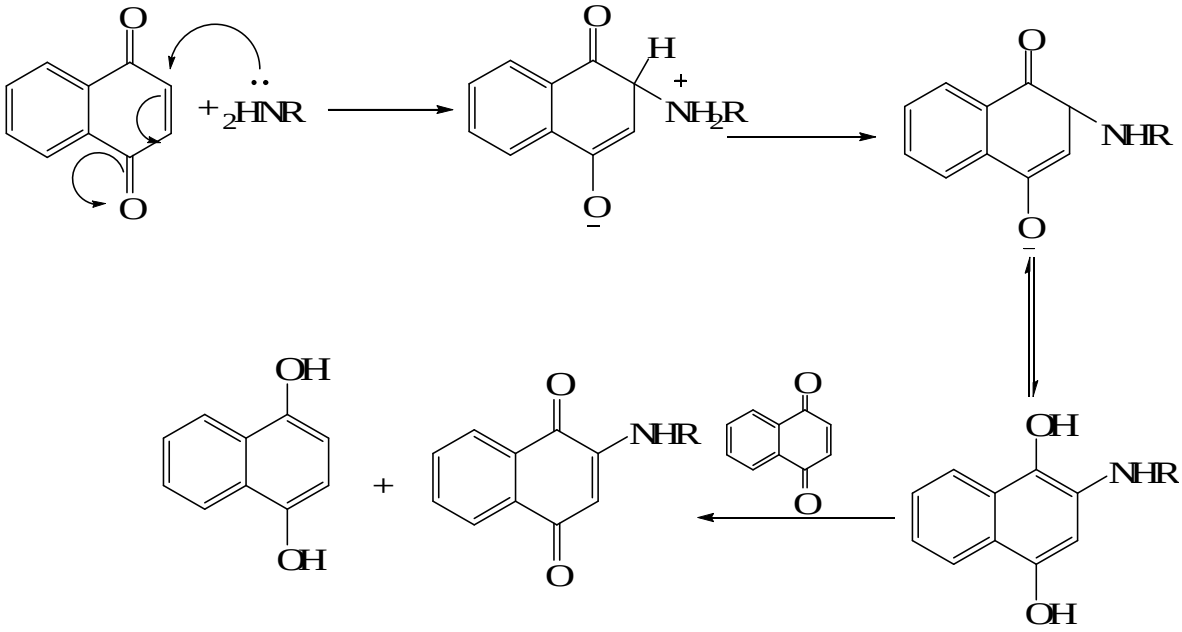
The synthetic designing of amino-*p*-quinones in this work was adopted through the disconnection approach according to well documented methods. The retrosynthetic analysis of these compounds can be shown below by which the standard carbon-carbon bonds were firstly disconnected.



The same approach was adopted for the disubstituted p-benzoquinone

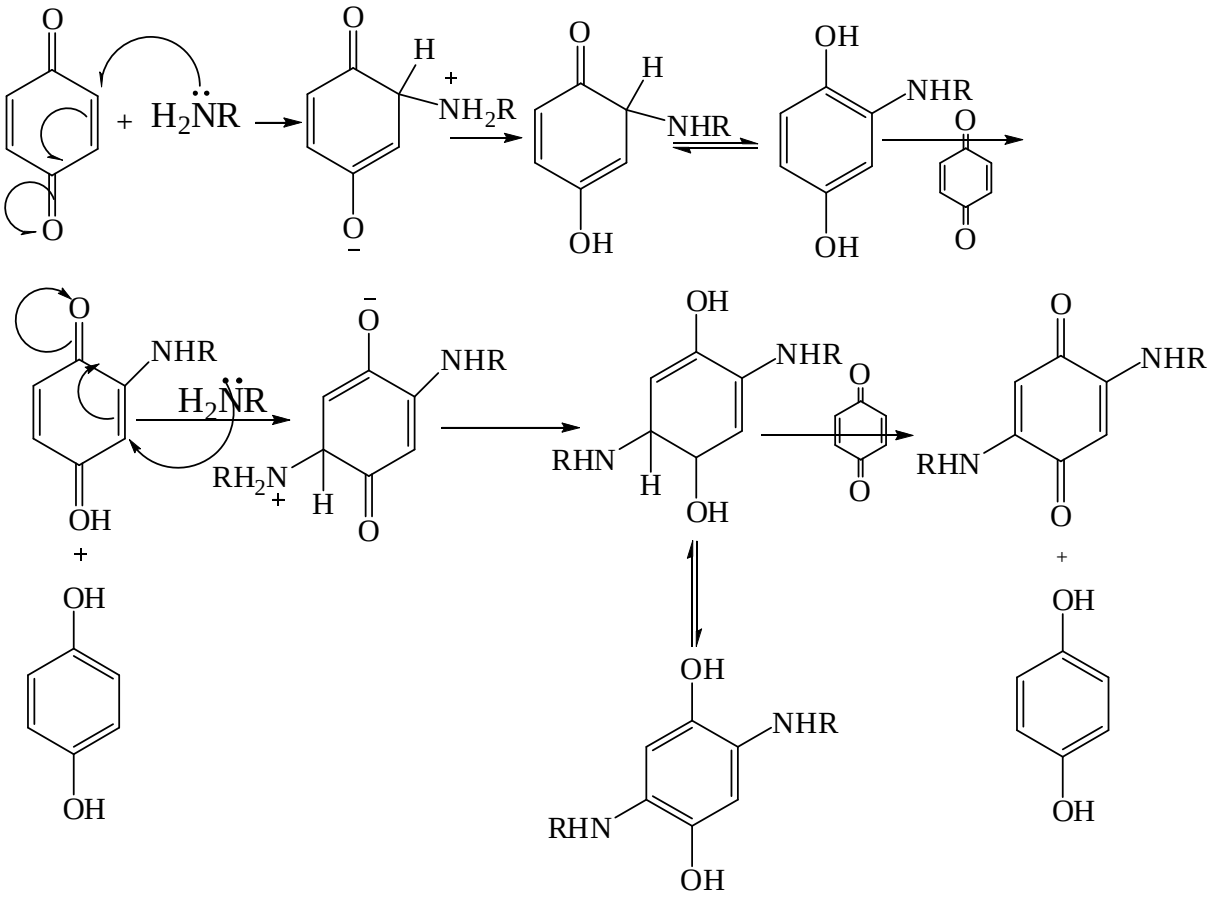


Therefore reaction of 2:1 molar ratio of required p-quinone and amine can furnish mono substituted product, the mechanism of such reaction can be illustrated below:



The amino compounds acting as nucleophiles tend to add in conjugate fashion to the olefinic carbon atom as the electron donor group lowers the electrode potential, the amino quinol formed can be oxidized in the presence of an excess of the parent quinone leading to the amino quinone.

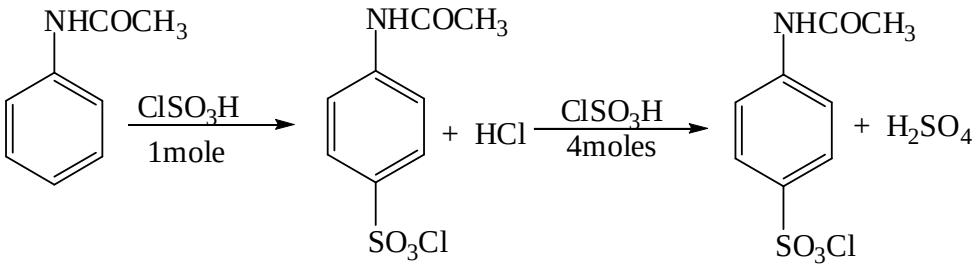
In the case of diamino benzoquinone the same mechanism worked, whereby after the formation of the monoamino benzoquinone a second amino group was added.



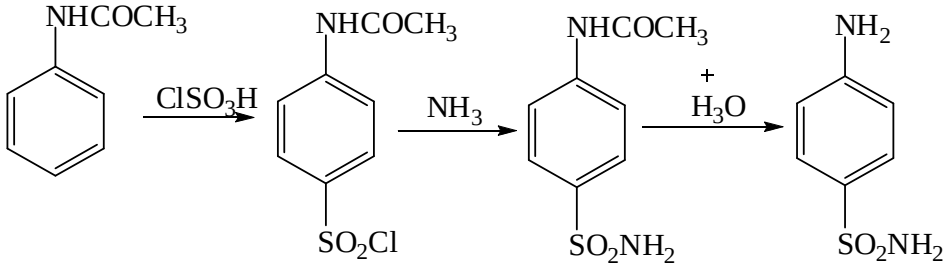
The identity of the prepared compounds was confirmed by spectral (Infrared, NMR, MS), chromatographic and classical data (m.p , color).

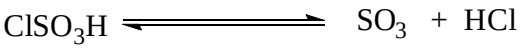
3.1. Mechanism of Chlorosulfonation

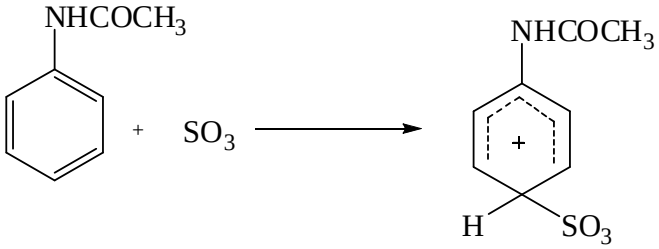
A simple one step reaction can be used to introduce the sulfonyl chloride group, to *p*-position of acetanilide to produced *p*-acetamedobenzenesulfonylchloride (two moles of the chlorosulphonic acid are required).

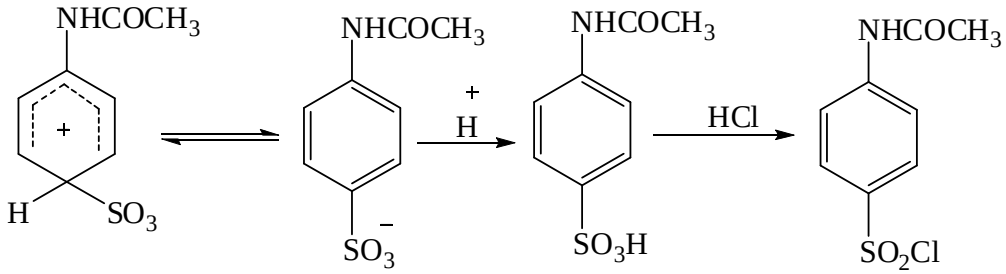


The reaction mechanism of chloro sulfonation involves the following steps.







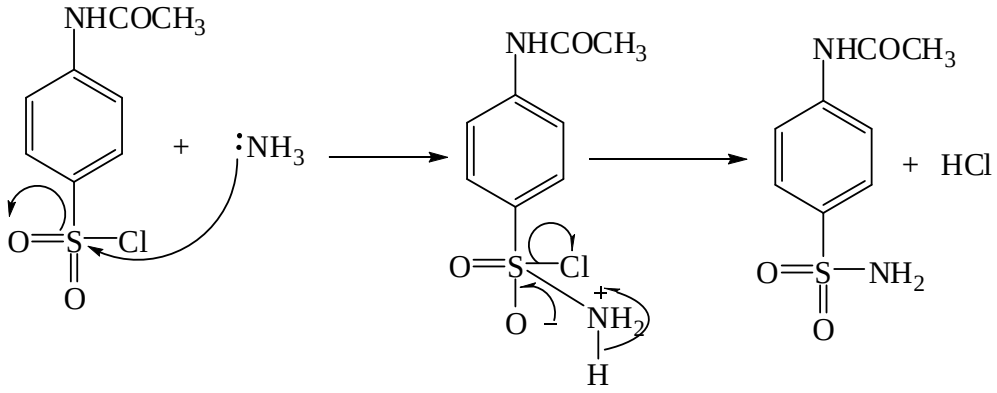


Reaction mechanism of chloro sulfonation.

In the first step, the generation of electrophilic sulfurtrioxide is simply an acid – base equilibrium this time between molecules of chlorosulfonic acid. In the second step electrophilic reagent, SO_3 attaches itself to the aromatic ring to form the intermediate carbocation. Step three is the loss of a proton to furnish the resonance- stabilized substitution product. This time the anion of p-acetamedo benzene sulfonic acid which being strong acid is highly disassociated. When it reacts with hydrochloric acid to converted to *p*-aminobenzenesulfonylchloride.

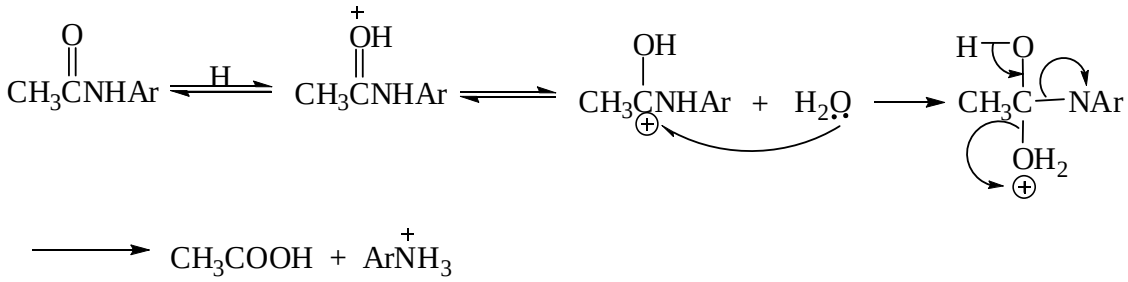
3.2 Mechanism of amination p.acetamedobenzensulfonylchloride

The mechanism of the reaction between *p*.acetamedobenzensulfonylchloride and ammonia can be illustrated as follows:



Ammonia act as nucleophile attaching to the sulfur atom and caused cleavage of the π bond to work oxygen which accept the negative charge. In the process the amine losses a proton to a second molecule of ammonia. The negative charge on oxygen make π bond with sulfur atom and this lead to the displacement of chlorine as leaving group (Marrison & Boyde.1992).

3.3 Reaction mechanism of hydrolysis of amide



It is understandable those acid derivatives are hydrolyzed more readily in either alkaline or acidic solution than neutral solution to hydrogen ion, which attaches itself to the carbonyl oxygen and thus renders the molecule vulnerable to attack by the weakly nucleophilic reagent water. Oxygen acquires the π electrons without accepting negative charge. Amine liberated as aleaving group when negative charge oxygen make π bond with carbon atom.

3.4 Spectroscopic analysis

The identification of all synthesized compounds (III - XXII) in this study, were confirmed using some physical properties like (mp) and spectroscopic analysis techniques like (IR, ^{1}H-NMR, ^{13}C-NMR and Mass spectra. Infrared spectroscopy is one of the most common spectroscopic techniques used by organic and inorganic chemists. The main goal of IR spectroscopic analysis is to determine the functional groups in the sample. Different functional groups absorb characteristic frequencies of IR radiation. Using various sampling accessories, IR spectrometers can accept a wide range of sample types such as gases, liquids, and solids. Thus, IR spectroscopy is an important and popular tool for structural elucidation and compound identification. Infrared spectra of synthesized compounds have been scanned in KBr pellets by using Perkin Elmer-838 FT-IR spectrophotometer instrument in region from 4000 cm^{-1} to 667 cm^{-1}. The IR region extends from long –wave limit to the visible region, the portion of spectrum most used in organic chemistry ranges from 4000 to 666 cm^{-1}. This is the range of the vibration –

rotation spectra (Tedder and Nach vata,1975). Some molecules were as others were associated with certain functional groups; the effects of these vibrations on the chemical bonds between the atoms are classified into two major classifications stretching and bending (Parikh, 1973). Frequencies of stretching and bending vibrations depend largely on the vibrating atomic masses and on the bond orders of the chemical bonds joying them. The lighter atoms have higher frequency vibrations. Similarly higher bond order with higher frequency of vibration, thus a bond vibrates at a lower frequency (lower wave number 2100 cm^{-1}) than a bond wave number (2900cm^{-1}), and C-C triple bond has higher vibration frequency (2300-2100)cm^{-1},than C-C double bond which in turn vibrates at a higher frequency (1700-1500cm-1) than C-C single bond (1300-800cm^{-1}),however, stretching vibrations generally required more energy and thus occur at higher vibrations of some groups ((Parikh, 1973 and Furrniss 1989).

All the prepared compounds showed characteristic IR bands. These compounds showed SO_2 st. vib bands in the region 1130-1155 cm^{-1} and 1300-1350 cm^{-1} (asym). N-H st.vib. bands appeared in the region 3250-3450 cm^{-1} while their bending vibration in the region 1560-1610 cm^{-1}, carbon-carbon partial double bond in the aromatic system appeared in the 1450-1610 cm^{-1}. Detailed ban ds for each compound individually were given in the tables (2.3.1- 2.3.4) however, with exception of p-aminobenzene sulphonamido derivatives and compounds (IV, VI, and VIII, X, XII), all the other prepared compounds showed the characteristic carbonyl group st.vib. in the region 1620-1695 cm^{-1}. The lowered values absorption was attributed to resonance and conjugation effects besides possible hydrogen bonding. This specific absorption was used as evidence for completion of hydrolysis reaction during the conversion of the acetamido group into amino group.

3.5 The nuclear Magnetic Resonance Spectroscopy (NMR)

Nuclear magnetic resonance spectroscopy (NMR) is one of the latest physical methods of investigating the organic compounds. The shift of the nuclear resonance signal as a result of the electronic environment is called chemical shift. It permits both qualitative and quantitative determination of different kind of bonds between atoms. High resolution ^{1}H- NMR is considered another powerful technique and has been used in the investigation of organic compound structures.

The ^{1}H-NMR spectroscopy was most popular technique worldwide in the structure elucidation. NMR provides the most accurate information about different proton environment. The chemical shift signal beside the value of capacity constant provide certain information about the different proton and their interactions, (Silvertien *et al*.,1981).

The ^{1}H-NMR spectra analysis of some synthesized quinones and sulphonamide derivatives in this study, may be explained in the followings. The ^{1}H-NMR of compound III and compound IV which are contain the same structure with different only in the substituted group which changed to amino group in the compounds IV where it formed after hydrolysis of compound III therefore showed the same 1H-NMR chemical shifits with differ in the one proton of amino of acetomido which is appeared at 5.88 (s,1H-NH) and the three protons of methyl group of acetomedo showed at 1.93 (s,3H,CH3) for other chemical shifts of the compounds III and IV see table (2.4.5 & 2,4,6). The ^{1}H-NMR analysis of compound XIV which is formed from the coupling reaction of compound III and Nathquinone which is give the following chemical shifts ,7.25 – 7.32 (5m) of benzene ring, 7.45 (1,s) proton of naphathaquinone, 9.407 (1,s); proton of NH, 7.81(2H,d, J = 3Hz); and 7.91 (2H,d, J = 4Hz) four protons of benzene ring of

sulphanamide, ; 9.21 (1H,s); of amino group attached to sulphonyl group, 8.08 (1H,s); phenazone ring, 7.92 – 7.98 (5, m) benzene ring attached to phenzone.

The ^{1}H-NMR of compound V and compound VI which contain the same structure with different, only, in the substituted group which changed to amino group in the compounds V where it formed after hydrolysis of compound VI therefore showed the same ^{1}H-NMR chemical shifits where differ in the one proton of amino of acetomido which is appeared at 10.13 (s,1H-NH) and the three protons of methyl group of acetomedo showed at 2.06 (s,3H,CH3) for other chemical shifts of the compounds V and VI see table (2.4.5 & 2,4,6). The 1H-NMR analysis of compound XIV which is formed from the coupling reaction of compound V and Nathquinone which is give the following chemical shifts ,7.80 – 7.85 (5m) of benzene ring, 7.24 (1,s) proton of naphathaquinone, 11.29 (1,s); proton of NH, 7.59(2H,d, J = 3Hz); and 7.27 (2H,d, J = 4Hz) four protons of benzene ring of sulphanamide, ; 9.21 (^{1}H,s); of amino group attached to sulphonyl group, 7.70 (1H,s); xazole ring .the chemical shifts of coupling compound of methyl benzoquinone and compound V give the same chemical shits with diffence in the 6.69 (1,s); c, 6.25 (1,s) which indicated for the protons of benzoquinone ring and the chemical shift of N-H proton which appeared at 5.4 (1,s).

The ^{1}H-NMR spectrum bands of compounds VII and VIII which have the same structures as before where ffer in some protons, for compound VII which is contain acetamedo group give the chemical shift 10.30 (1,s) is indicated to one proton singlet of amino of acetamedo group , and the amino group of compound VIII which produced according to hydrolysis of compound VII it appeared chemical shift for (2H-NH2) at 2.50, for other chemical shits of these compounds see table (2.4.9 & 2.4.10). The compounds XV and XX formed according to coupling reaction of compounds VIII and naphthquinone and methylbenzoquinone, so the

chemical shifts of two compounds may not more differ but some difference may be available, the proton of amino group which connects sulfonamide and quinone, in case of naphthoquinone the proton appeared 3.35 (1,s), but in the methylbenzoquinone it showed at 4.05 (1,s). For more chemical of compounds (XV & XX) see tables (2.4.11 & 2.4.12).

Compounds IX and X which are contain the same sulfonamide but have differ in acetamedo (IX), which showed following chemical shifts, 10.3 (1,s) indicated for amino group of acetamido, where the amino group in compound X showed at 10.4 (2H,s), in other case three protons of methyl group are appeared at 2.05 (3,s) which indicate to methyl group in compound IX for more see tables (2.4.13 & 2.4.14). For compounds (XVI and XXI) which are coupling of compound X with nathoquinone and methylbenzoquinone, there appeared the following chemical shift, compound XVI showed chemical shift at 3.35 (1H,s) of amino group connected compound IX to naphthoquinone where in compound XXI it appeared at 5.40 (1H,s), there are three protons appeared at 2.44 (3H,s) indicated for the methyl group in benzoquinone, for more see tables (2.4.15 & 2.4.16).

Compounds XI and XII which contain the same sulfonamide but differ in acetamedo (XI),showed following chemical shifts, 10.34 (1,s) indicated for amino group of acetamido, where the amino group in compound XII showed at 6.0 (2H,s), in other case three protons of methyl group are appeared at 2.06 (3,s) which indicate to methyl group in compound XI for more see tables (2.4.17 & 2.4.18). For compounds (XVII and XXII) which are coupling of compound XII with nathoquinone and methylbenzoquinone, there appeared the following chemical shift, compound XVII showed chemical shift at 12.2 (1H,s) of amino group connected compound XII to naphthoquinone where in compound XXII it

appeared at 5.40 (1H,s), there are three protons appeared at 2.54 (3H,s) indicated for the methyl group in benzoquinone, for more see tables (2.4.19 & 2.4.20).

The ^{13}C-NMR spectra analysis of synthesized quinones and sulphonamide derivatives in this study may be explained in the followings. The ^{13}C-NMR of compound III and compound IV which are contain the same structure with different only in the substituted group which changed to amino group in the compound IV where it formed after hydrolysis of compound III therefore showed the same ^{13}C-NMR chemical shifts with differ in some carbon atoms according to difference of their environments and groups attached and types of hydrogen nucleus which are coupling to the carbon atoms in certain molecule. The compounds III and IV showed some ^{13}C –NMR chemical shifts, two compounds have the same structure with differ in acetamedo group for compound III which is appeared the chemical of carbon atom attached to acetamedo group at (153.02) and for compound IV appeared at 155.37, for more see table (2.5.1 & 2,5,2). The coupling of compound IV with nathaquinone formed compound XIII and the coupling of the same reagent with methylbenzoquinone formed compound XVIII, the difference between two coupling compounds may be showed in the following ^{13}C-NMR chemical shifts , (155.41) indicated for carbon in naphthquinone attached to amino group of sulfonamide, the other coupling compound (XVIII) the ^{13}C-NMR analysis un appeared except the following, 16.39 indicated to methyl group, for more see tables, (2.5.3 & 2,5,4).

Compounds V and VI showed some ^{13}C –NMR chemical shifts, two compounds have the same structure differ in acetamedo group for compound V which is appeared the chemical of carbon atom attached to acetamedo group at (128.47) and for compound VI appeared at 133.34, also the carbon of carbonyl of acetamedo group in compound V appeared at 170.3, for more see table (2.5.5 &

2,5,6). The coupling of compound VI with nathaquinone formed compound XIV and the coupling of the same reagent with methylbenzoquinone formed compound XIX, the difference between two coupling compounds may be showed in the following ^{13}C-NMR chemical shifts , (157.92) indicated for carbon in naphthquinone attached to amino group of sulfonamide, the other coupling compound (XIX) the ^{13}C-NMR analysis un appeared except the following, 133.74 indicated to benzene ring carbons, for more see tables, (2.5.7 & 2,5,8).

