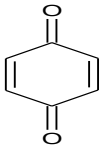
Chapter One

1. Introduction

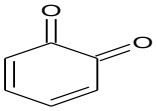
1.1. Definition and structure of quinones

Quinones are an α,β-unsaturated cyclic diketones. They are ubiquitous in nature and constitute an important class of naturally occurring compounds that are found in plants, fungi, and bacteria and that function primarily as components of the electron transport chains involved in cellular respiration and photosynthesis (Berger and Rieker, 1974). Quinones are coloured compounds because they are highly conjugated, generally yellow crystalline solids (Furniss *et al*, 2004). Two Quinones of benzene are possible: *o*-benzoquinone and *p*-benzoquinone:



1,4-benzoquinone

p -benzoquinone



1,2-benzoquinone

o - benzoquinone

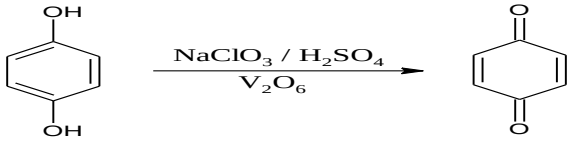
m-bezoquinone has not been prepared; it is impossible to arrange to carbonyl oxygen atoms in the ring in the *m*-position and still maintain a valency of four for carbon (Finar, 1963).

Quinonoid systems play a vital role in biosynthetic routes, are found as structural units in antibiotics and pigments, and are found in compounds having antihaemorrhagic activity (e.g. the Vitamin K group) (Furniss *et al*, 2004). Some quinones, for example Adriamycin possess antitumor activity and are important therapeutically (Gant *et al*, 1986).

1.2. Preparation of quinones

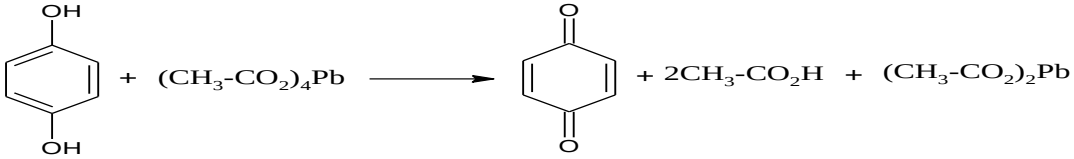
1.2.1. *p*-Benzoquinone

(*p*-Quinone) may be prepared by the oxidation of quinol with ferric chloride, manganese dioxide and sulphuric acid, or acid dichromate; the best oxidizing agent is sodium chlorate in dilute sulphuric acid in the presence of vanadium pentoxide as catalyst:

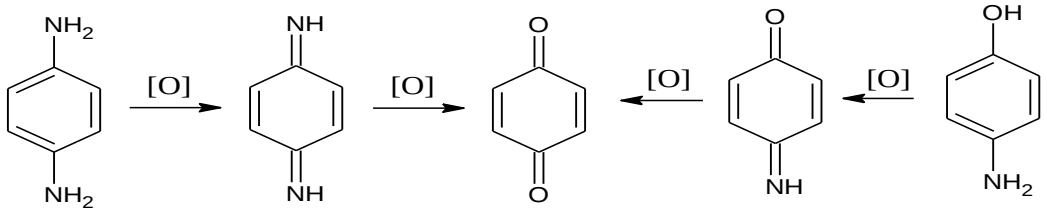


92 - 96 %

Quinol may also be oxidized to quinone by lead tetra-acetate:



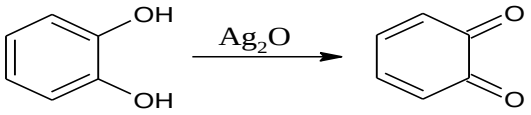
p-benzoquinone is usually prepared in the laboratory by oxidation of aniline with potassium dichromate and sulphuric acid (Finar, 1963). In general, *p*-quinone may be prepared by oxidation (using dichromate-sulphuric acid) of *p*-dihydroxy- *p*-diamino- or *p*-aminohydroxy-compounds e.g:



p-Benzoquinone crystals in yellow prisms, m.p 116 ^{o}C (Finar, 1963).

1.2.2. *o*-Benzoquinone

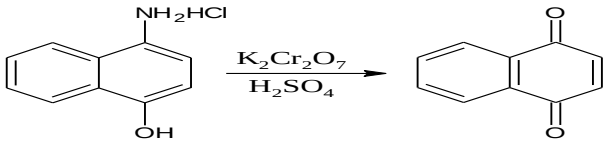
May be prepared by the oxidation of catechol with silver oxide in dry ethereal solution in the presence of anhydrous sodium sulphate (Finar, 1963). The latter is necessary to remove the water formed during the reaction, since *o*-benzoquinone is readily oxidized by silver oxide in the presence of water:



o-Benzoquinone exists in two forms, one as unstable green needles, and the other, stable light-red crystalline plates (Finar , 1963).