The ^{13}C-NMR analysis of compounds XI and XII showed chemical shifts, two compounds have the same structure w here differ in acetamedo group for compound XI which is appeared the chemical of carbon atom attached to acetamedo group at (143.48) and for compound XII appeared at 153.60, also the carbon of carbonyl of acetamedo group in compound VII appeared at 169.52, for more see table (2.5.9 & 2,5,10). The coupling of compound XII with nathaquinone formed compound XVII and the coupling of the same reagent with methylbenzoquinone formed compound XXII, the difference between two coupling compounds may be showed in the following ^{13}C-NMR chemical shifts , (157.92) indicated for carbon in naphthquinone attached to amino group of sulfonamide, the other coupling compound (XXII) the ^{13}C-NMR analysis un appeared except the following, 16.40 indicated for carbon of methyl group, some other chemical shifts indicated to benzene ring carbons, for more see tables, (2.5.11 & 2.5.12).

The ^{13}C-NMR analysis of compounds IX and X showed chemical shifts, two compounds have the same structure with differ in acetamedo group for compound IX which is appeared the chemical of carbon atom attached to acetamedo group at (143.88) and for compound X appeared at 153.60, also the carbon of carbonyl of acetamedo group in compound IX appeared at 169.52, for more see table (2.5.13

& 2.5.14). The coupling of compound X with nathaquinone formed compound XVI and the coupling of the same reagent with methylbenzoquinone formed compound XXI, the difference between two coupling compounds may be showed in the following ^{13}C-NMR chemical shifts , (143.92) indicated for carbon in naphthquinone attached to amino group of sulfonamide, the other coupling compound (XXII) the ^{13}C-NMR analysis unappeared any chemical shifts, for more see tables, (2.5.15 & 2.5.16).

The 13C-NMR analysis of compounds VII and VIII showed chemical shifts, two compounds have the same structure with differ in acetamedo group for compound VII which is appeared the chemical of carbon atom attached to acetamedo group at (133.05) and for compound VIII appeared at 150.99, also the carbon of carbonyl of acetamedo group in compound VII appeared at 169.53, for more see table (2.5.17 & 2.5.18). The coupling of compound VIII with nathaquinone formed compound XV and the coupling of the same reagent with methylbenzoquinone formed compound XX, the difference between two coupling compounds may be showed in the following 13C-NMR chemical shifts , (143.92) indicated for carbon in naphthquinone attached to amino group of sulfonamide, the other coupling compound (XXII) the 13C-NMR analysis un appeared any chemical shifts, for more see tables, (2.5.19 & 2.5.20).

The molecular mass spectra analysis for some synthesized compounds to determine their molecular weight. The mass spectra of compounds (III and IV) which have the same structure with difference in the acetamedo group for compound for III and amino group for compound IV, and the coupling of compound IV with naphthoquinone formed compound XIII and with methylbenzoquinone formed compound XVIII, MS spectra for synthesized compounds showed strong peaks respectively as the following (207, 85% , 281,

25%, table2.6.1), (267, 15%, 298, 10%, table 2.6.2), (280 ,25%, , 357, 24%, ,table2.6.3),(355, 25%, 429 , 27%,table2.6.4).

The mass spectra of compounds (V and VI) which have the same structure with difference in the acetamedo group for compound for V and amino group for compound VI, and the coupling of compound VI with naphthoquinone formed compound XIV and with methylbenzoquinone formed compound XIX, MS spectra for synthesized compounds showed strong peaks respectively as the following (209,17%,281,17%table2.6.5),(249,13%,283,13%,table2.6.6),(207, 25%, 271, 20% ,table2.6.7) ,(355 , 23%, 421, 22%,table2.6.8).

The mass spectra of compounds (XI and XII) which have the same structure with difference in the acetamedo group for compound for XI and amino group for compound XII, and the coupling of compound XII with naphthoquinone formed compound XVII and with methylbenzoquinone formed compound XXII, MS spectra for synthesized compounds showed strong peaks respectively as the followings (281, 15%, 342, 10%,table2.6.9),(209, 15%,281, 20%,table2.6.10), (341, 20%, 429, 20% ,table2.6.11) ,(282, 28%, 375, 22%,table2.6.12).

The mass spectra of compounds (IX and X) which have the same structure with difference in the acetamedo group for compound for IX and amino group for compound X, and the coupling of compound X with naphthoquinone formed compound XVI and with methylbenzoquinone formed compound XXI, MS spectra for synthesized compounds showed strong peaks respectively as the followings (246, 25%, 281, 27%,table2.6.13),(207.00, 95%, 281, 25% ,table2.6.14), (179, 48%, 341, 25%,table2.6.15) ,(236, 55%, 281, 65% ,table2.6.16).

The mass spectra of compounds (VII and VIII) have the same structure with difference in the acetamedo group for compound for VII and amino group for compound VIII, and the coupling of compound VIII with naphthoquinone formed compound XV and with methylbenzoquinone formed compound XX, MS spectra for synthesized compounds showed strong peaks respectively as the following: (76, 75%, 230, 25%.table 2.6.17),(281, 25%, 267, 20% ,table 2.6.18), (46, 100%, 285, 23%, table 2.6.19) ,(46, 100%, 289, 20%, table2.6.20).

Conclusion and recommendations

The following points may be concluded or recommended according to the results of this study:

- The method used for the synthesis of the intermediate compounds (sulphnamide) was chlorosulfonation.
- From the previous studies and the products of sulfonamide prepared in this study we conclude that, the sulfonamide are very active compounds, therefore, may react with different regents to form various compounds (p-actamedo and aminocompounds compounds).
- In this study,most of synthesized p-actamedo and aminocompounds were treated with two synthesized reagents (naphthaquinones and methylbenzoquinone).
- The two intermediate reagents naphthoquinones and methylbenzoquinone were prepared by the treatment of naphthalene and crezole respectively.
- The coupling compounds formed through reaction of some synthesized amines (which were formed through hydrolysis of acetamedo compounds) and naphthoquinone and methylbenzoquinone.
- All synthesized compounds in this study were purified by recrystalization and TLC techniques. The structures of all synthesized compounds in this thesis were characterized by study of spectral analysis IR,^{1}H -NMR,^{13}C -NMR and mass spectra.
- Many of the synthesized compounds in this work were novel.

- It highly recommended that the final and intermediate synthetic compounds be screened for the following possible biological activities:

  a- Anti tuborculestatic activity.

  b- Anti malarial and anti tumor activities.

  c- Anti microbial activity.

- Based upon biological activities a molecular modeling study including QSAR and molecular docking is highly recommended.
- Design of new derivatives based upon computational studies.

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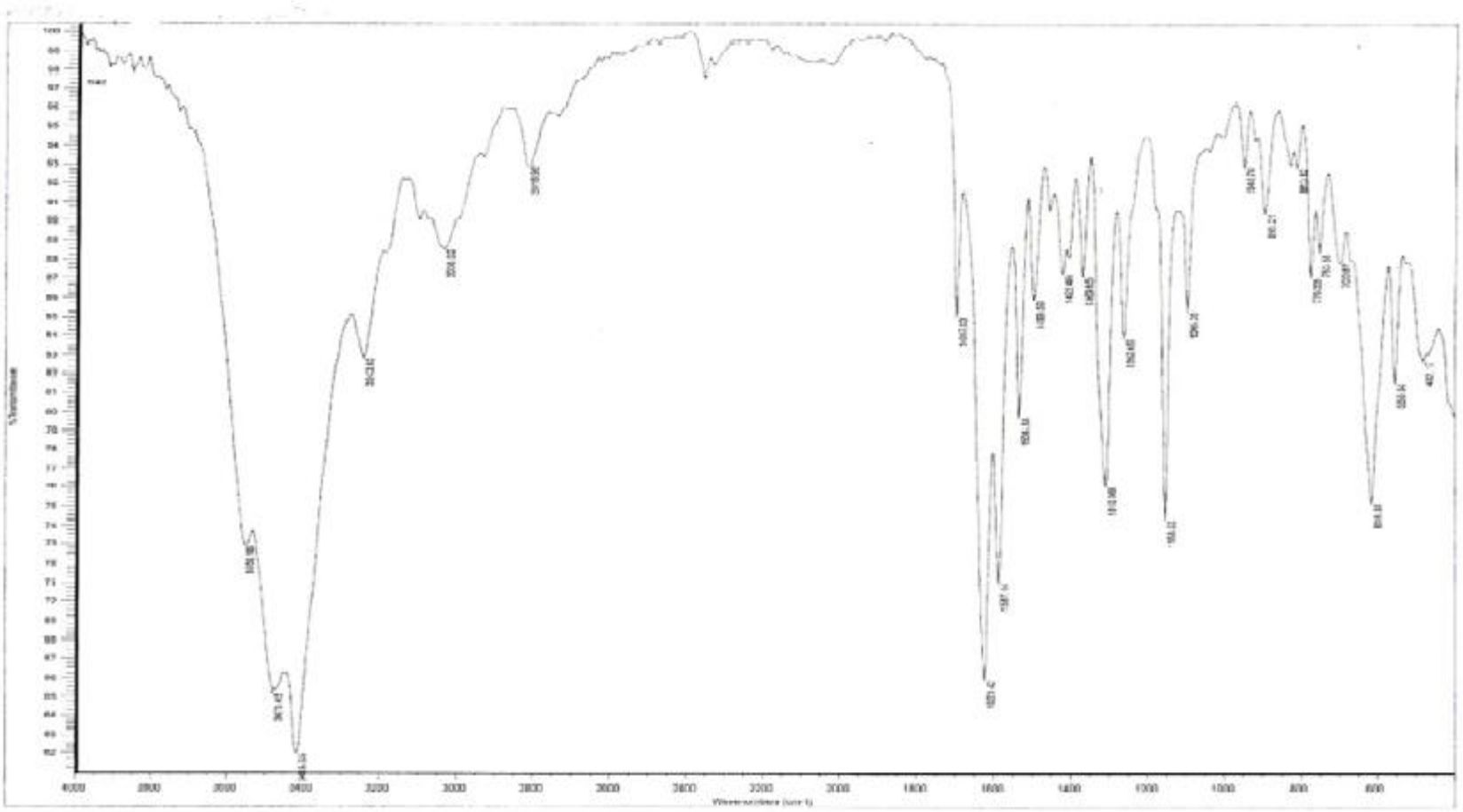
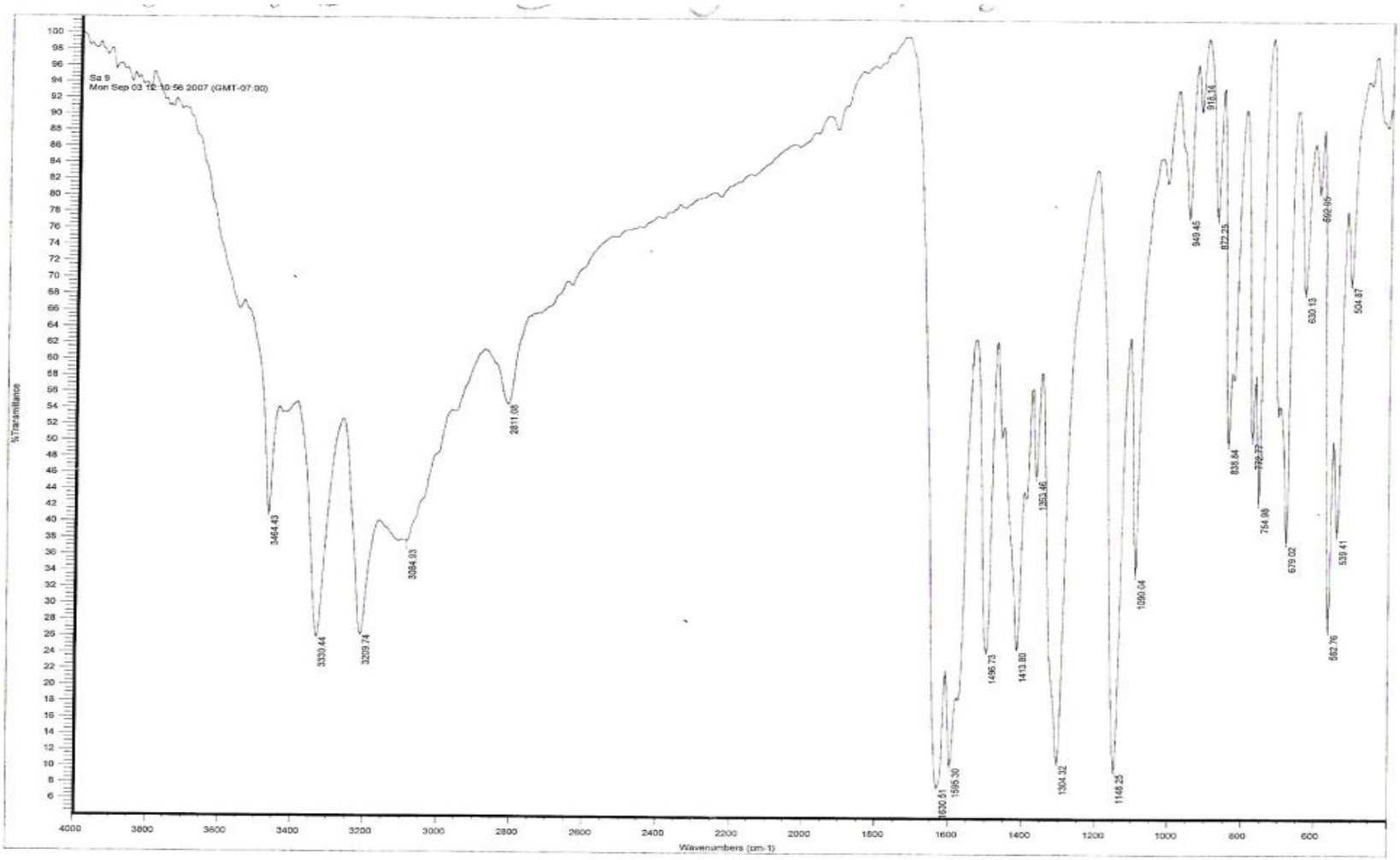
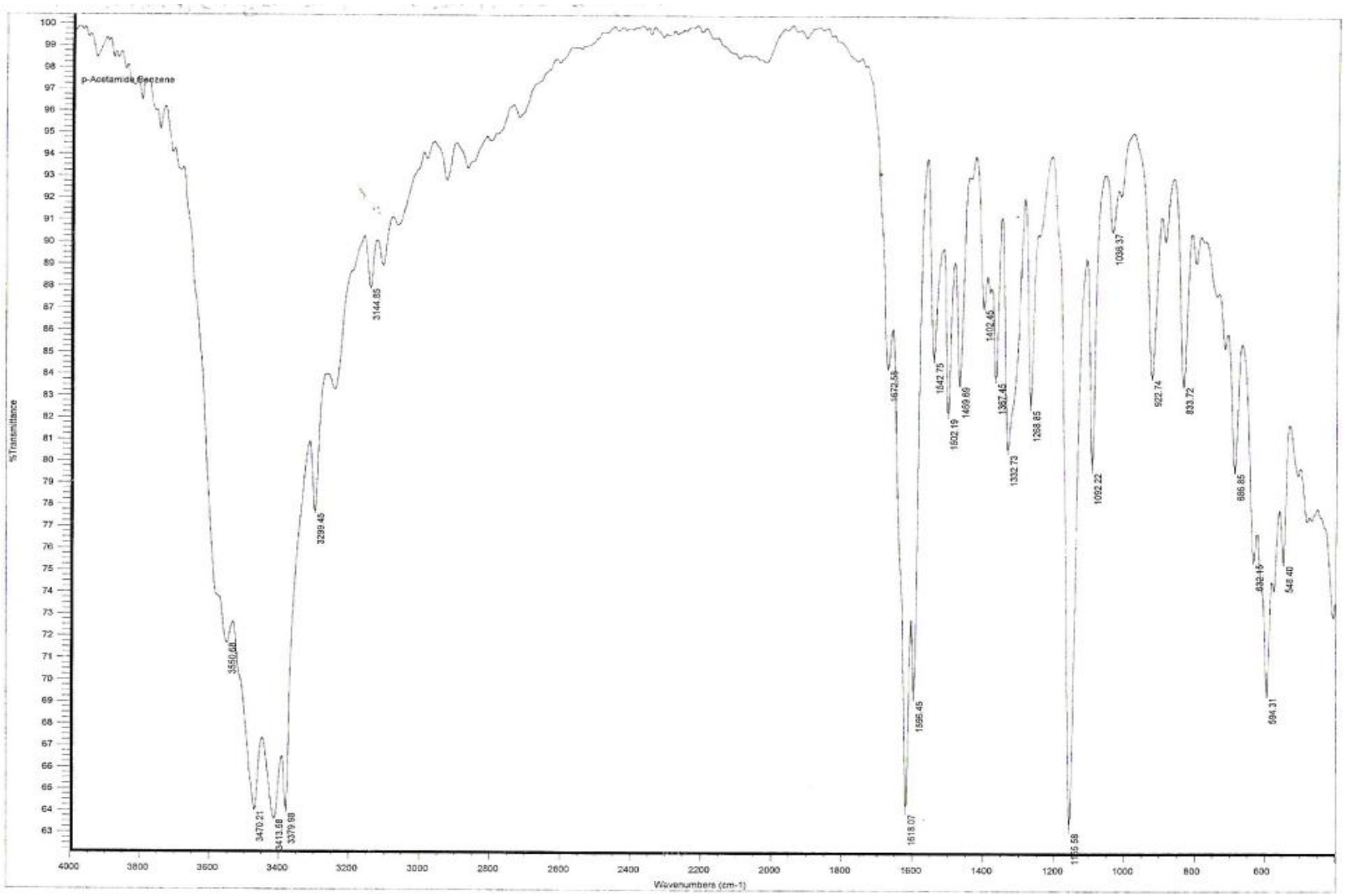
Appendices



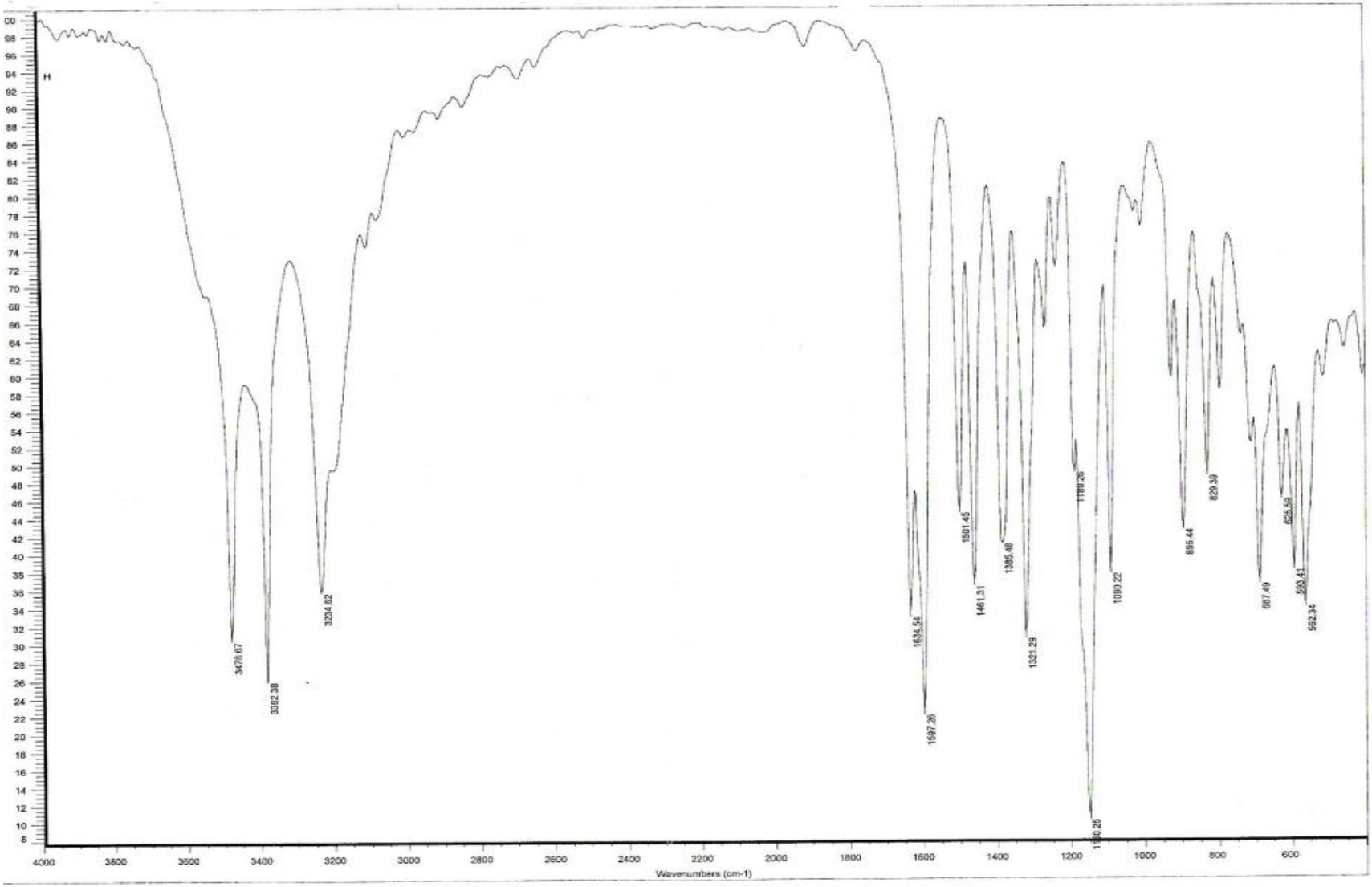
Appendix (1):IR spectra of N-(4-(N-(5-oxo-1-phenylpyrazolidin-4-yl)sulfamoyl)phenyl)acetamide compound (**III**)



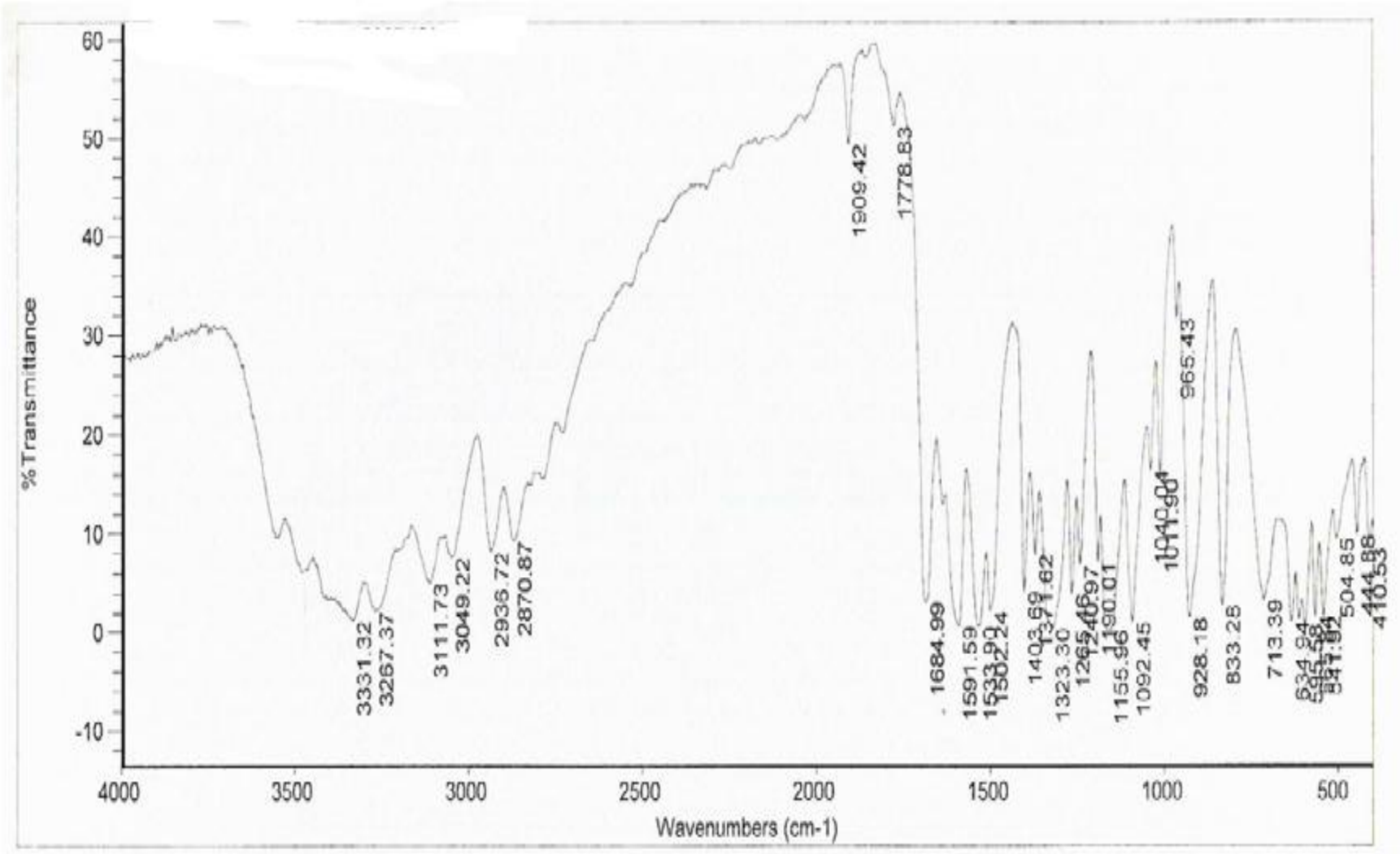
Appendix (2):IR spectra of 4-amino-N-(5-oxo-1-phenylpyrazolidin-4-yl)benzenesulfonamide compound (**IV**)



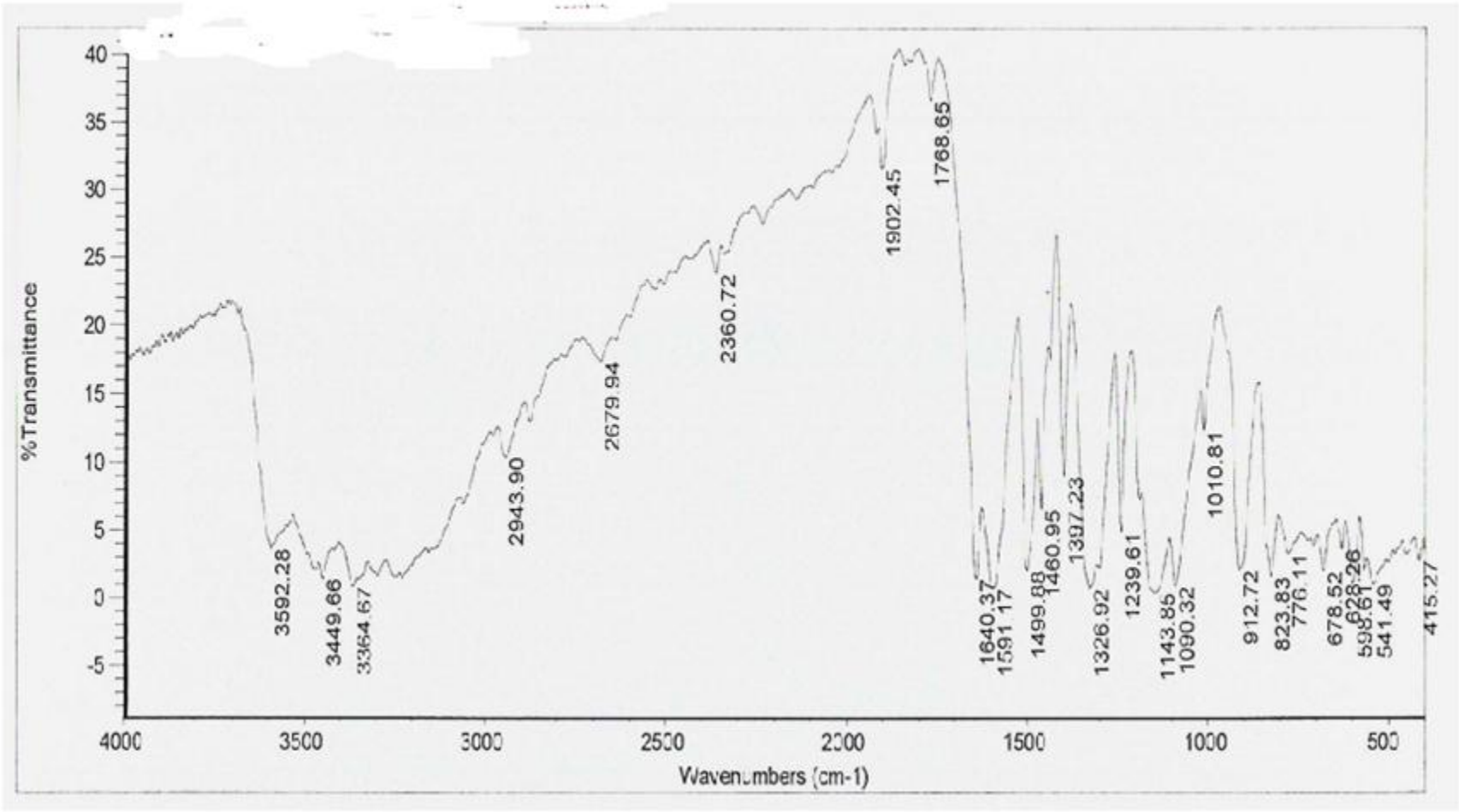
Appendix (3):IR spectra of N-(4-(4-(5-methylisoxazole-3-sulfonamido)phenylsulfonamido)phenyl)acetamide compound (**V**)



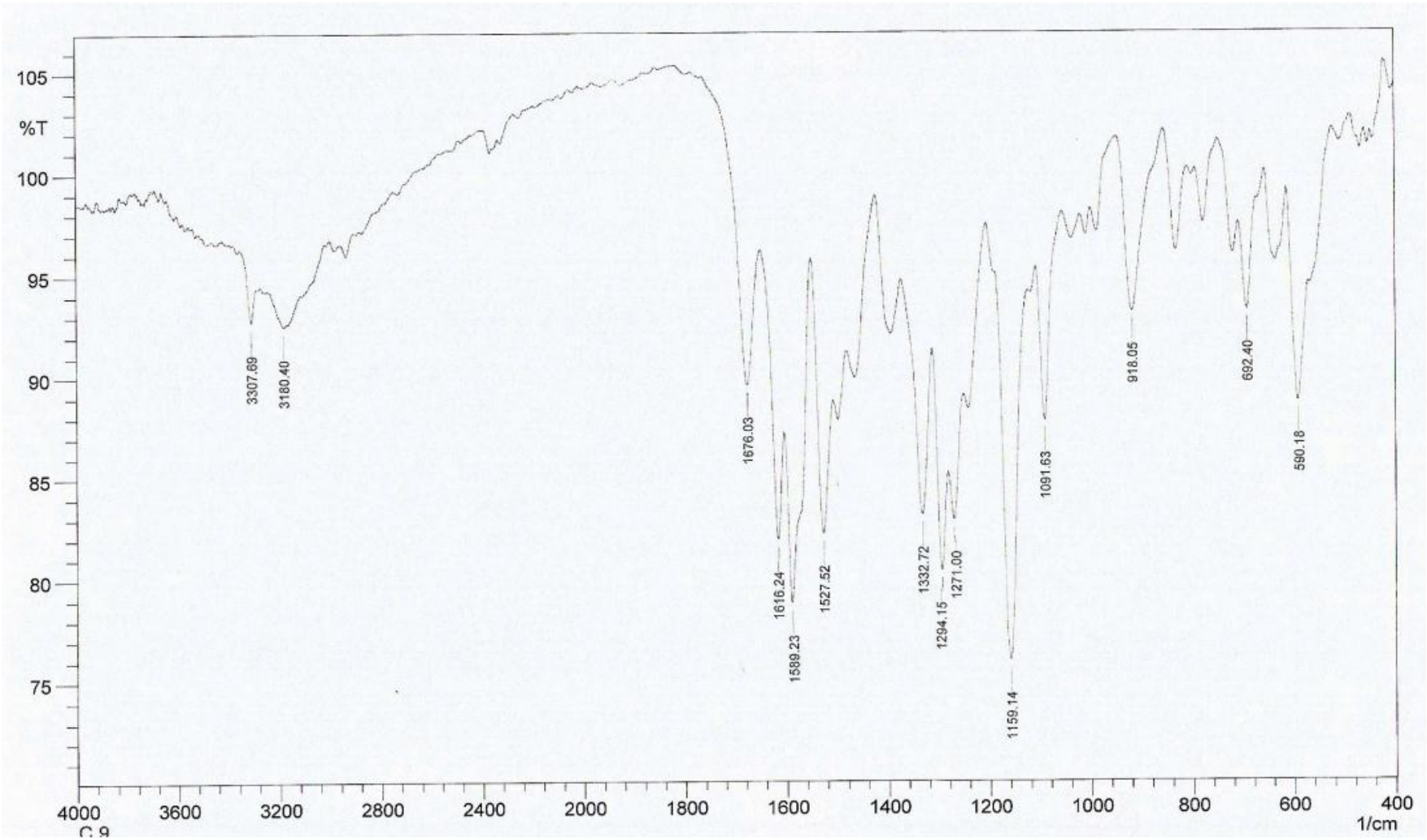
Appendix (4):IR spectra of 4-amino-N-(4-(N-(5-methylisoxazol-3-yl)sulfamoyl)phenyl)benzenesulfonamide compound (**VI**)



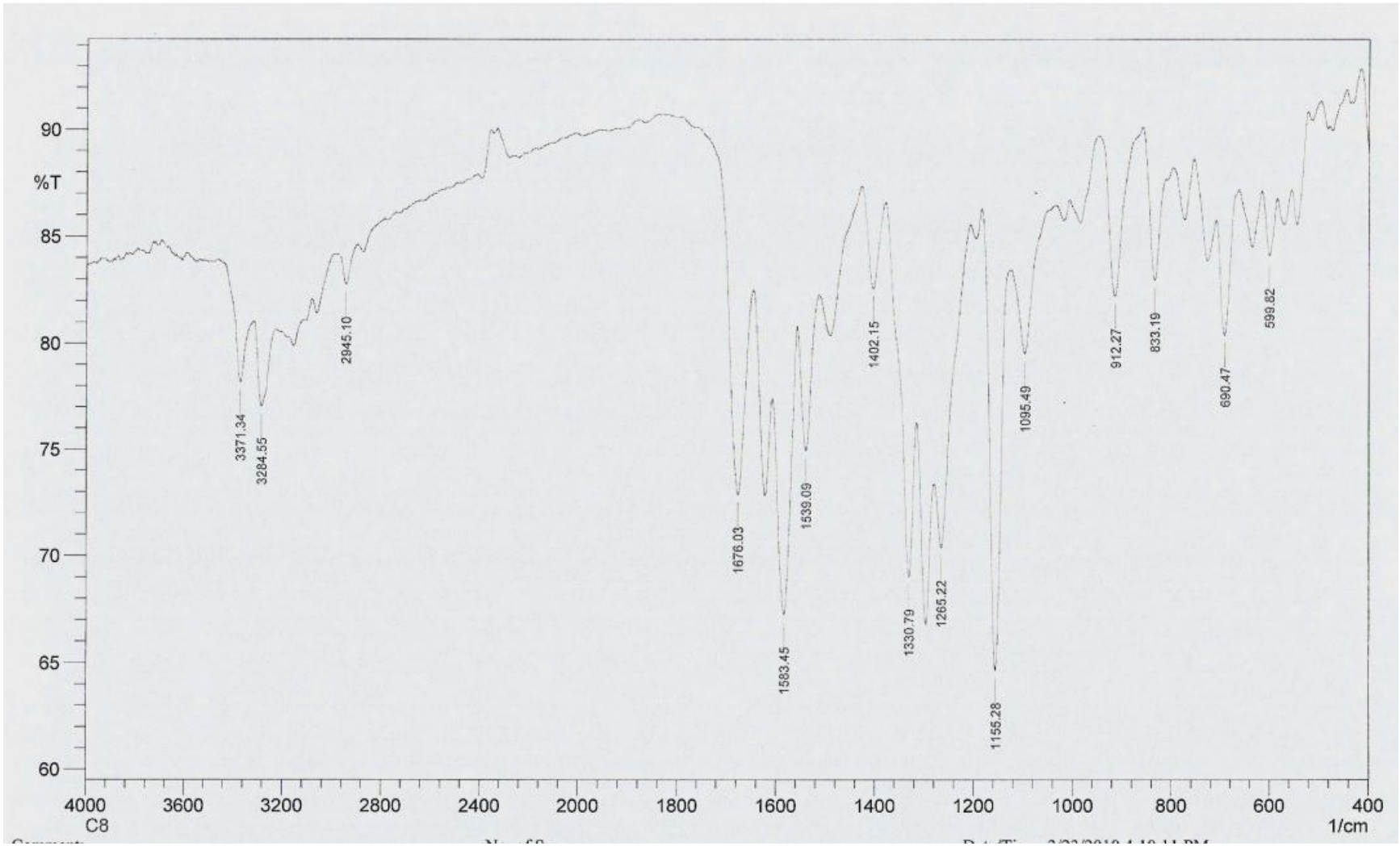
Appendix (5):IR spectra of N-(4-(N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)sulfamoyl)phenyl)acetamide compound (**IX**)



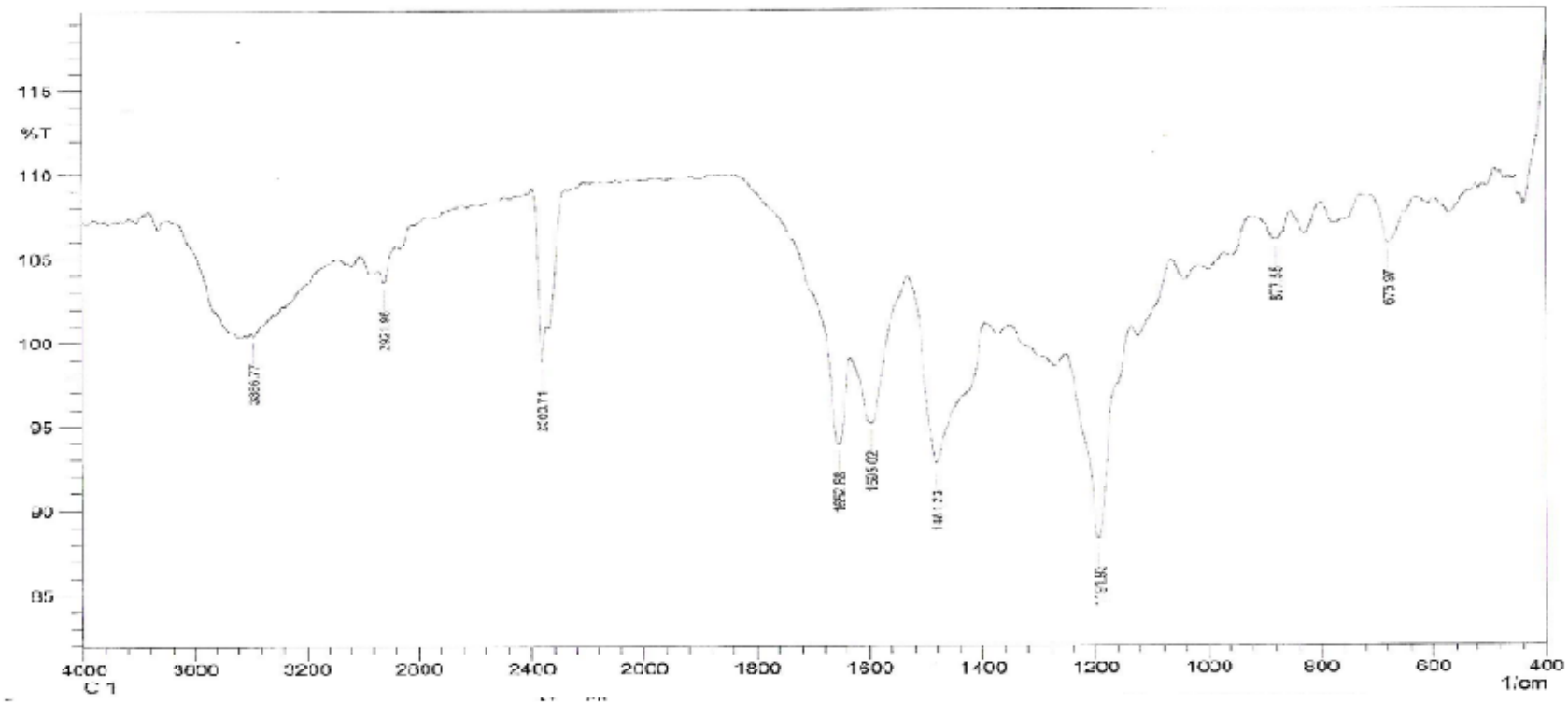
Appendix (6):IR spectra of 4-amino-N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)benzenesulfonamide compound (**X**)



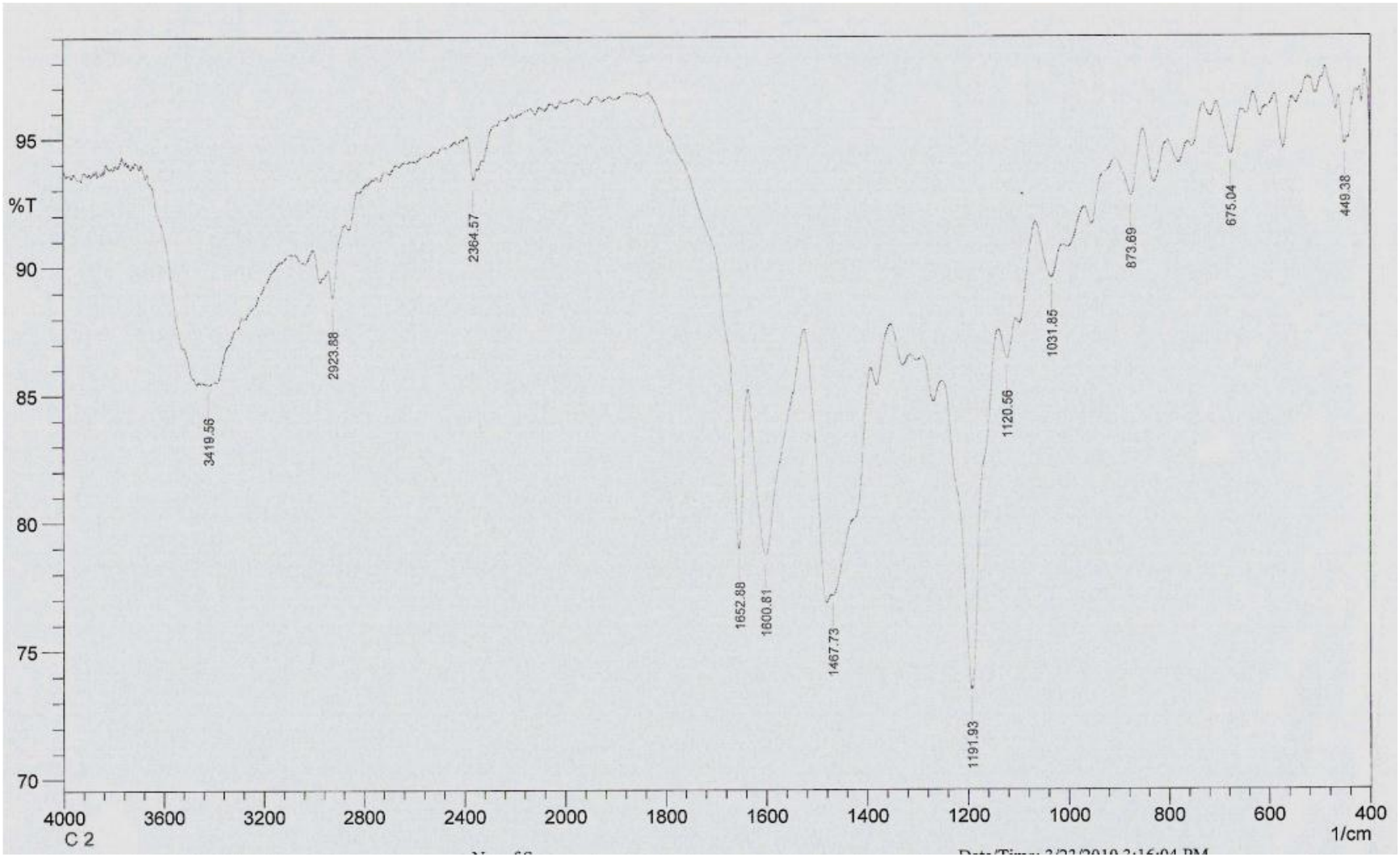
Appendix (7):IR spectra of 4-(1,4-dioxo-1,4-dihydronaphthalen-2-ylamino)-N-(5-methylisoxazol-3-yl)benzenesulfonamide compound (**XIV**)



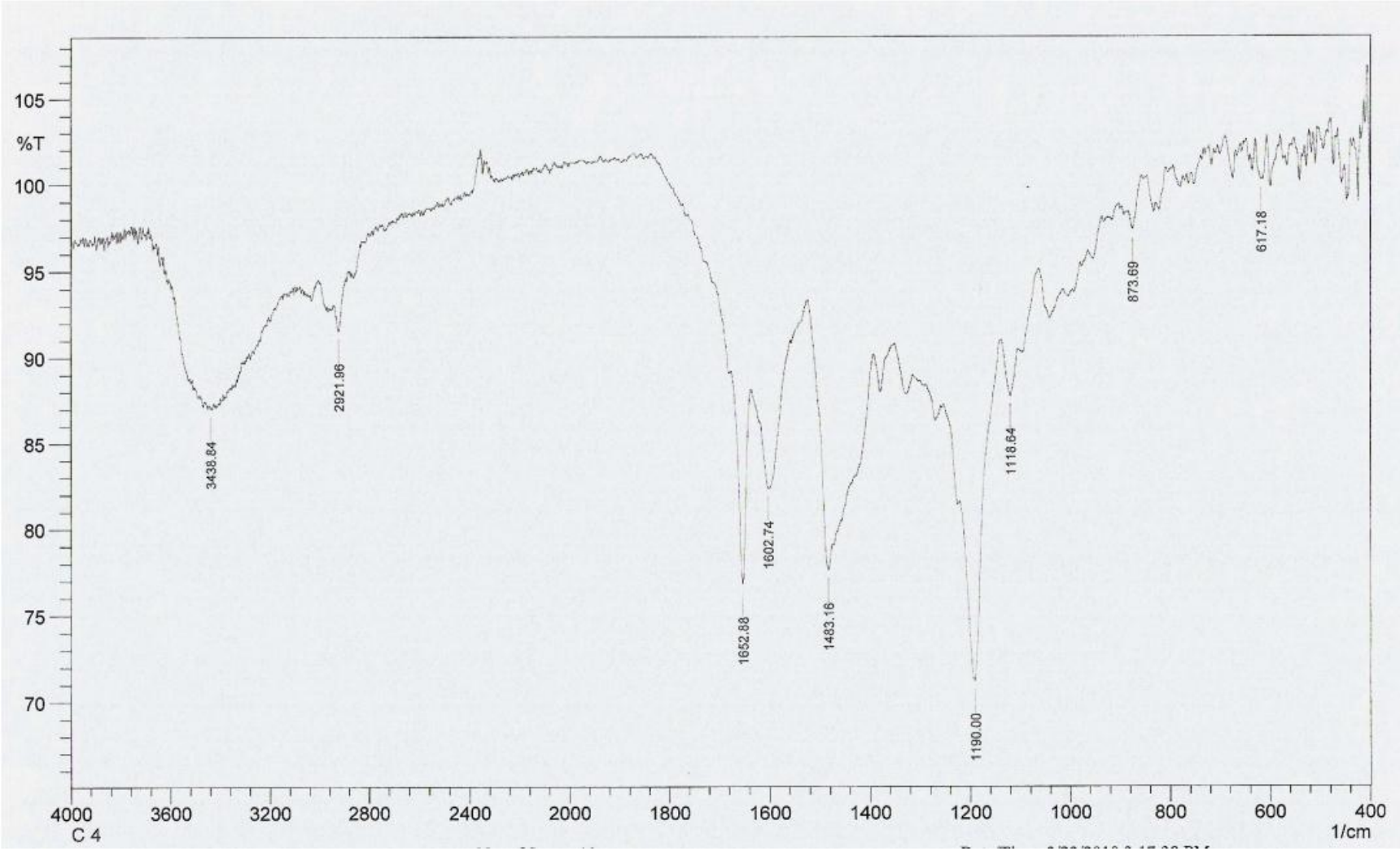
Appendix (8):IR spectra of N-(4-aminophenyl)-4-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)benzenesulfonamide compound (**XVI**)



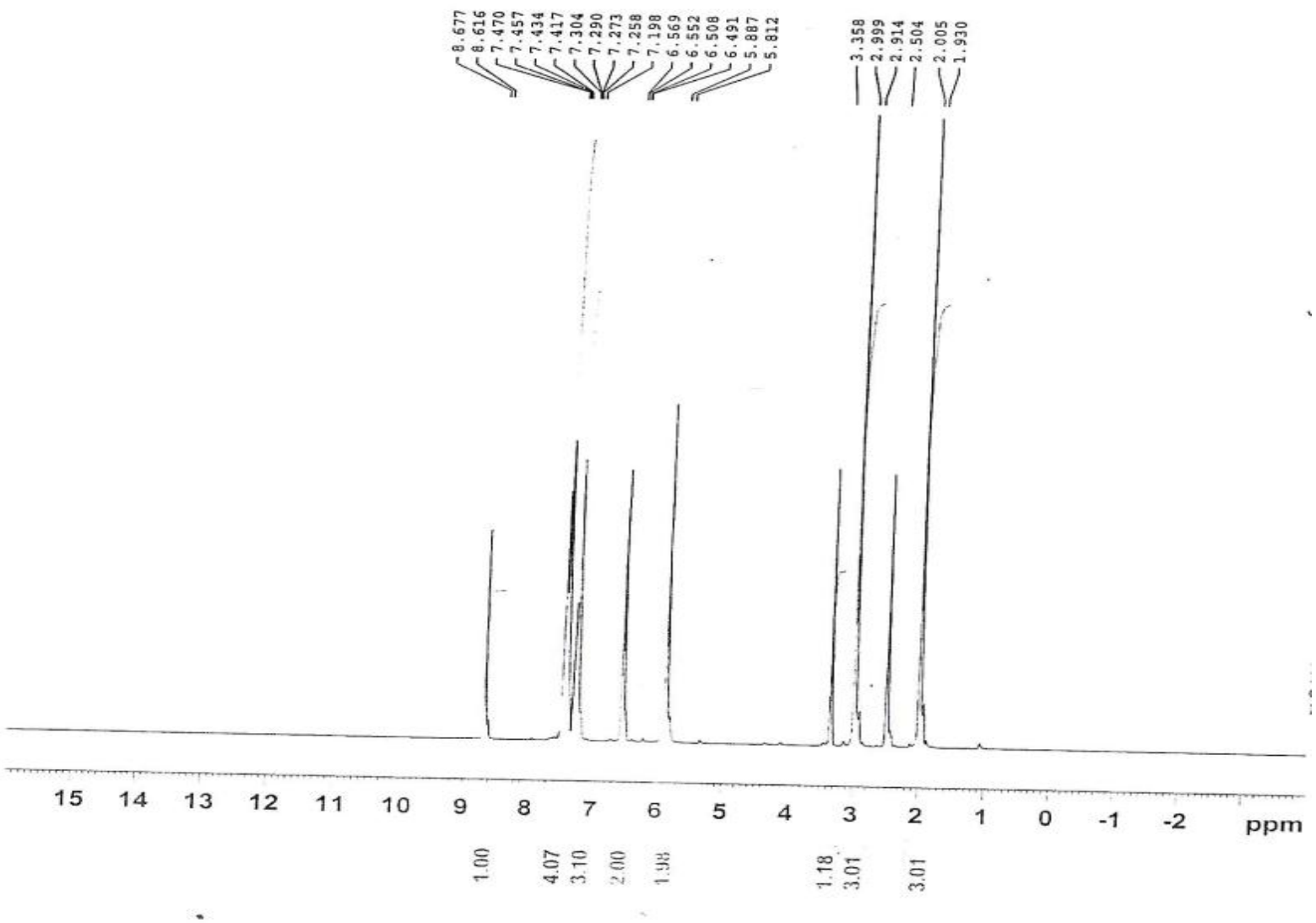
Appendix (9):IR spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) benzenesulfonamide compound (**XVIII**)



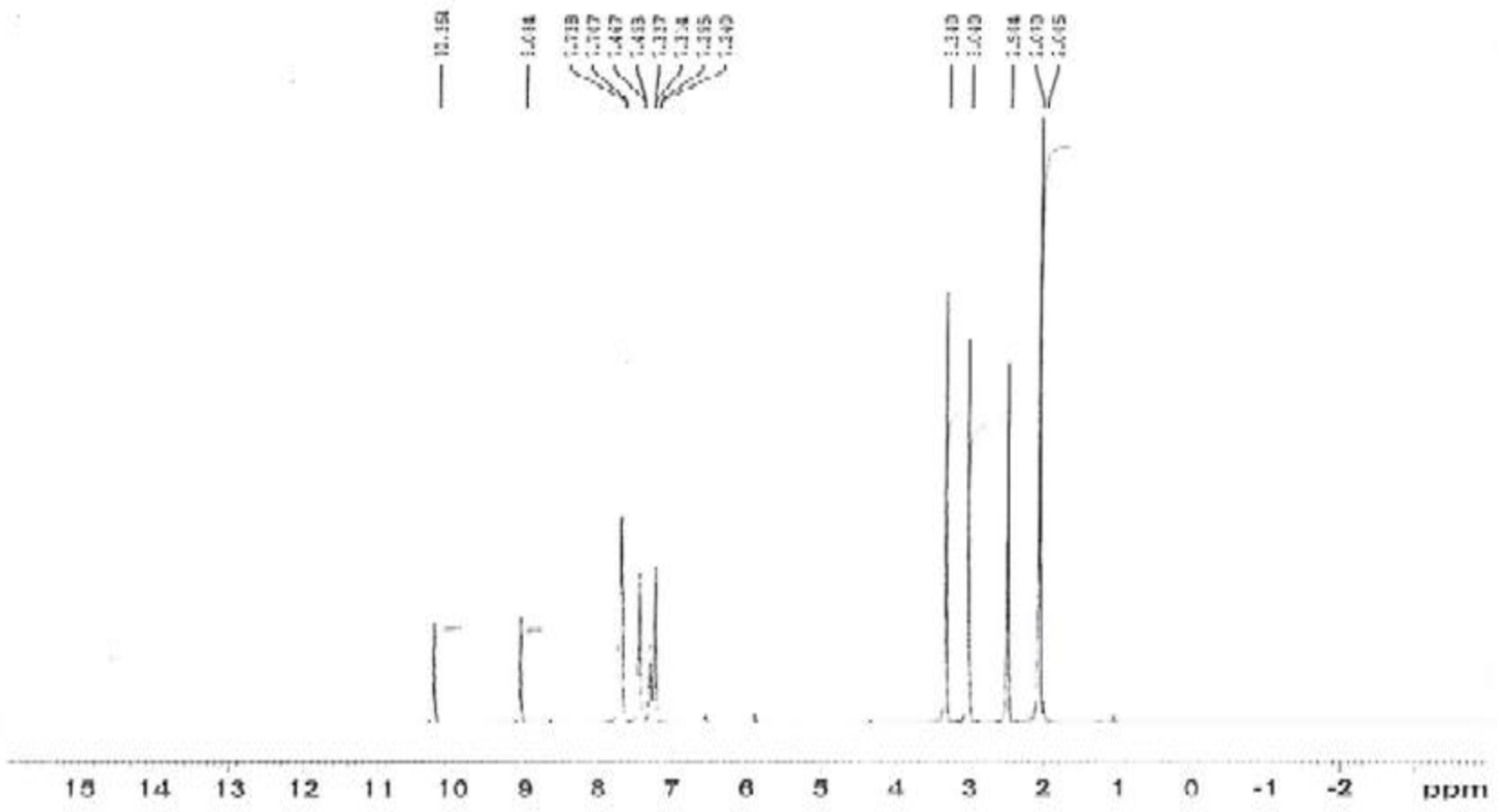
Appendix (10):IR spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(5-methylisoxazol-3-yl)sulfamoyl)phenyl)benzenesulfonamide compound (**XIX**)



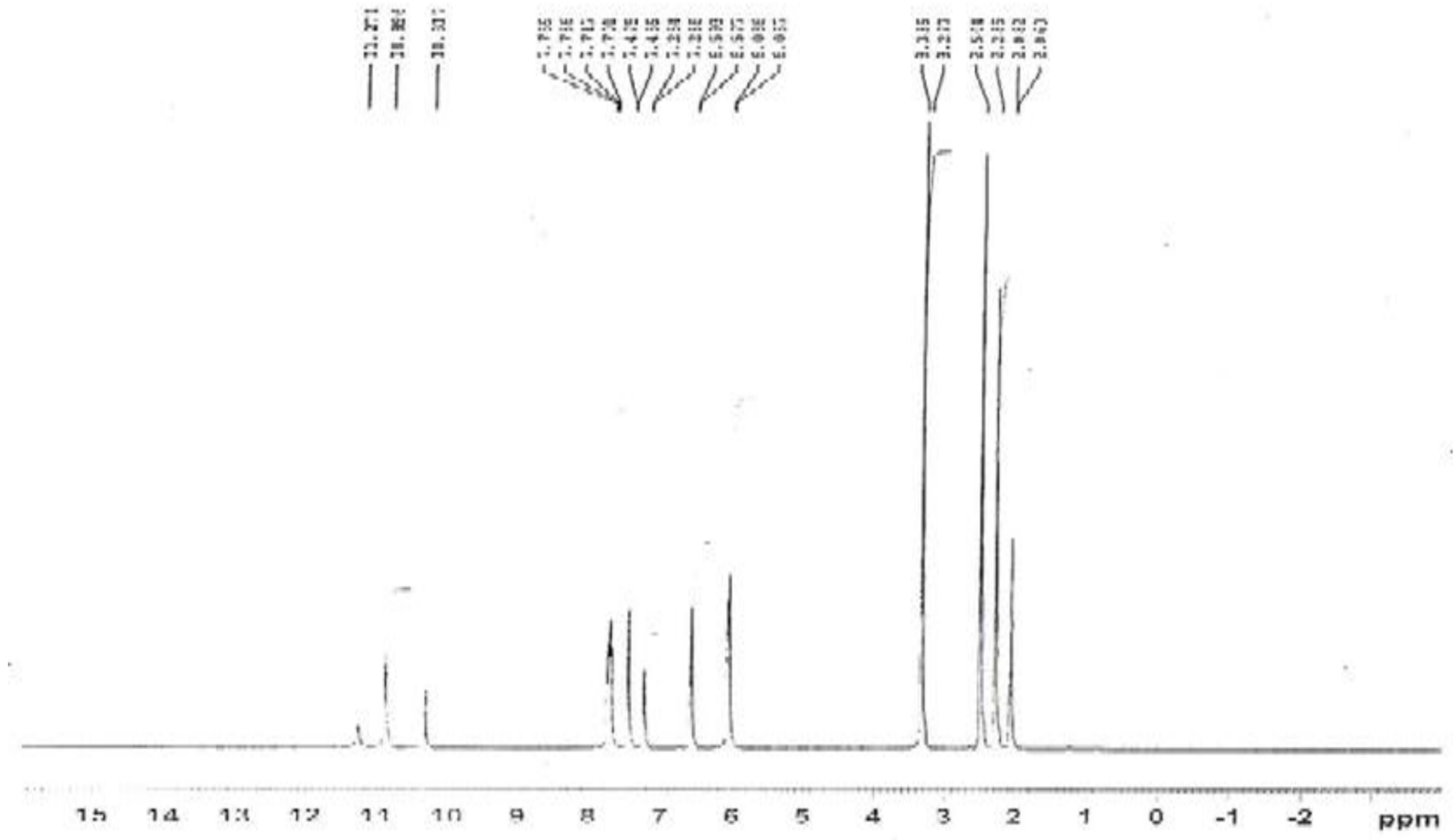
Appendix (11):IR spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl) benzenesulfonamide compound (**XXI**)



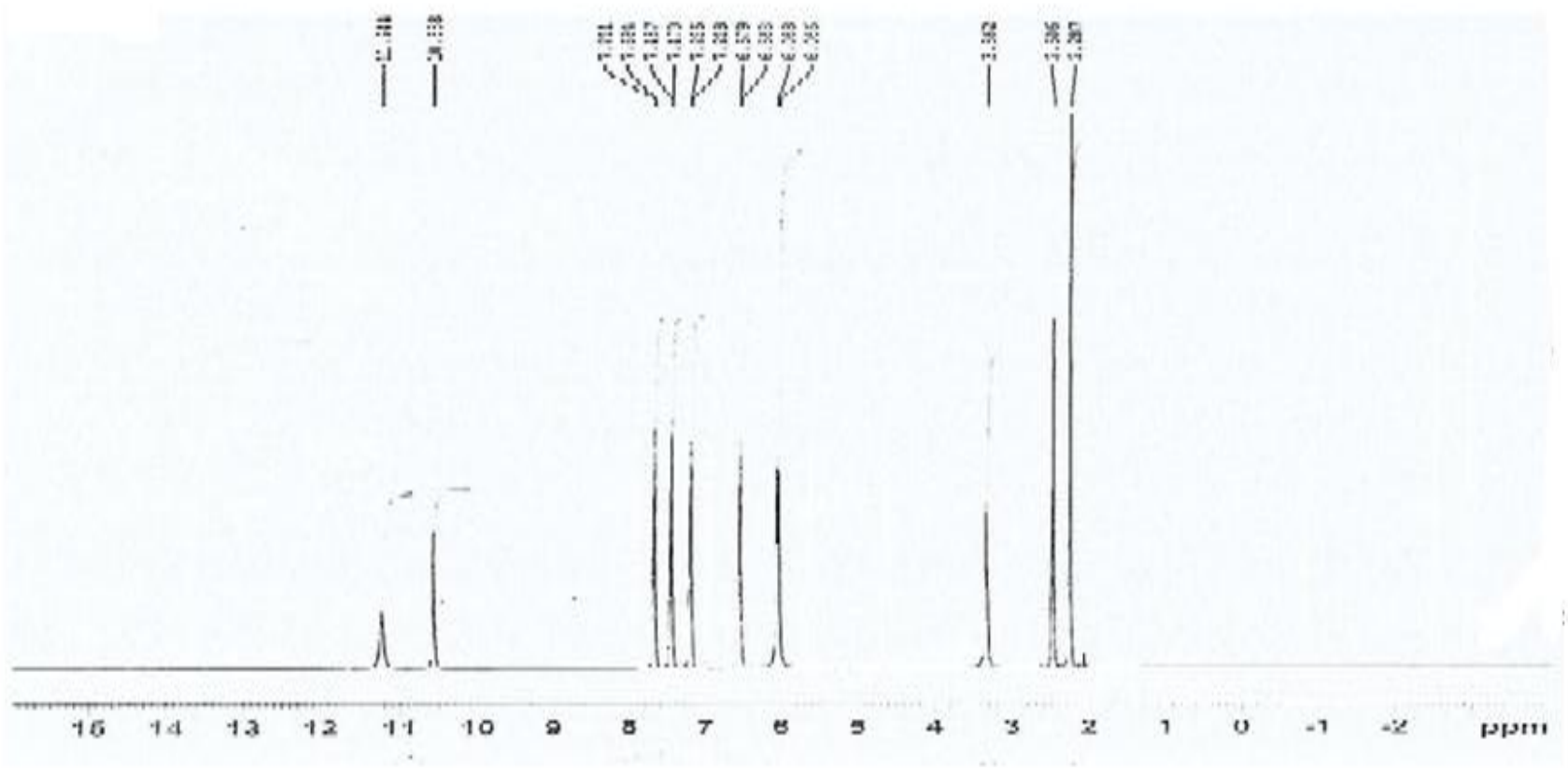
Appendix (12):H^1-NMR spectra of N-(4-(N-(5-oxo-1-phenylpyrazolidin-4-yl)sulfamoyl)phenyl)acetamide compound (**III**)



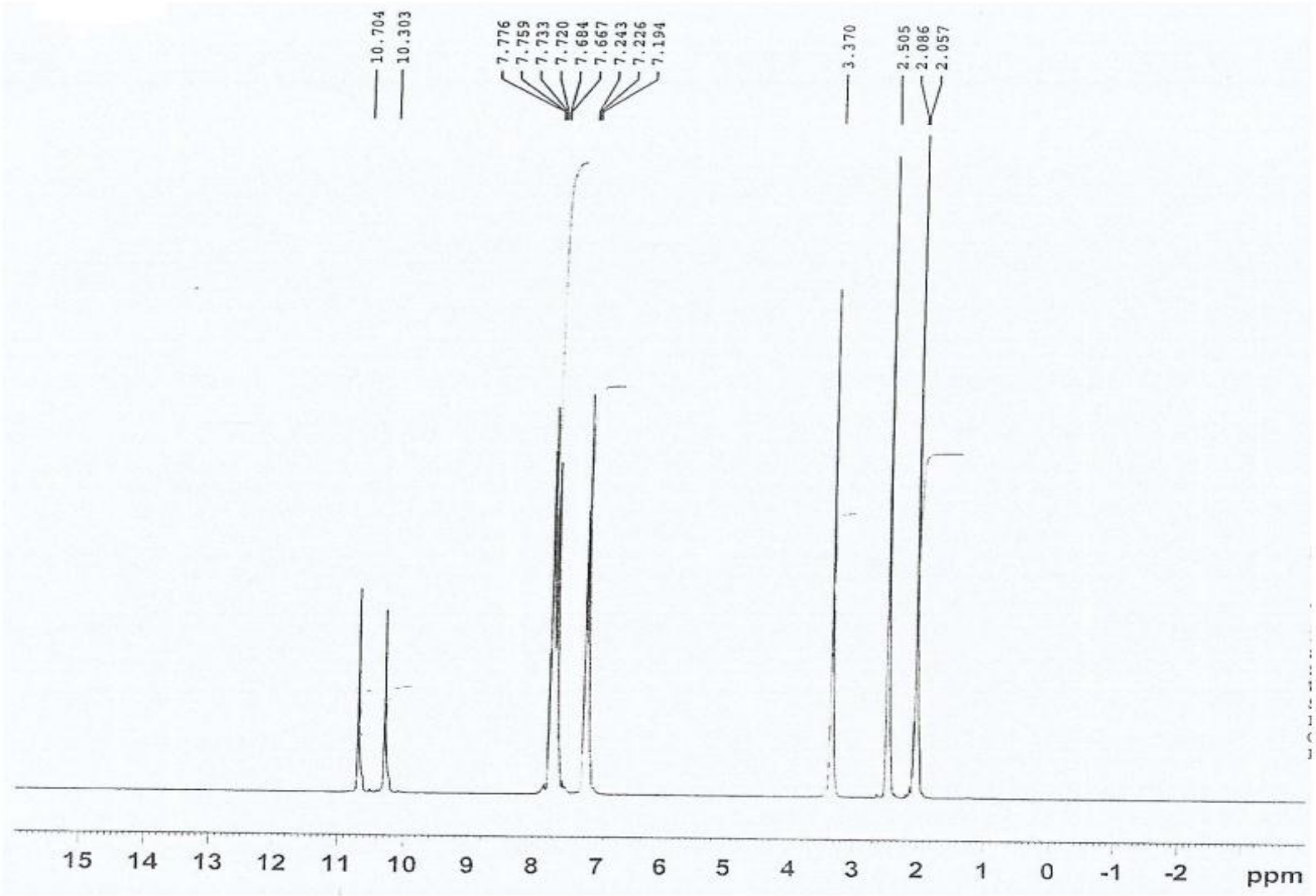
Appendix (13):H^1-NMR spectra of 4-amino-N-(5-oxo-1-phenylpyrazolidin-4-yl)benzenesulfonamide compound (**IV**)



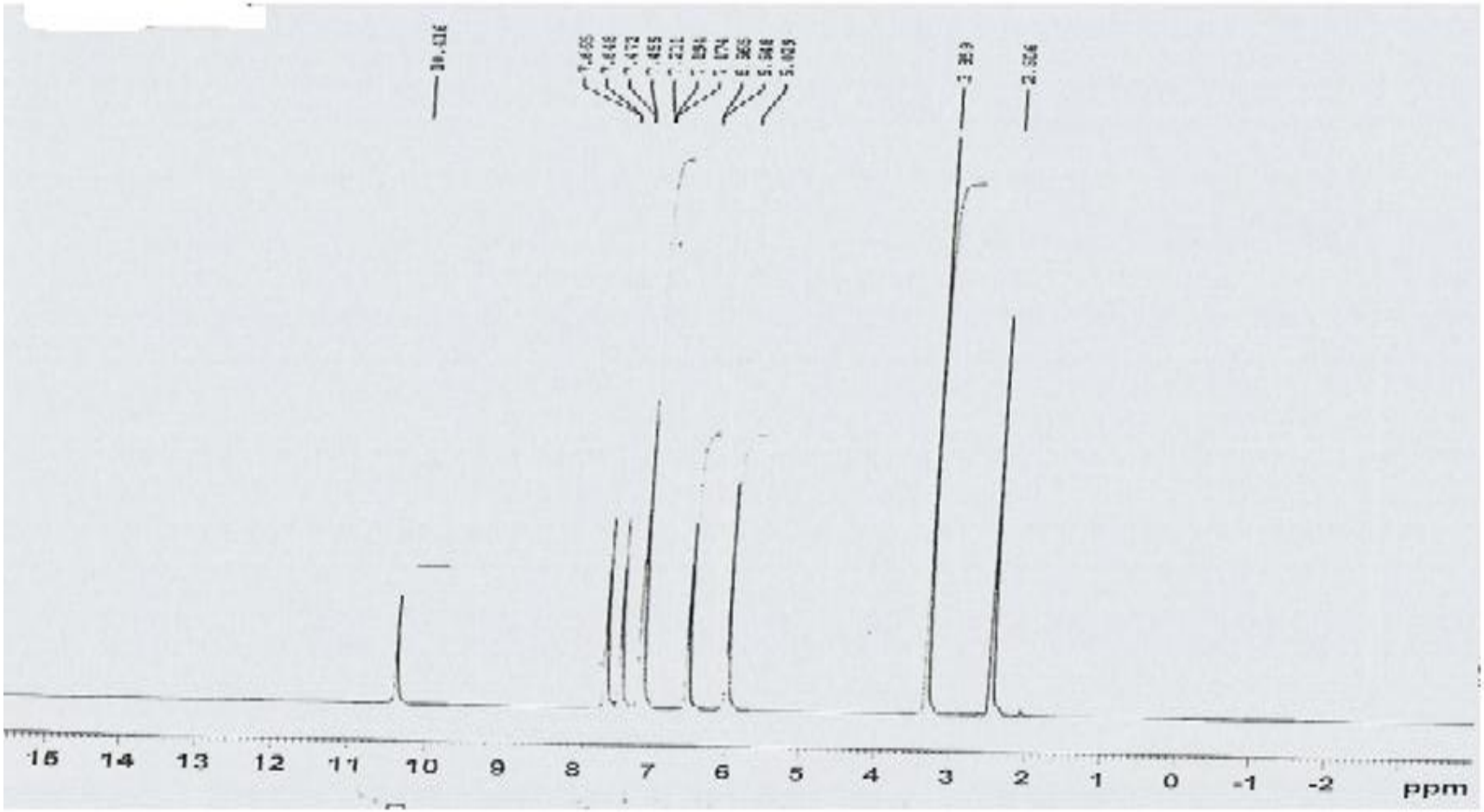
Appendix (14):H^1-NMR spectra of N-(4-(4-(5-methylisoxazole-3-sulfonamido)phenylsulfonamido)phenyl)acetamide compound (**V**)



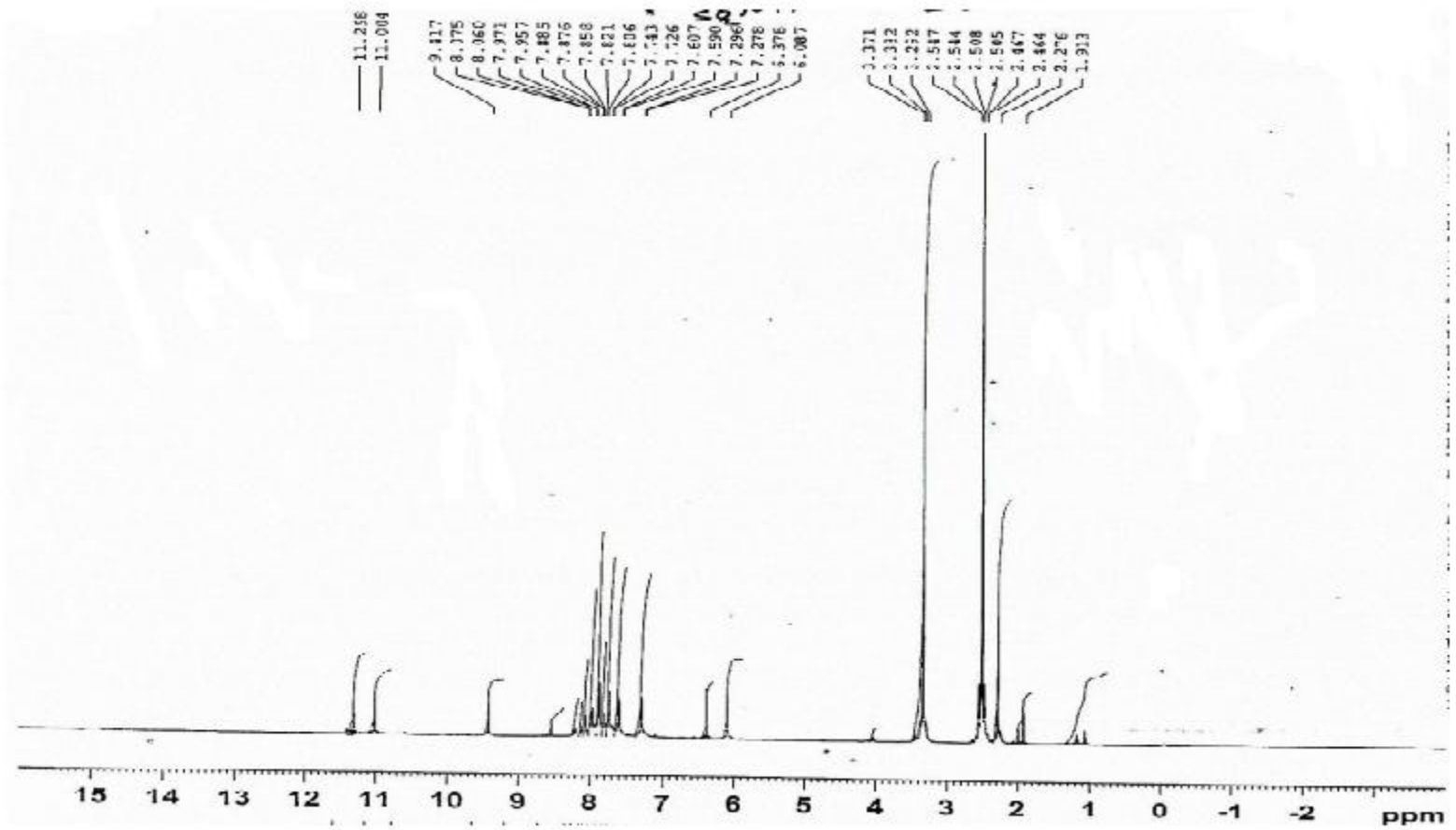
Appendix (15):H^1-NMR spectra of 4-amino-N-(4-(N-(5-methylisoxazol-3-yl)sulfamoyl)phenyl)benzenesulfonamide compound (**VI**)



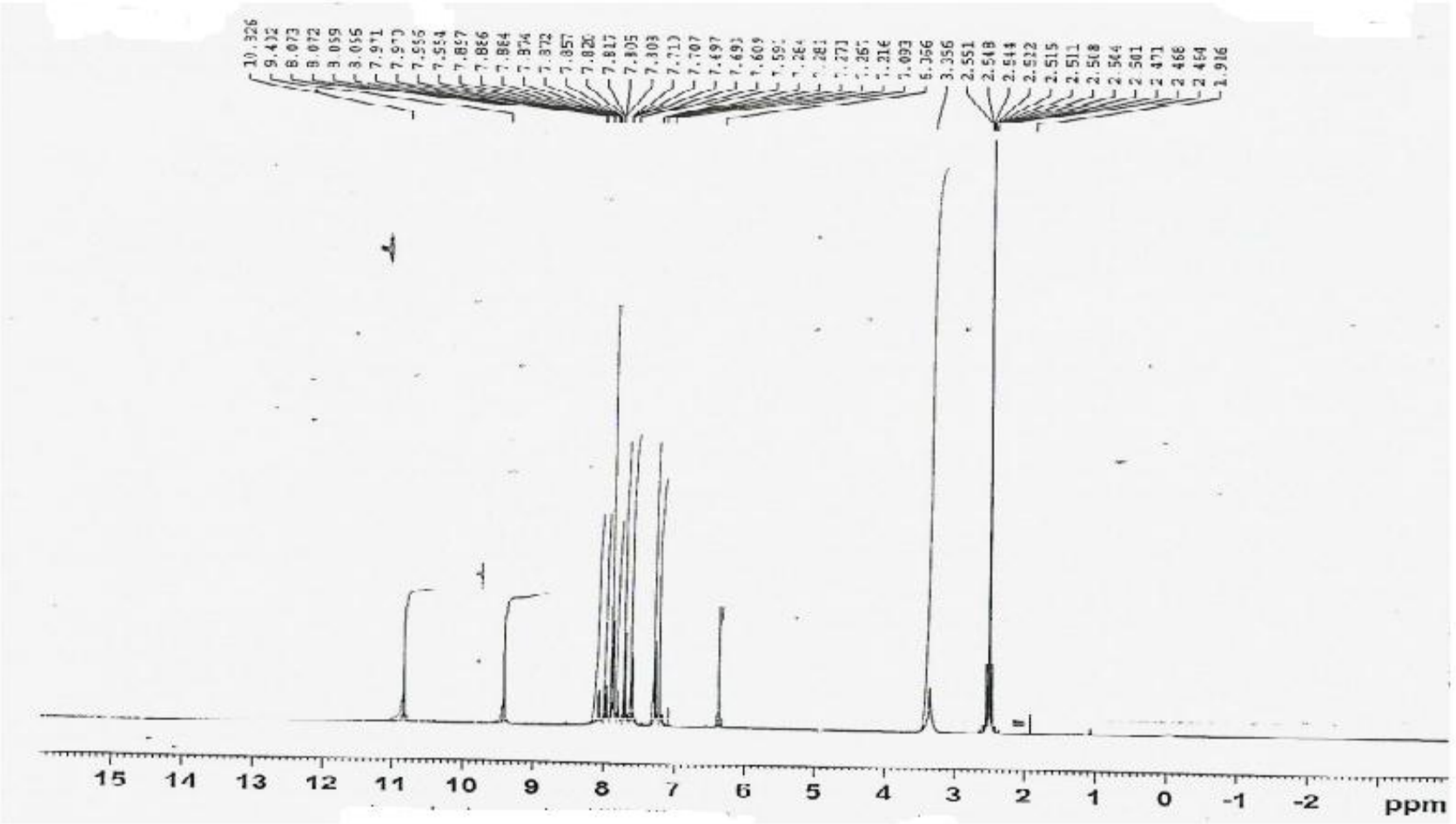
Appendix (16):H^1-NMR spectra of N-(4-(N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)sulfamoyl)phenyl)acetamide compound (**IX**)



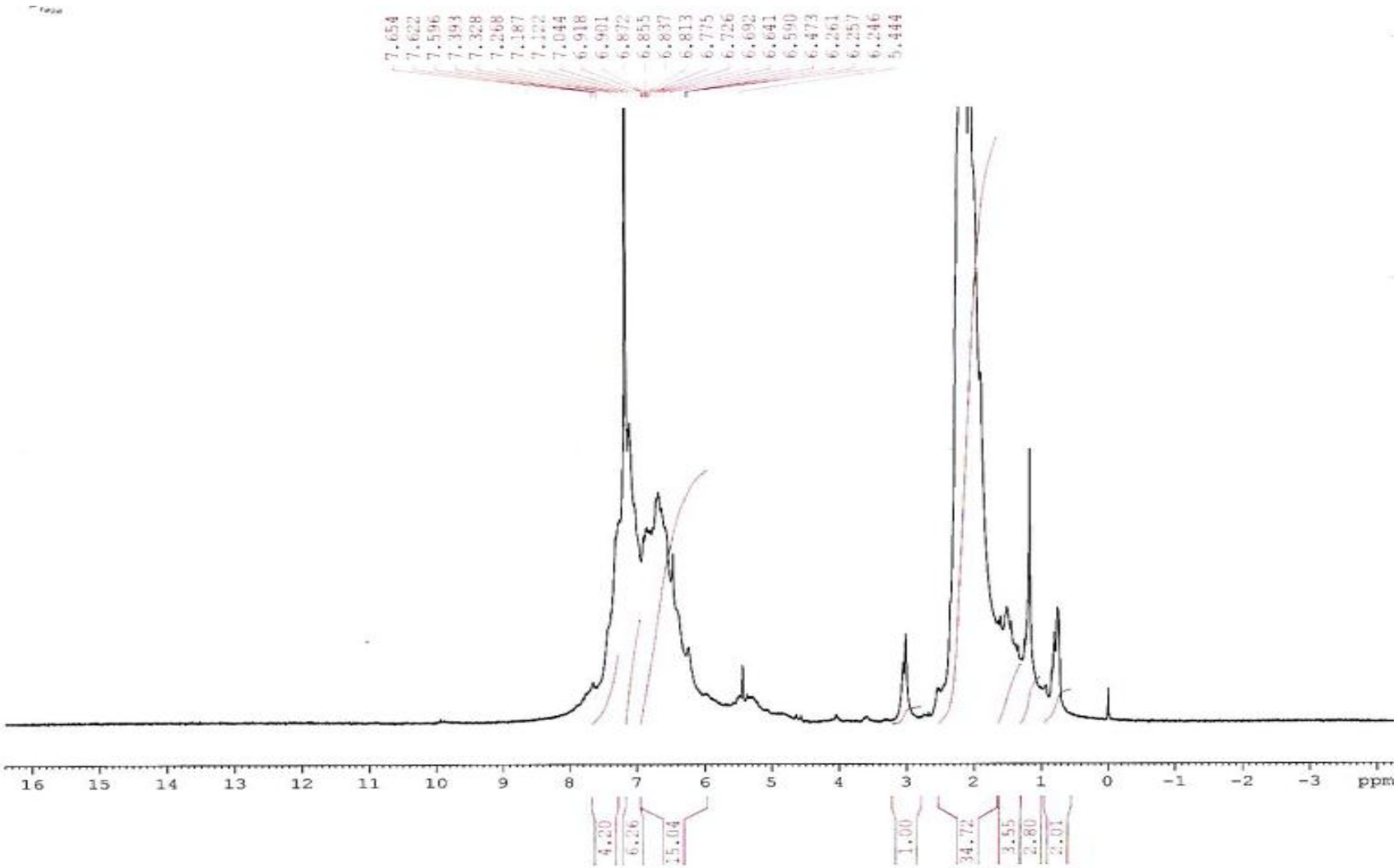
Appendix (17):H^1-NMR spectra of 4-amino-N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)benzenesulfonamide compound (**X**)



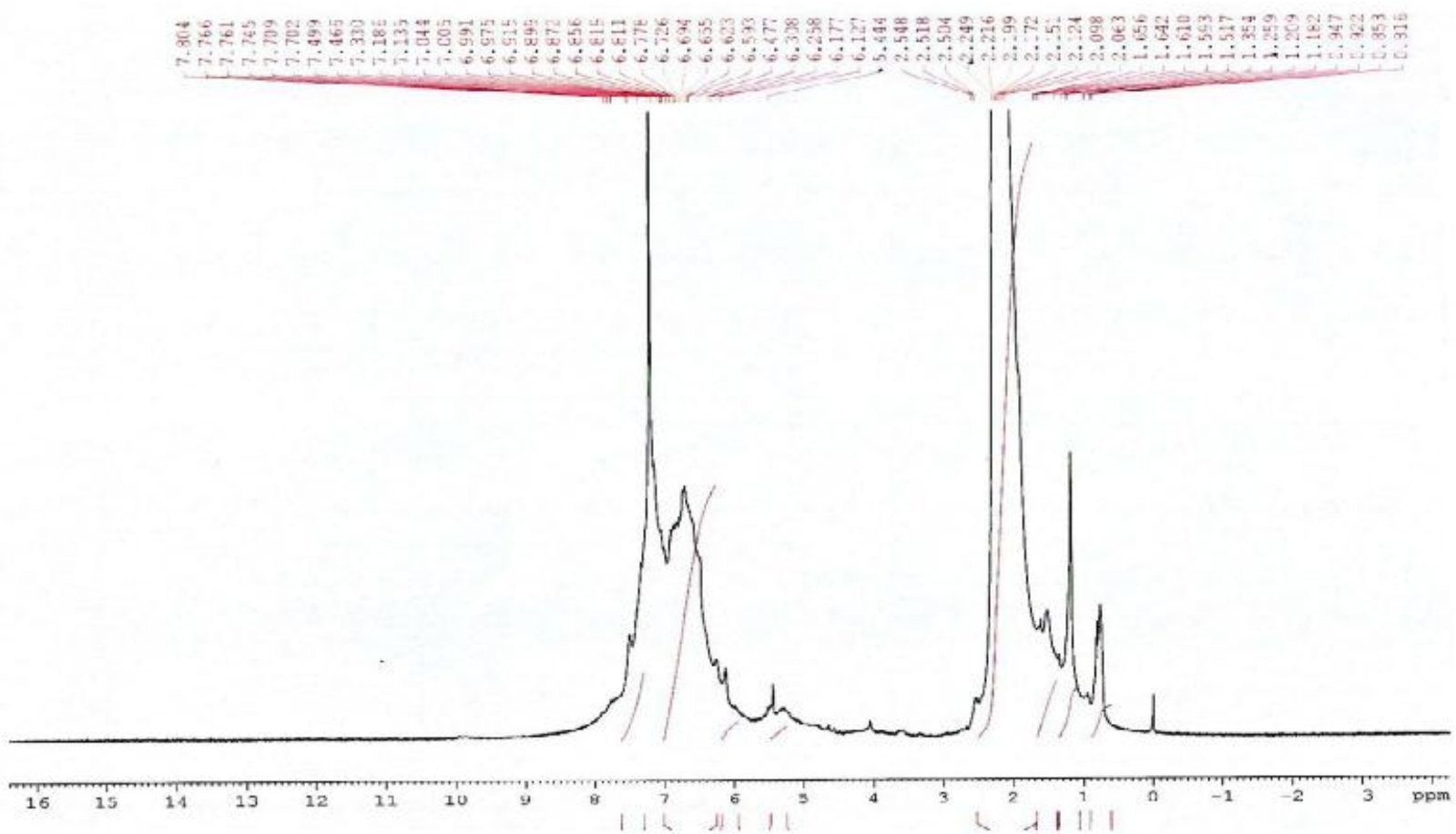
Appendix (18):H^1-NMR spectra of 4-(1,4-dioxo-1,4-dihydronaphthalen-2-ylamino)-N-(5-methylisoxazol-3-yl)benzenesulfonamide compound (**XIV**)



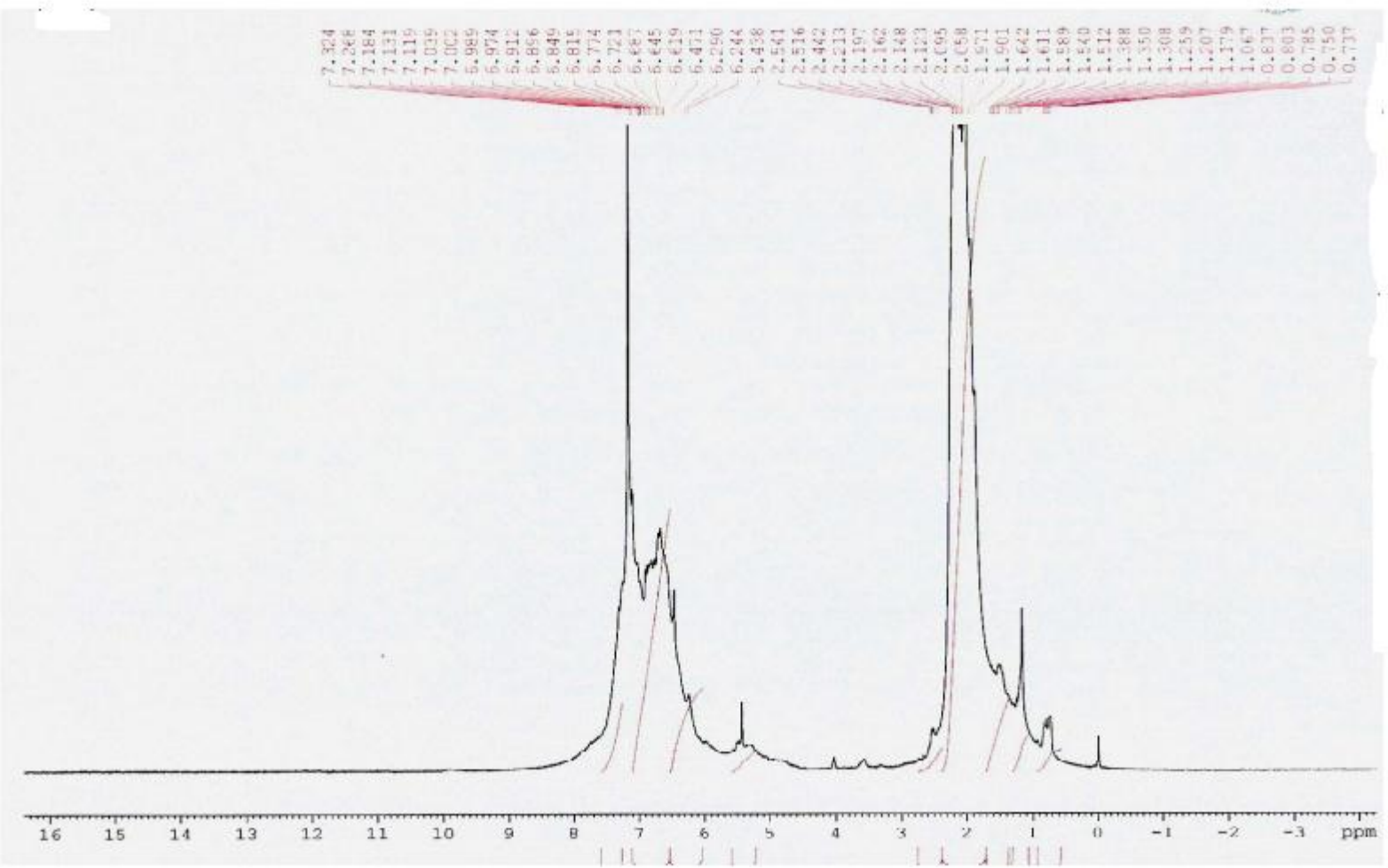
Appendix (19):H^1-NMR spectra of N-(4-aminophenyl)-4-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)benzenesulfonamide compound (**XVI**)



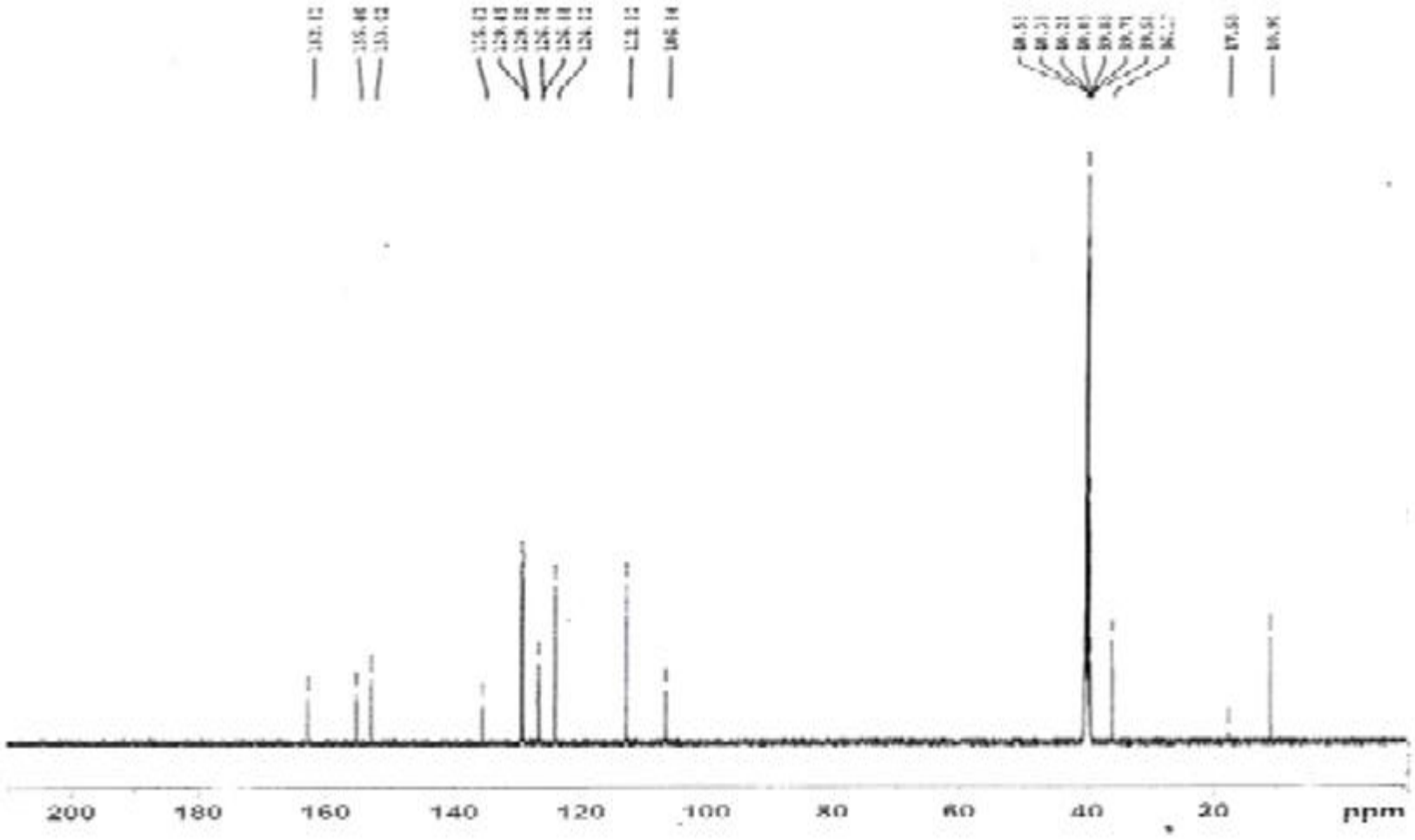
Appendix (20):H^1-NMR spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4yl) benzenesulfonamide compound (**XVIII**)



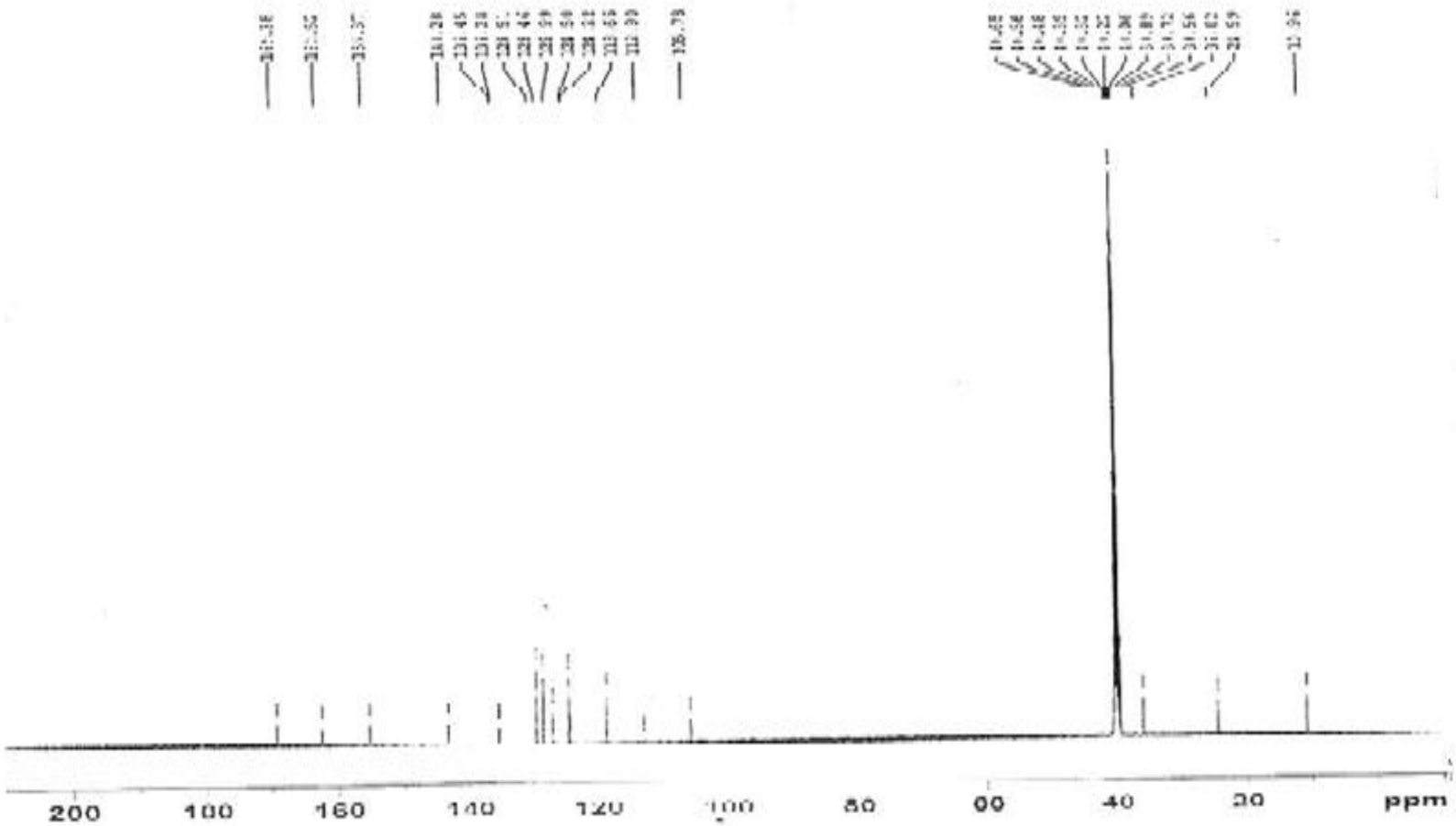
Appendix (21):H^1-NMR spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(5-methylisoxazol-3-yl) sulfamoyl)phenyl)benzenesulfonamide compound (**XIX**)



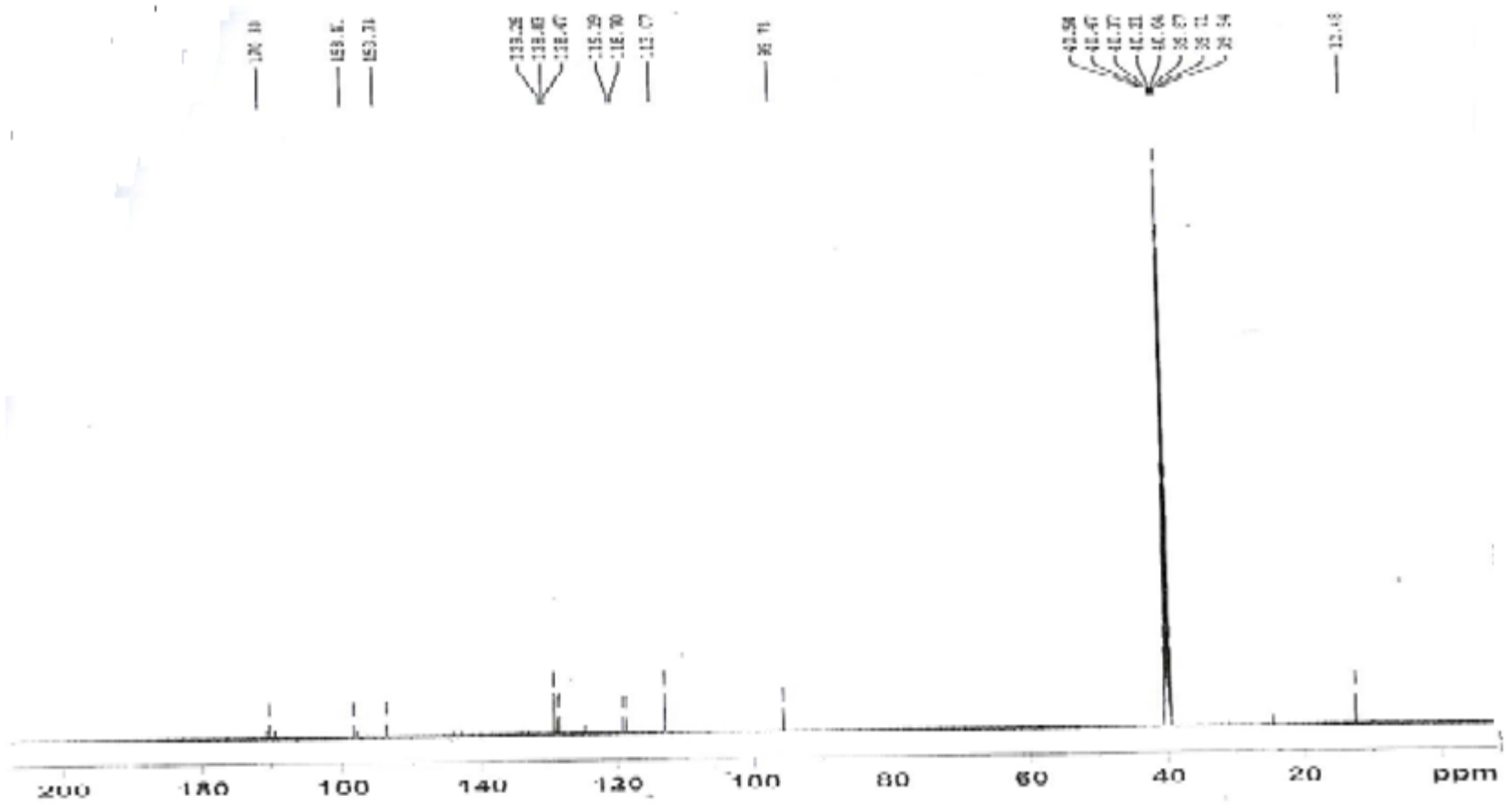
Appendix (22):H^1-NMR spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(4-sulfamoylphenyl) sulfamoyl)phenyl)benzenesulfonamide compound (**XXI**)



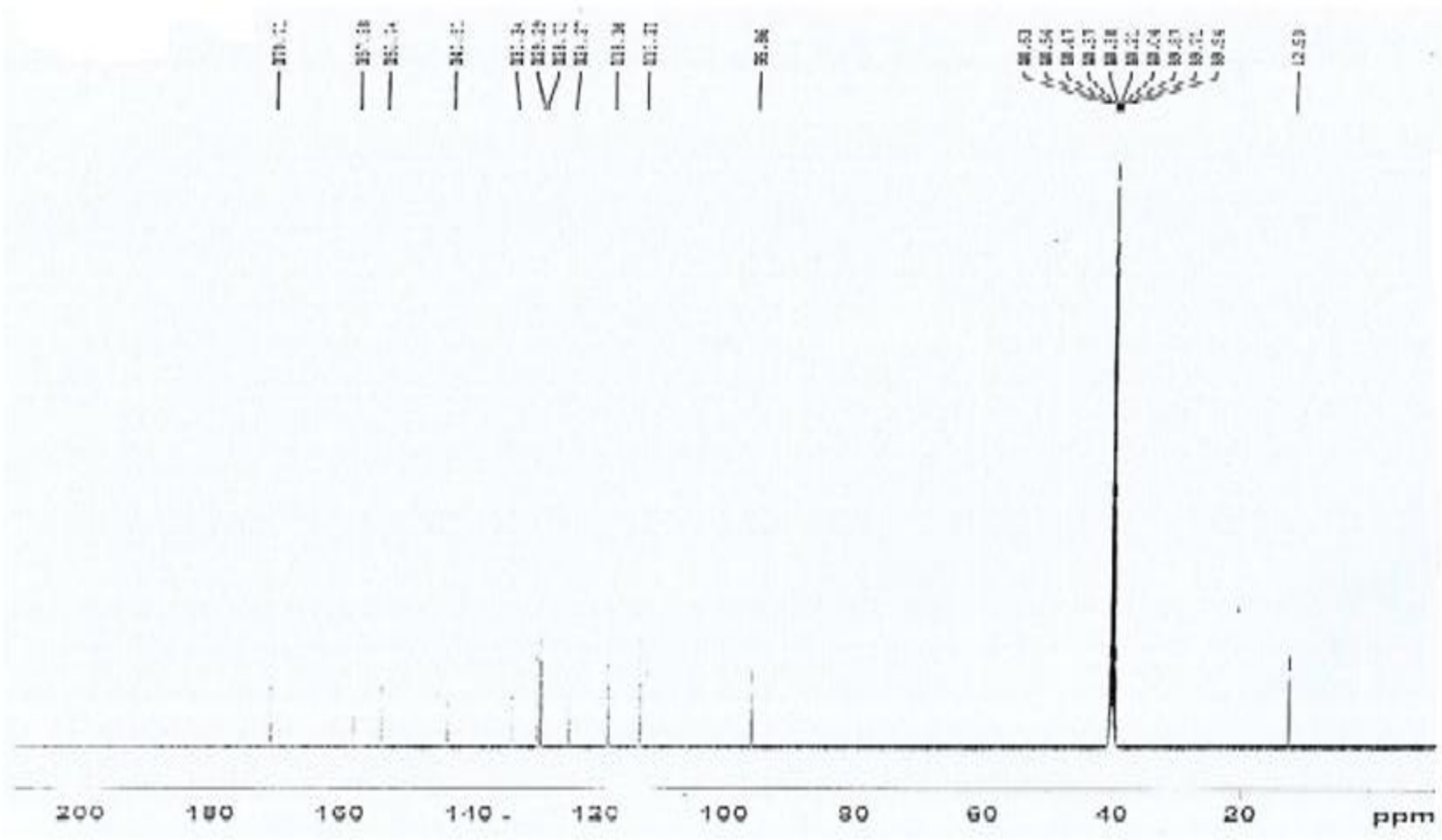
Appendix (23):C^{13}-NMR spectra of N-(4-(N-(5-oxo-1-phenylpyrazolidin-4-yl)sulfamoyl)phenyl)acetamide compound (**III**)



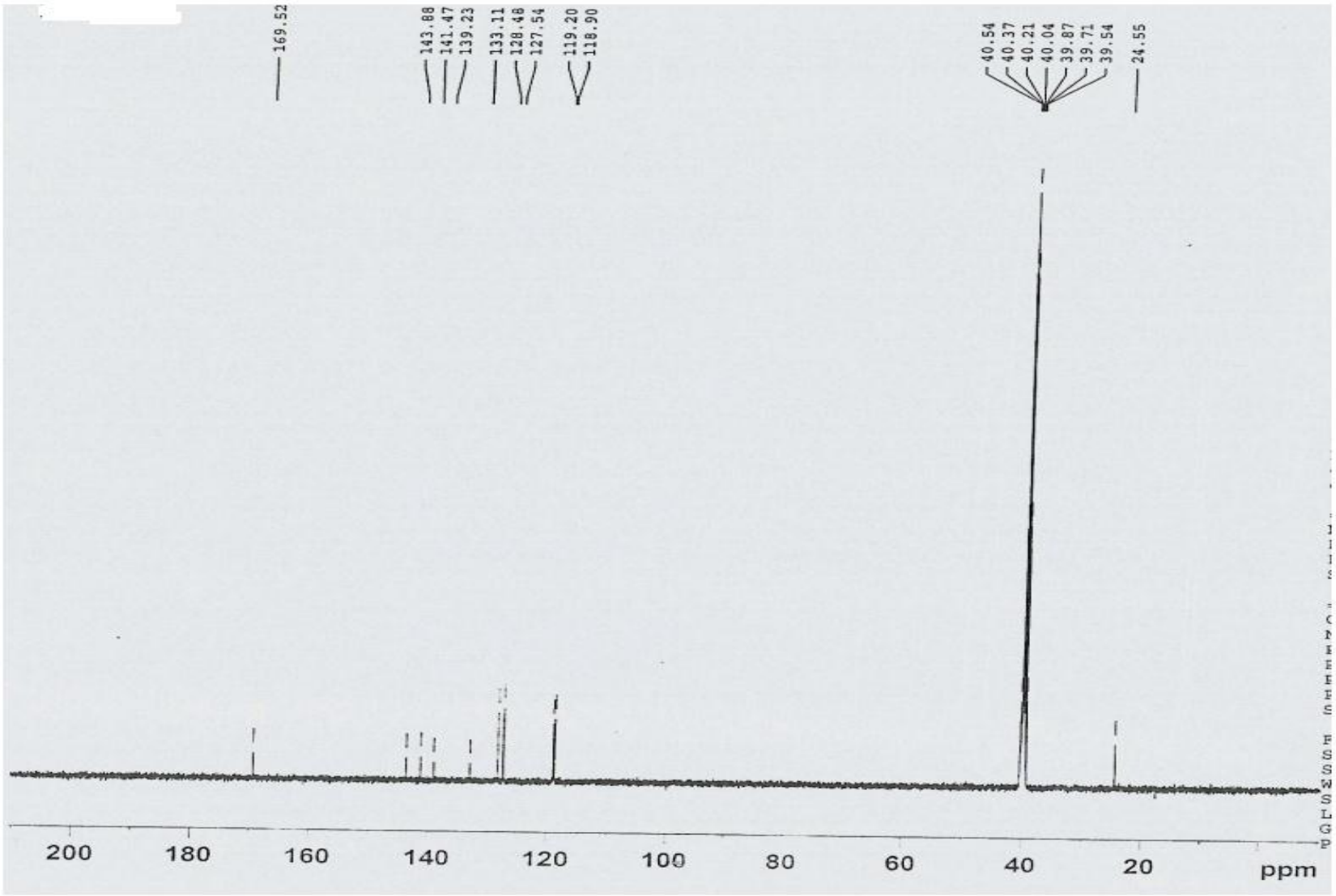
Appendix (24):C^{13}-NMR spectra of 4-amino-N-(5-oxo-1-phenylpyrazolidin-4-yl)benzenesulfonamide compound (**IV**)



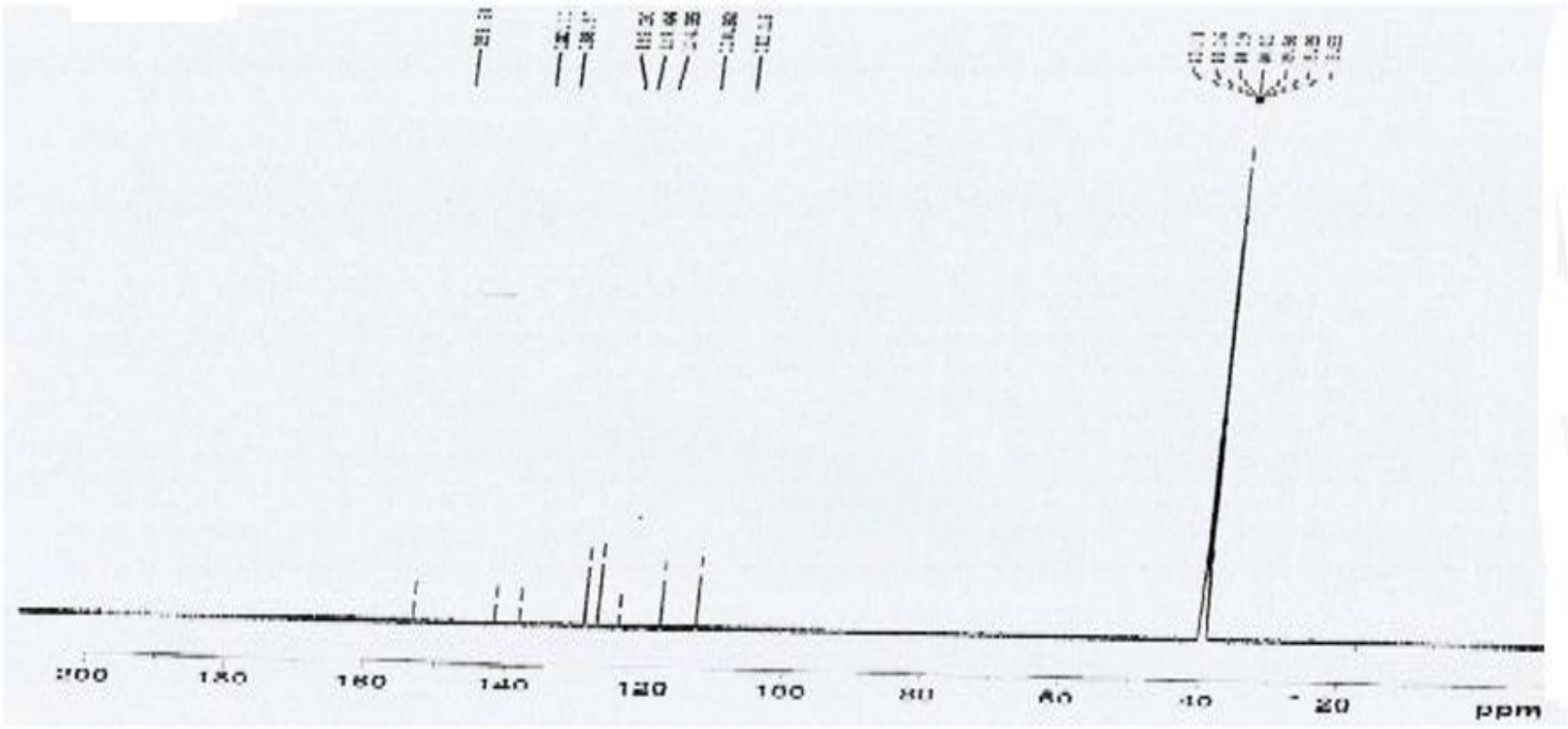
Appendix (25):C^{13}-NMR spectra of N-(4-(4-(5-methylisoxazole-3-sulfonamido)phenylsulfonamido)phenyl)acetamide compound (**V**)



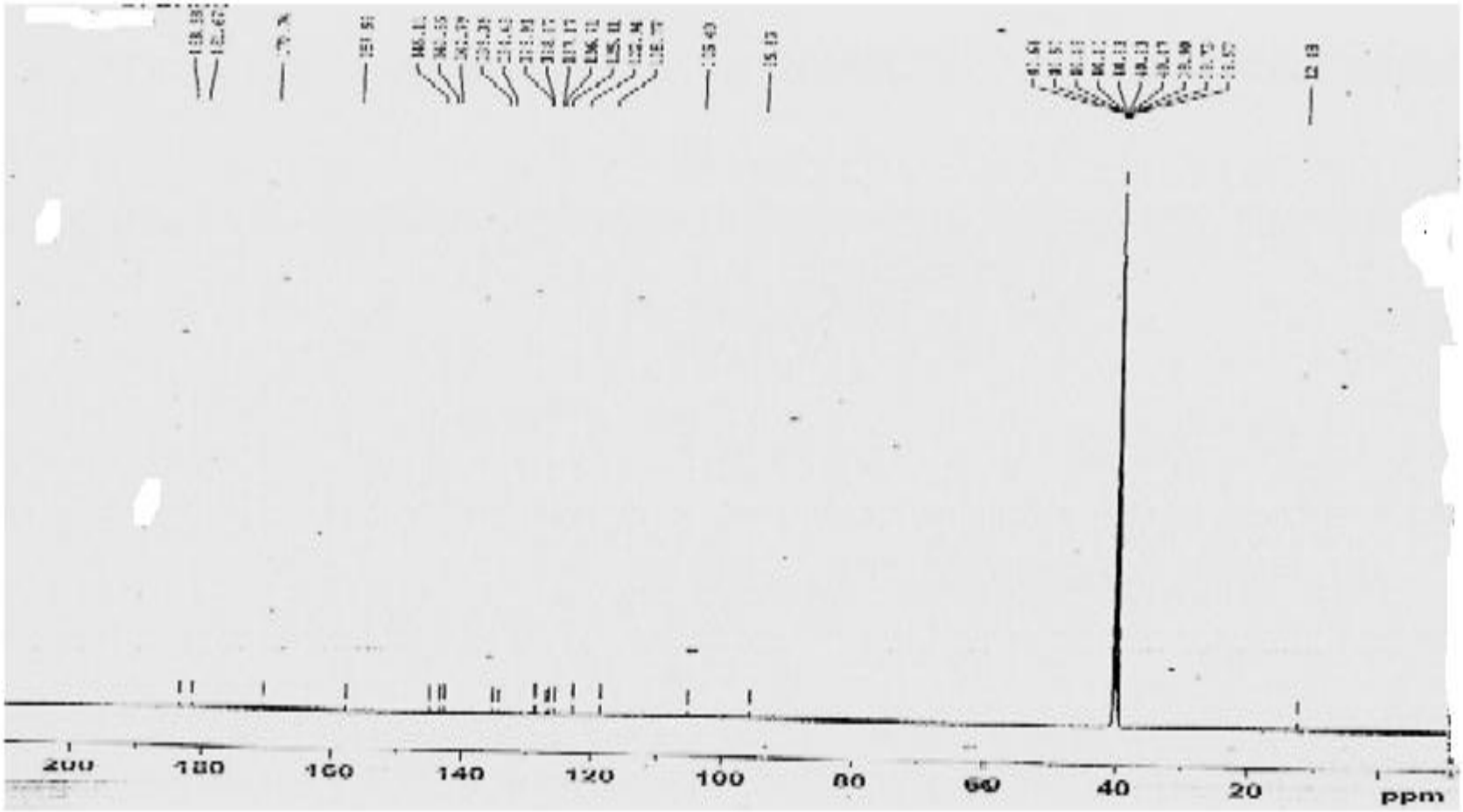
Appendix (26):C^{13}-NMR spectra of 4-amino-N-(4-(N-(5-methylisoxazol-3-yl)sulfamoyl)phenyl)benzenesulfonamide compound (**VI**)



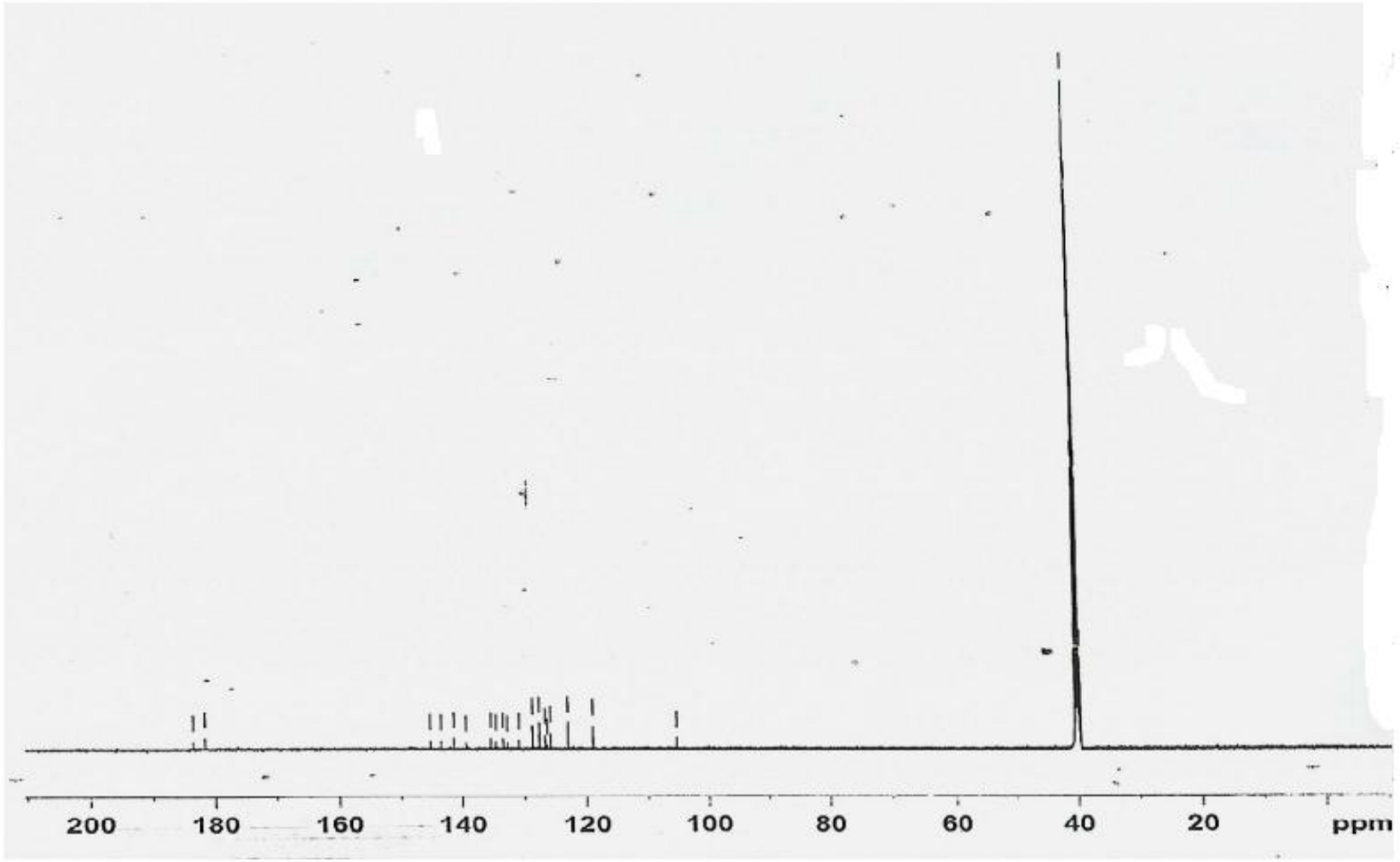
Appendix (27):C^{13}-NMR spectra of N-(4-(N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)sulfamoyl)phenyl)acetamide compound (**IX**)



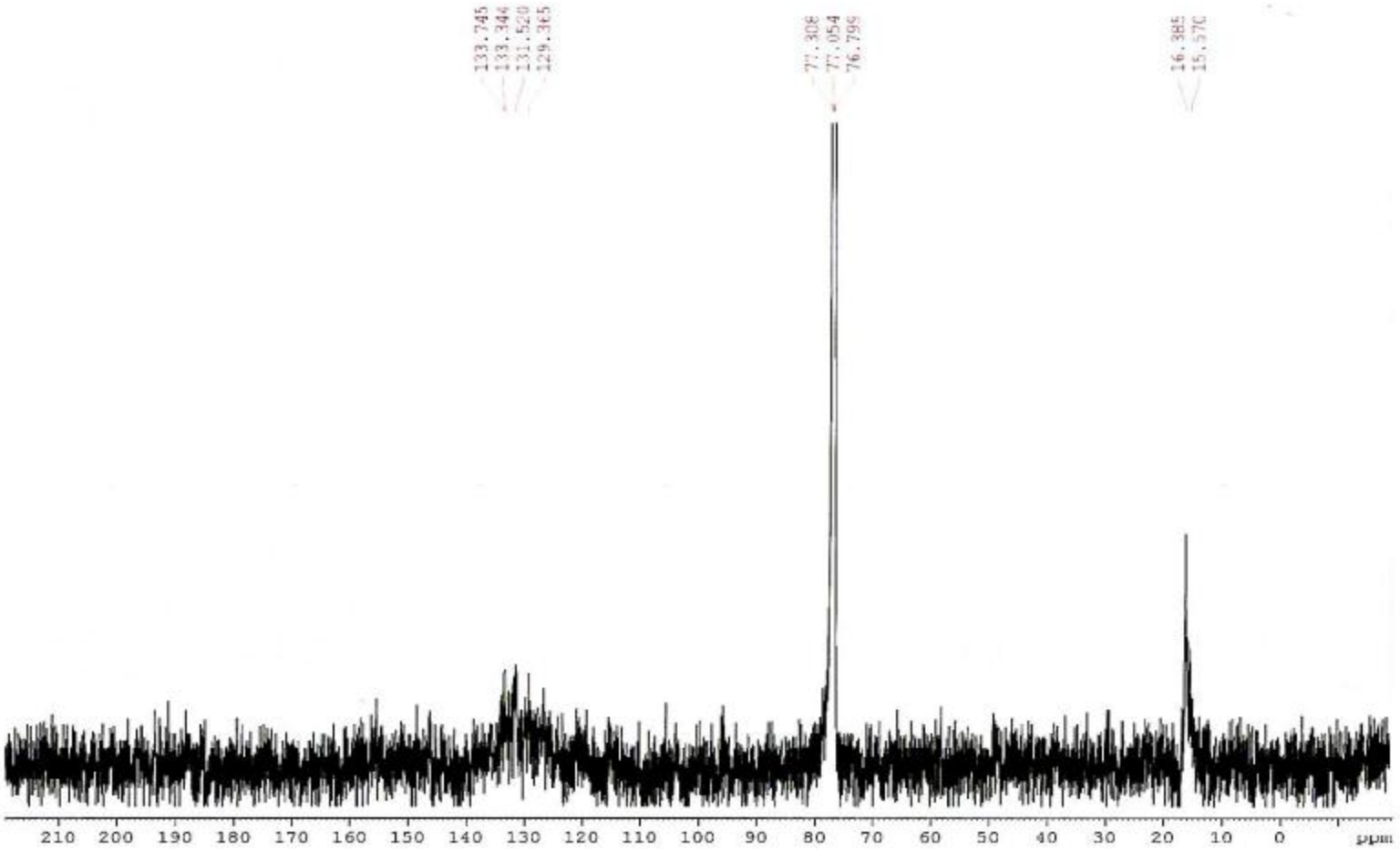
Appendix (28):C^{13}-NMR spectra of 4-amino-N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)benzenesulfonamide compound (**X**)



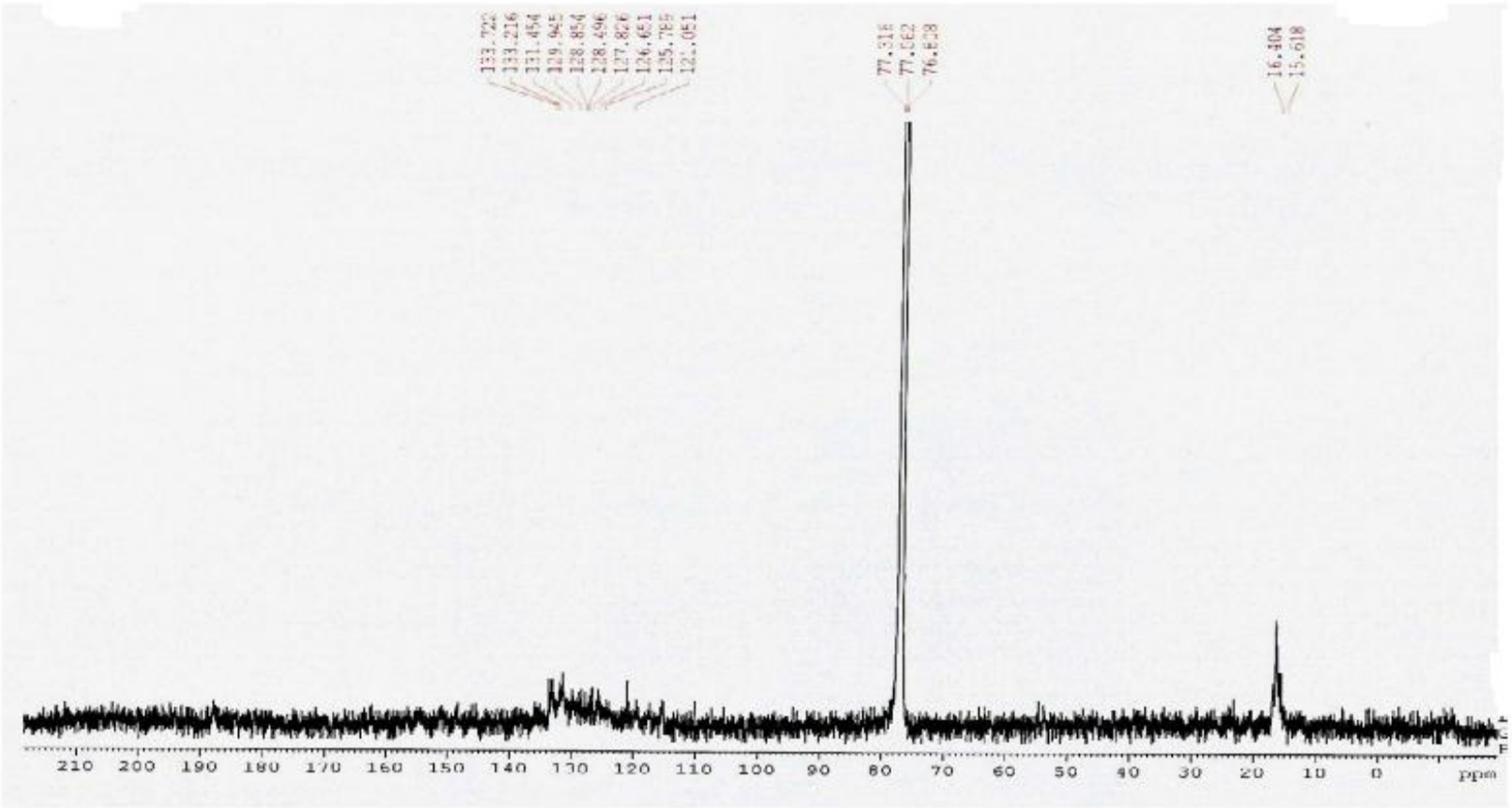
Appendix (29):C^{13}-NMR spectra of 4-(1,4-dioxo-1,4-dihydronaphthalen-2-ylamino)-N-(5-methylisoxazol-3-yl)benzenesulfonamide compound (**XIV**)



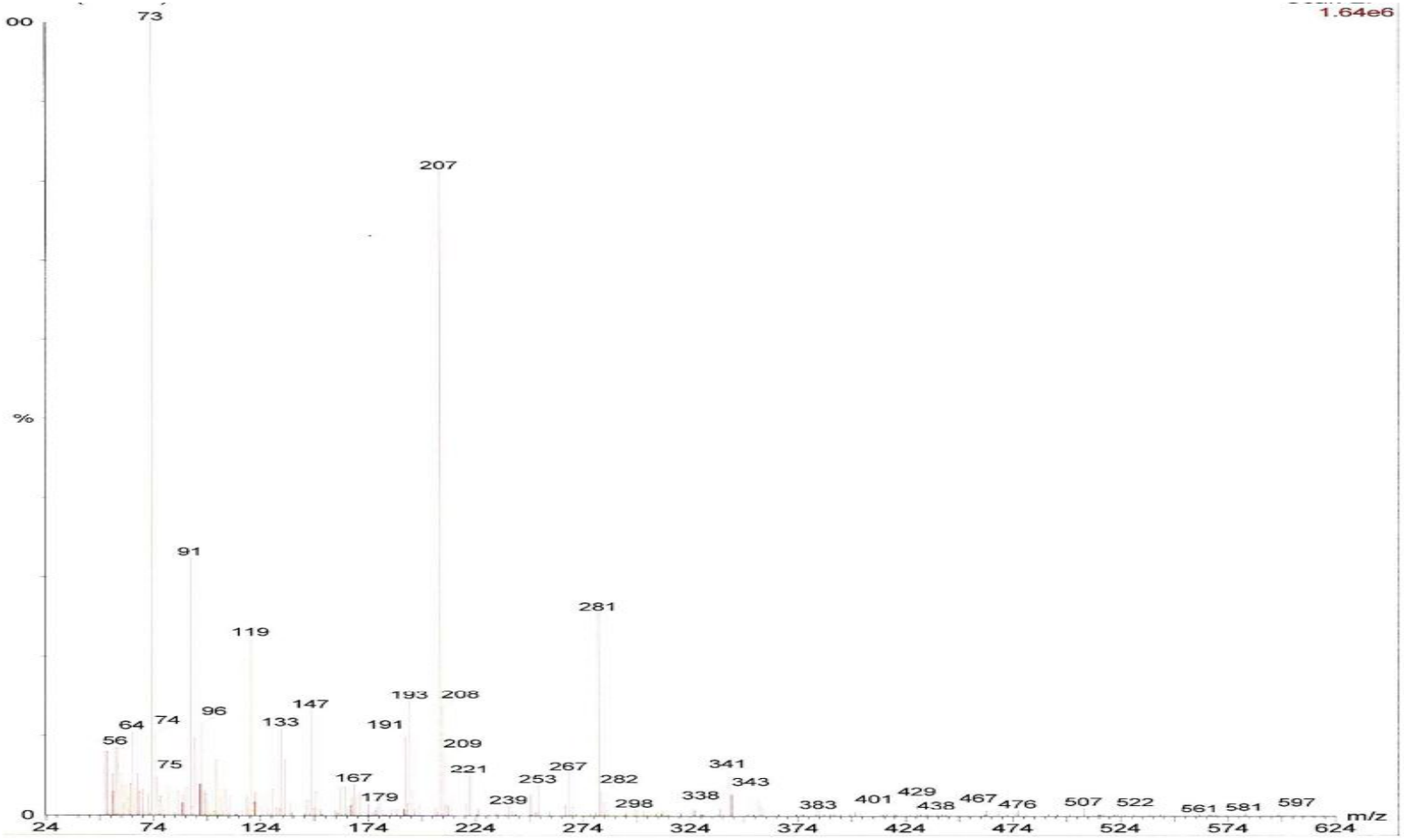
Appendix (30):C^{13}-NMR spectra of N-(4-aminophenyl)-4-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)benzenesulfonamide compound (**XVI**)



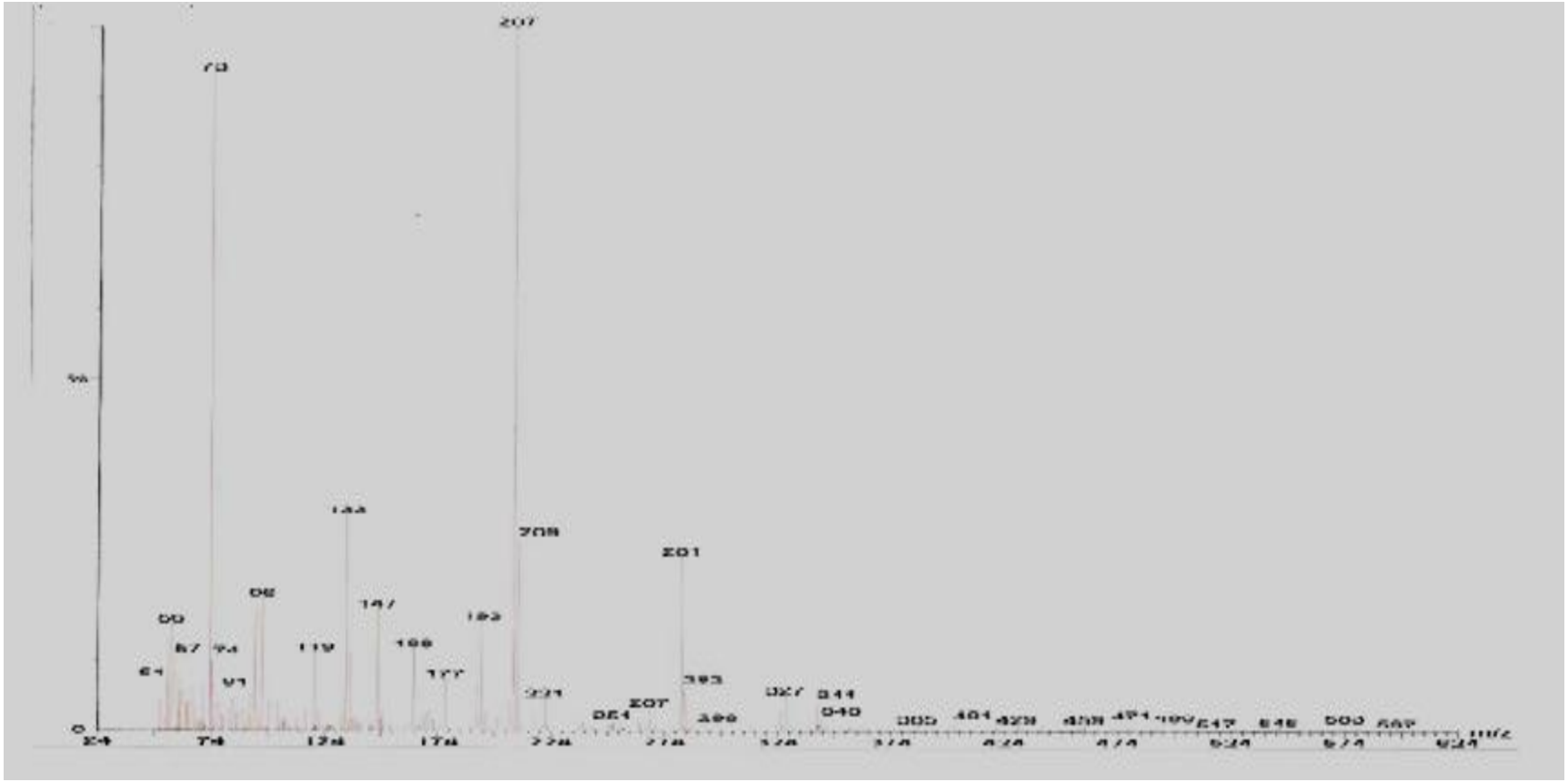
Appendix (31):C^{13}-NMR spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(5-methylisoxazol-3-yl) sulfamoyl)phenyl)benzenesulfonamide compound (**XIX**)



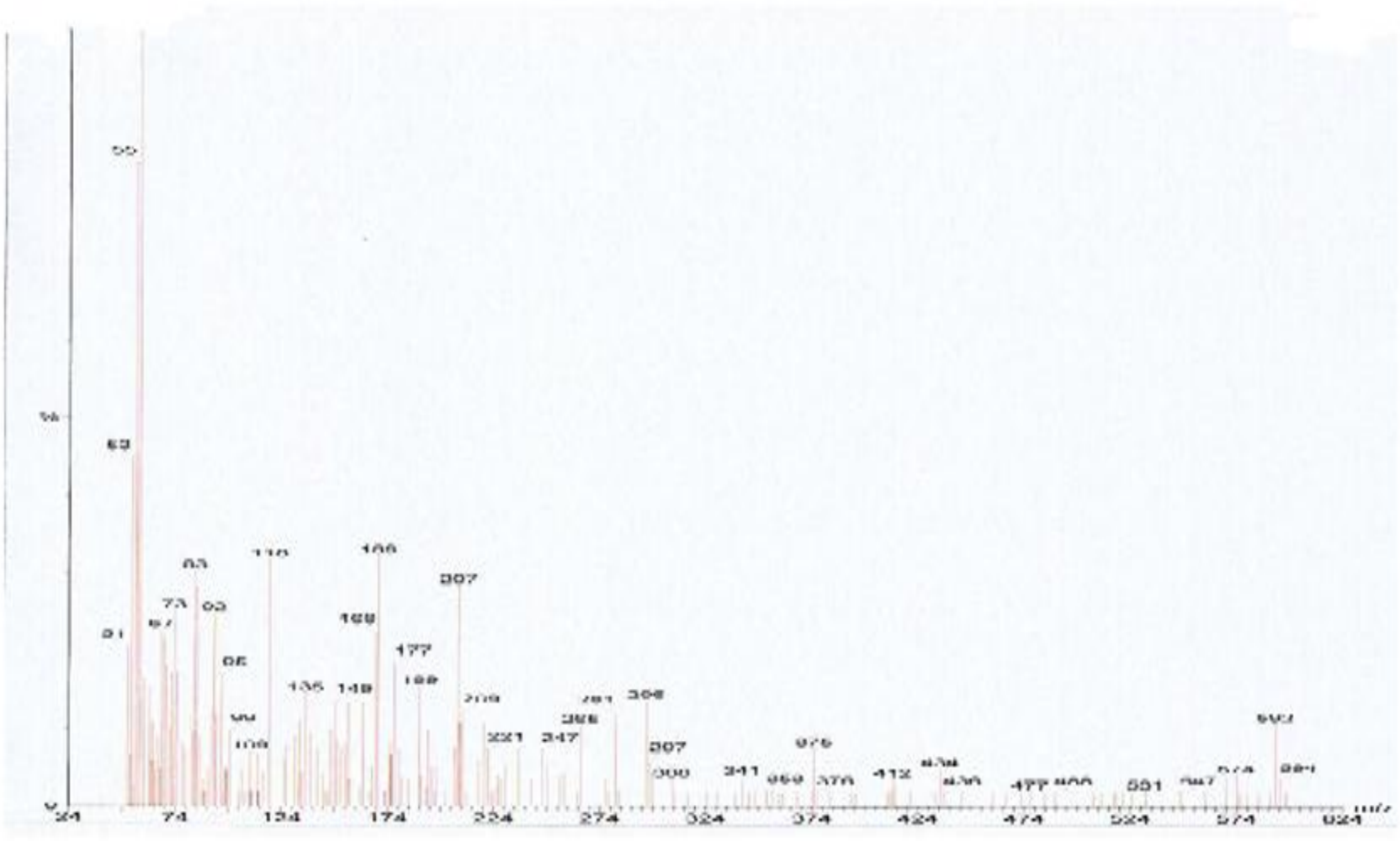
Appendix (32):C^{13}-NMR spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(4-sulfamoylphenyl) sulfamoyl) phenyl)benzenesulfonamide compound **(XXI**)



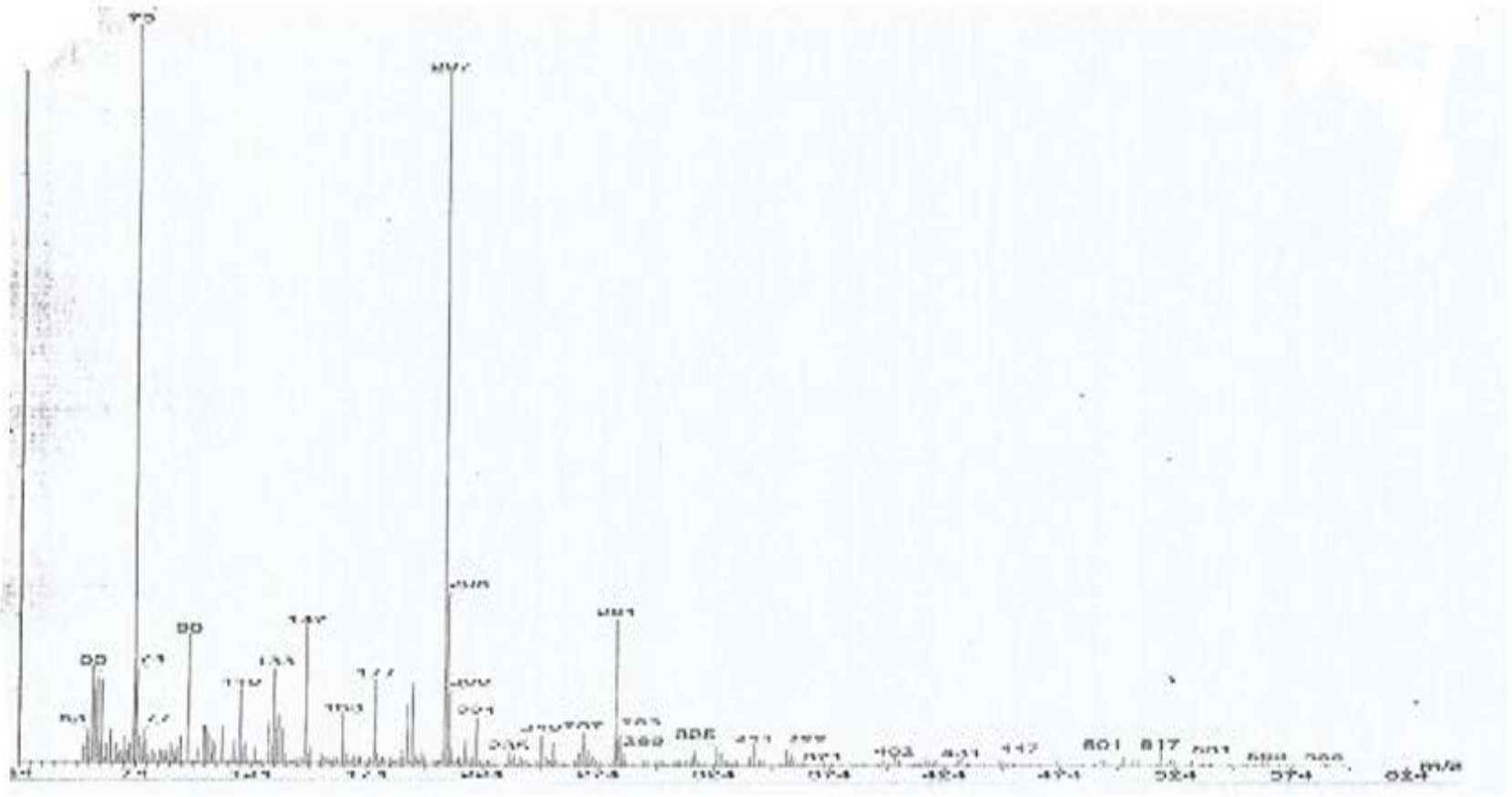
Appendix (33):MS spectra of N-(4-(N-(5-oxo-1-phenylpyrazolidin-4-yl)sulfamoyl)phenyl)acetamide compound (**III**)



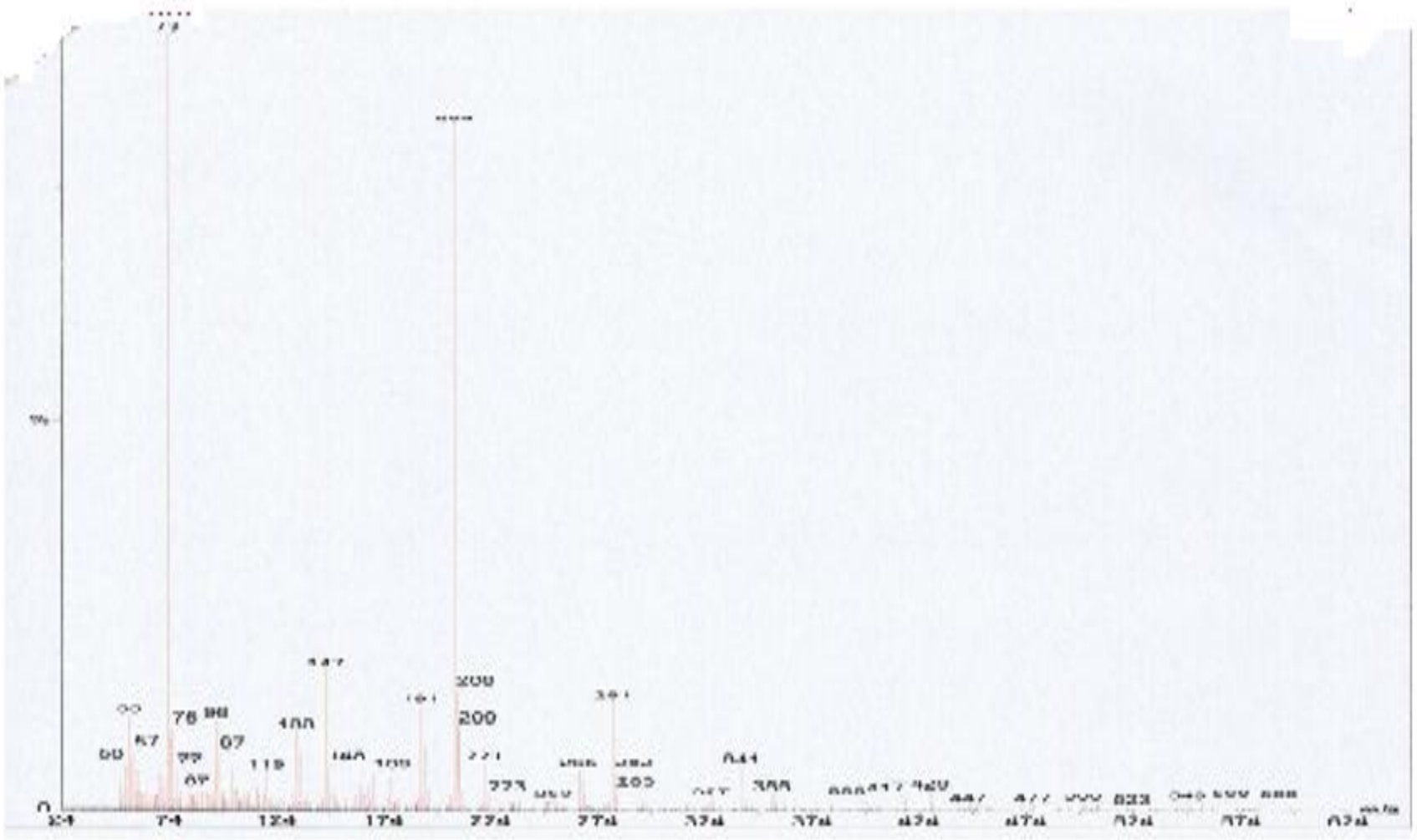
Appendix (34):MS spectra of 4-amino-N-(5-oxo-1-phenylpyrazolidin-4-yl)benzenesulfonamide compound (**IV**)



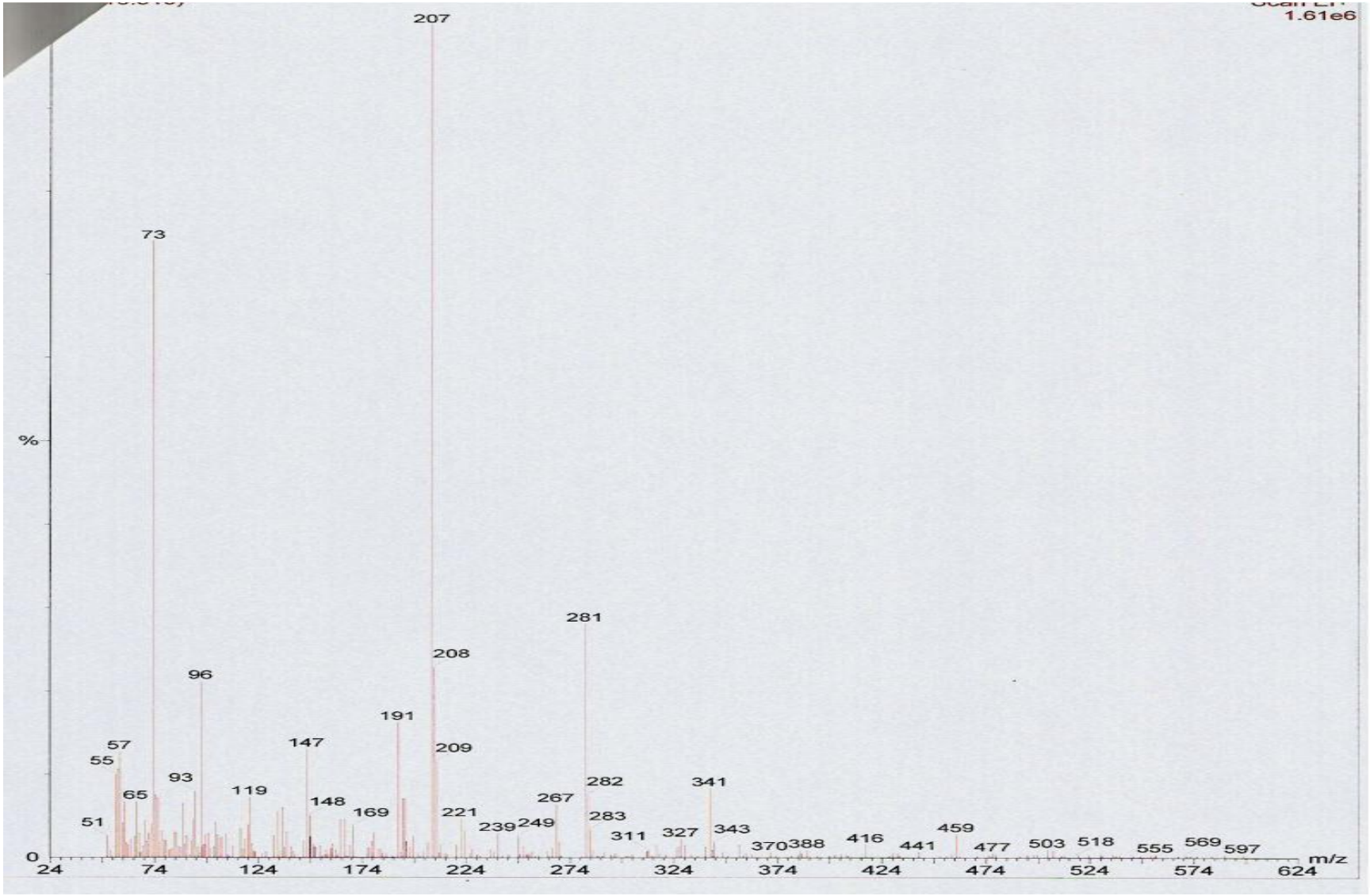
Appendix (35):MS spectra of N-(4-(4-(5-methylisoxazole-3-sulfonamido)phenylsulfonamido)phenyl)acetamide compound (**V**)



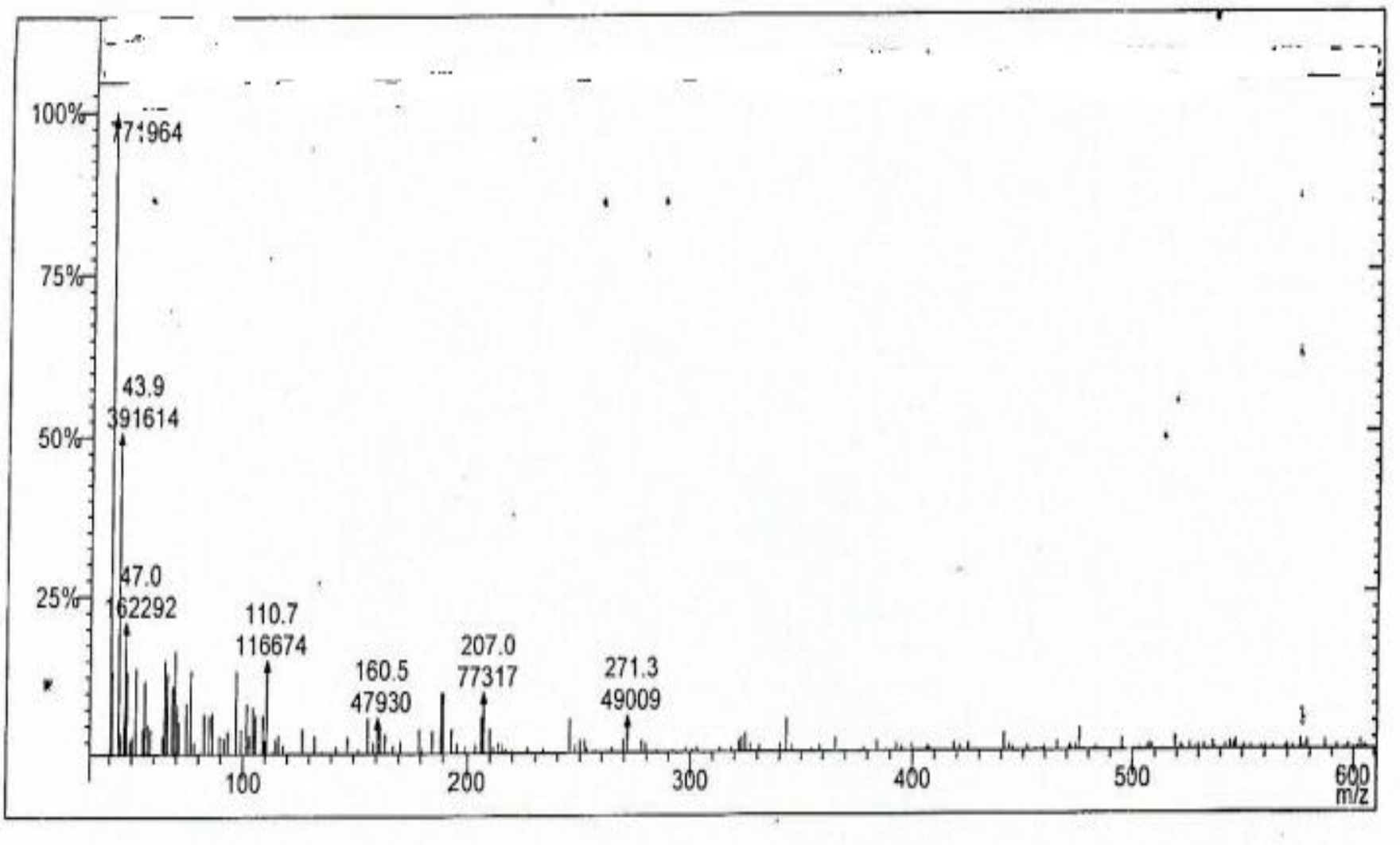
Appendix (36):MS spectra of 4-amino-N-(4-(N-(5-methylisoxazol-3-yl)sulfamoyl)phenyl)benzenesulfonamide compound (**VI**)



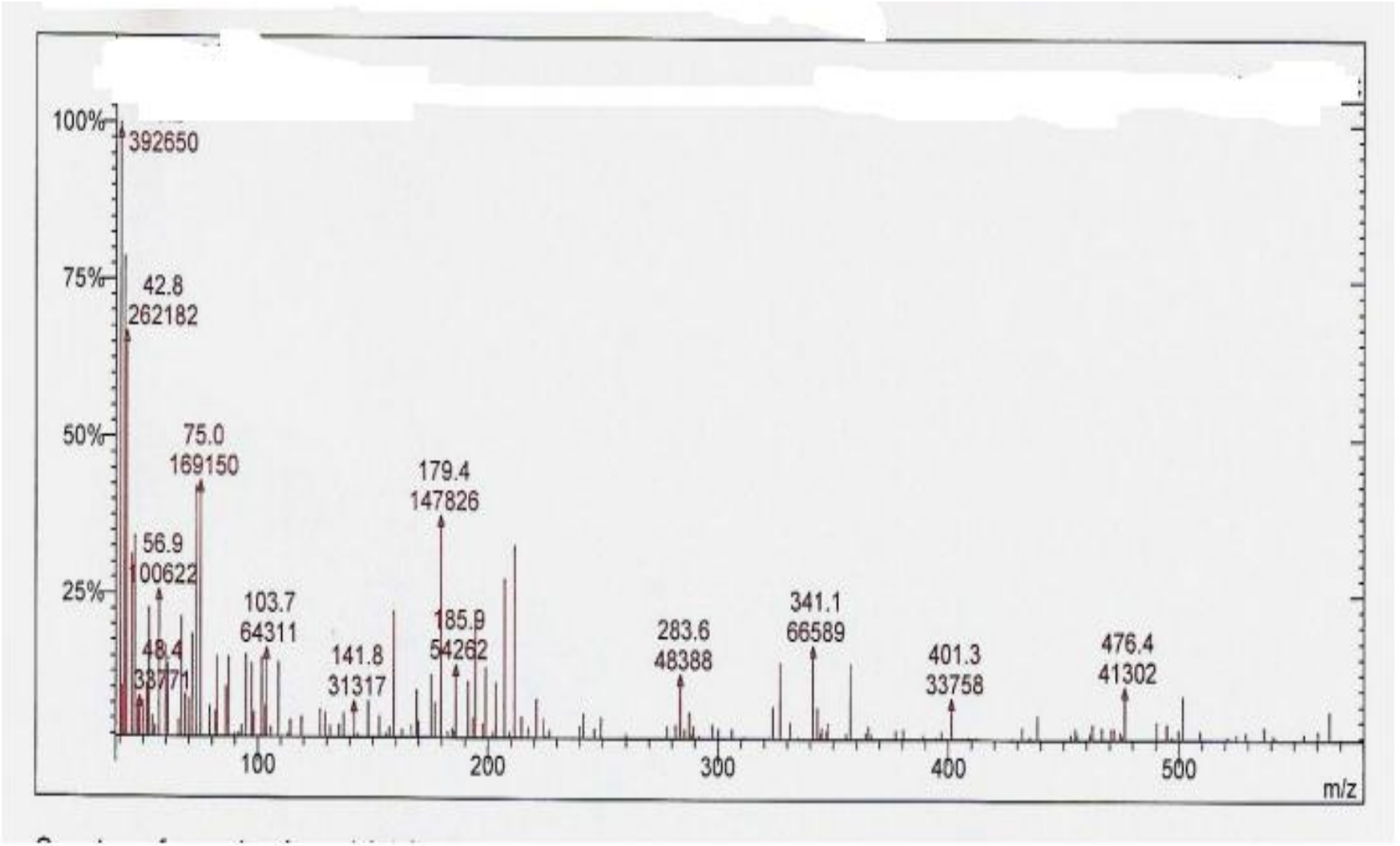
Appendix (37):MS spectra of N-(4-(N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)sulfamoyl)phenyl)acetamide compound (**IX**)



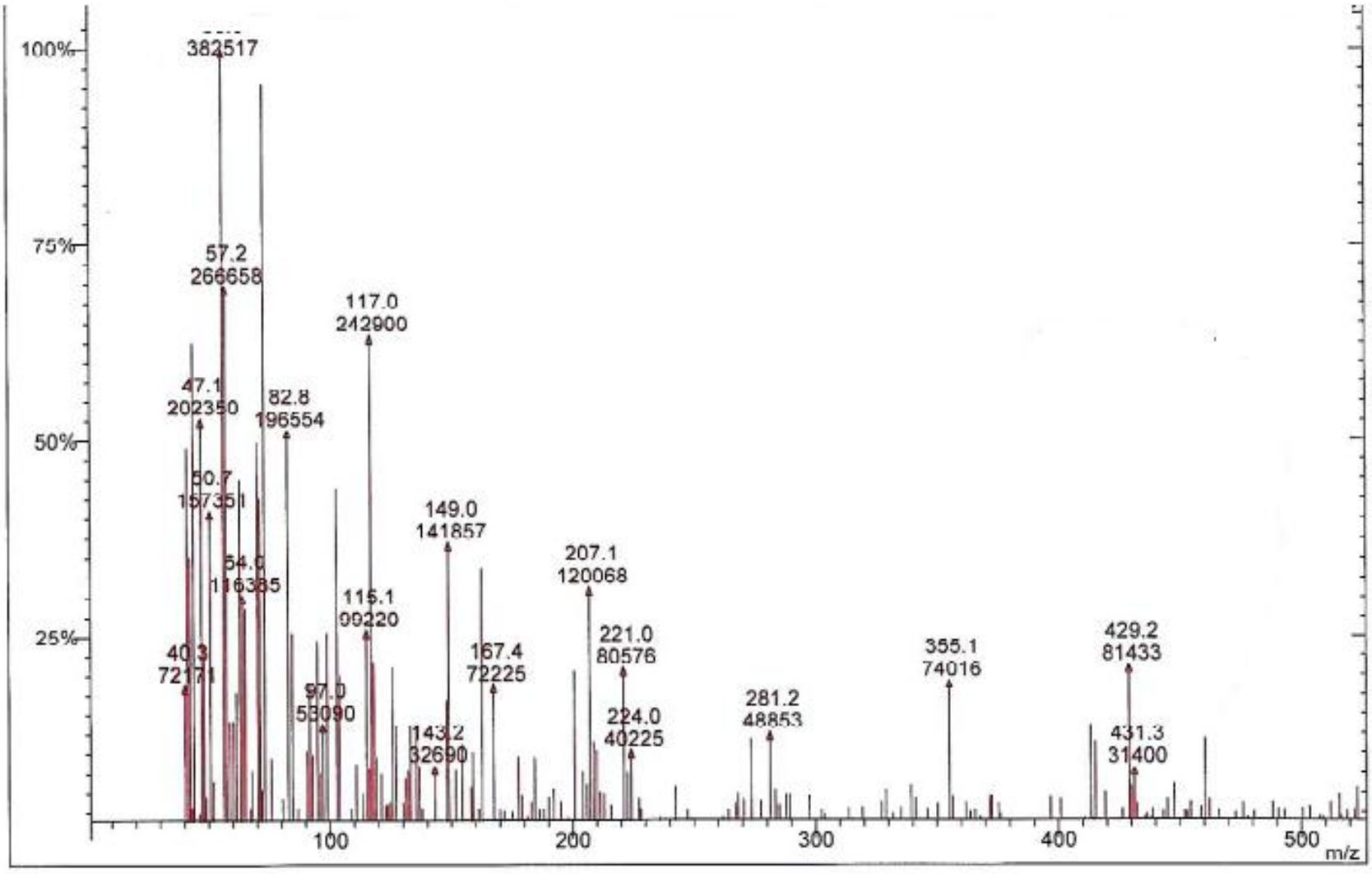
Appendix (38):MS spectra of 4-amino-N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl)benzenesulfonamide compound (**X**)



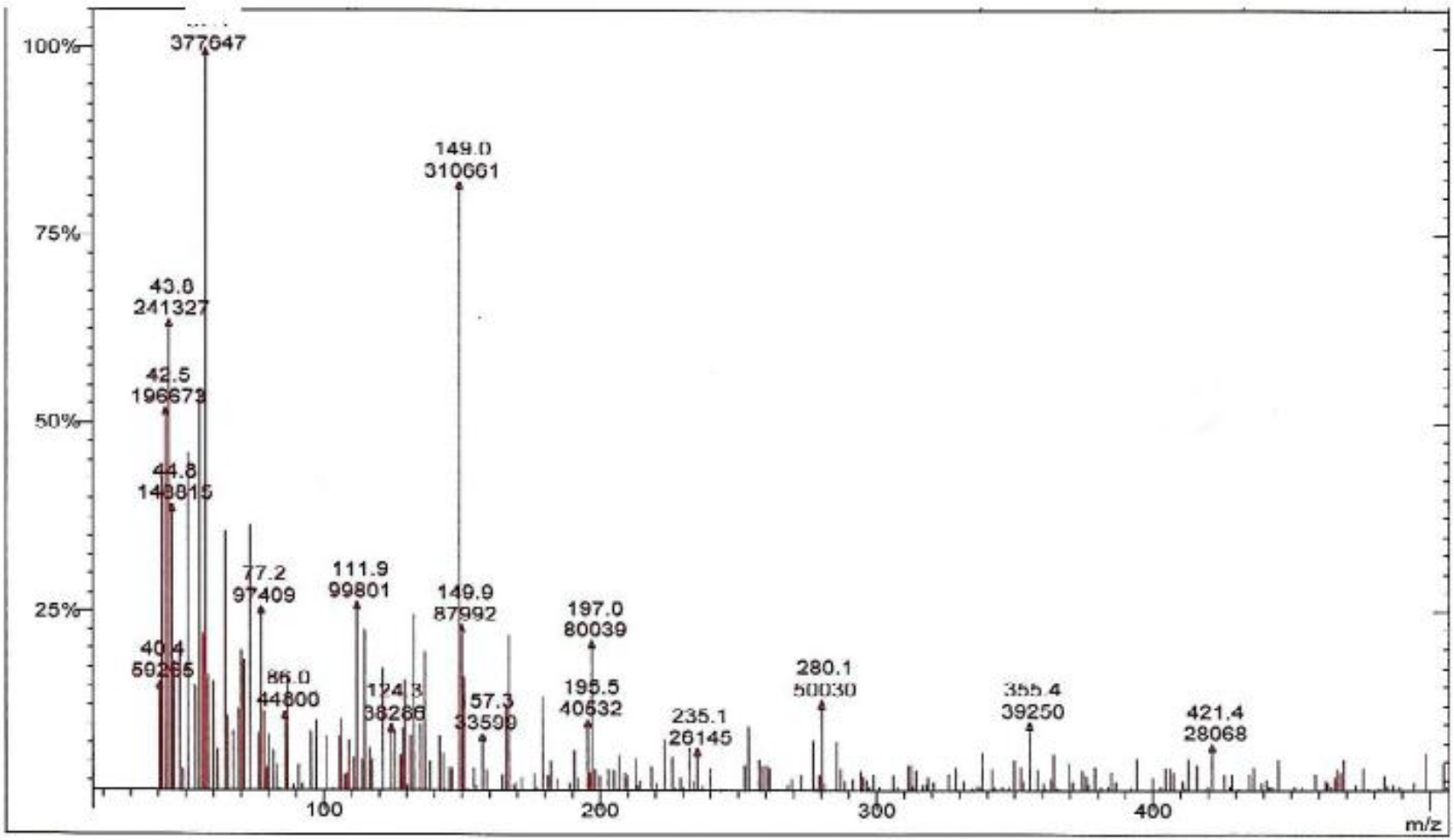
Appendix (39):MS spectra of 4-(1,4-dioxo-1,4-dihydronaphthalen-2-ylamino)-N-(5-methylisoxazol-3-yl)benzenesulfonamide compound (**XIV**)



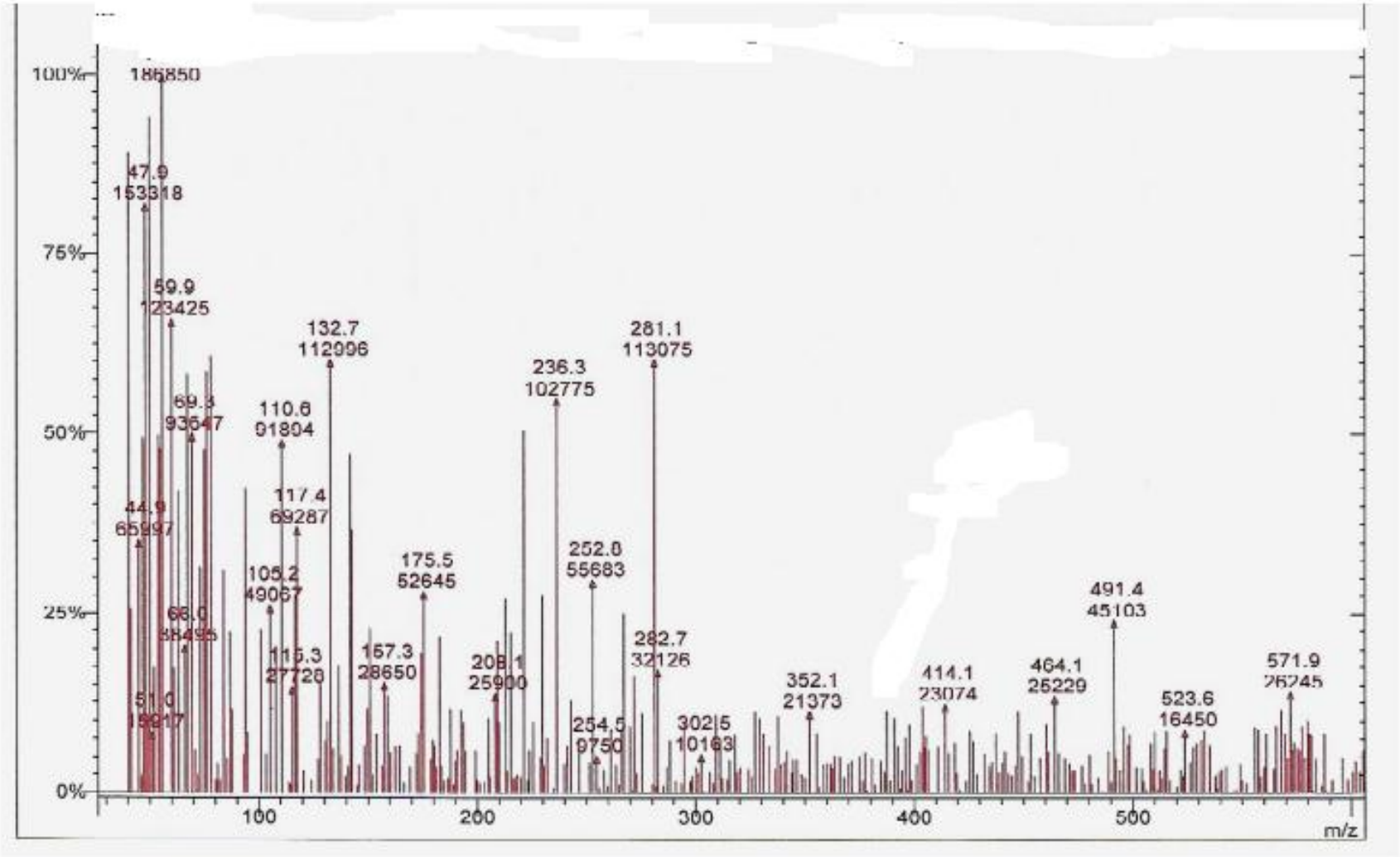
Appendix (40):MS spectra of N-(4-aminophenyl)-4-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)benzenesulfonamide compound (**XVI**)



Appendix (41):MS spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(3-oxo-2-phenyl-2,3-dihydro-1H-pyrazol-4-yl) benzenesulfonamide compound (**XVIII**)



Appendix (42):MS spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(5-methylisoxazol-3-yl)sulfamoyl)phenyl) benzenesulfonamide compound (**XIX**)



Appendix (43):MS spectra of 4-(4-methyl-3,6-dioxocyclohexa-1,4-dienylamino)-N-(4-(N-(4-sulfamoylphenyl)sulfamoyl)phenyl) benzenesulfonamide compound (**XXI**