1.2.3. 1,4-Naphthoquinone

May be prepared by the oxidation of 1,4-diamino-, dihydroxy- or aminohydroxynaphthalene, e.g:

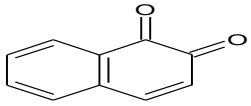


78 - 81%

It may be prepared by the direct oxidation of naphthalene with dichromate and sulphuric acid, or chromium trioxide in glacial acetic acid (yield 40 per cent). 1,4-naphthoquinone is a volatile yellow solid, m.p 125 ^{o}C (Furniss *et al*, 2004).

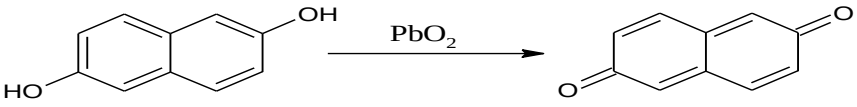
1.2.4. 1,2-Naphthoquinone

May be prepared by oxidizing 1-amino-2-naphthol with dichromate and sulphuric acid (yield 75 %). It is a non-volatile, odourless, red solid which decomposes at 115 – 120 ^{o}C (Finar, 1963).



1.2.5. 2,6-Naphthoquinone

May be prepared by oxidizing 2,6-dihydroxynaphthalene in benzene solution with ‘‘ active ’’ lead dioxide (this may be prepared by decomposing lead tetra-acetate with water; (Finar, 1963):

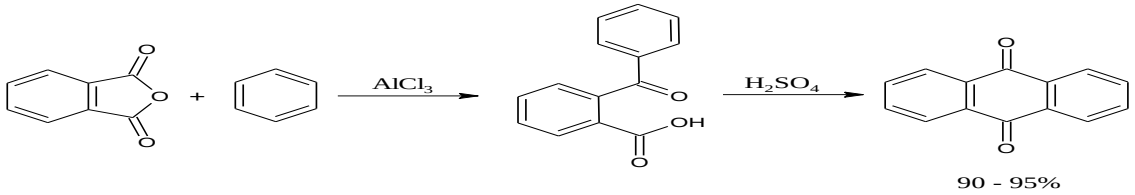


It is an orange, non-volatile, odourless solid, m.p 135 ^{o}C (Finar, 1963).

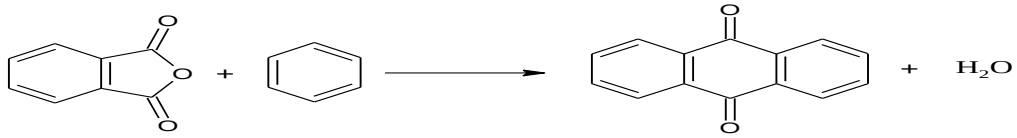
1.2.6. Anthraquinone

There are nine possible isomeric quinones of anthracene, but only three are known: 1,2-, 1,4- and 9,10-. The most important one is the 9,10-compound, and this is referred to simply as anthraquinone (Finar, 1963).

Before 1914, anthraquinone was made by oxidizing anthracene with sodium dichromate and sulphuric acid (yield 90 per cent). Later, instead of isolation anthracene free from carbazole, the mixture of these compounds was oxidized under conditions whereby anthracene was converted into anthraquinone and the carbazole completely oxidized (Finar, 1963). This method is cheaper than the original, but the cheapest method today is a synthetic one:



By using chlorobenzene or toluene instead of benzene, chloro- or methyl-anthraquinone is obtained; these are used in manufacture of dyes. A possible future industrial method may be that of Sachanen and Caesar (1946), who showed that anthraquinone can be obtained in one step from phthalic anhydride and benzene by using a silica-alumina catalyst at 370 ^{o}C:



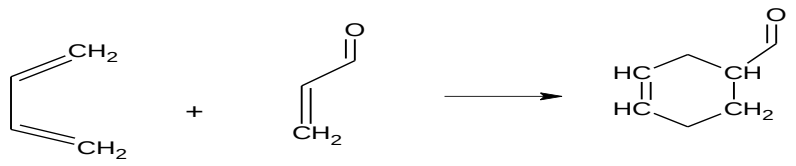
Anthraquinone is pale yellow compound which sublimes in needles that melt at 268 ^{o}C (Finar, 1963).

1.3. *p*-Quinones reactions

p-Quinones undergo a wide range and variety of reactions:

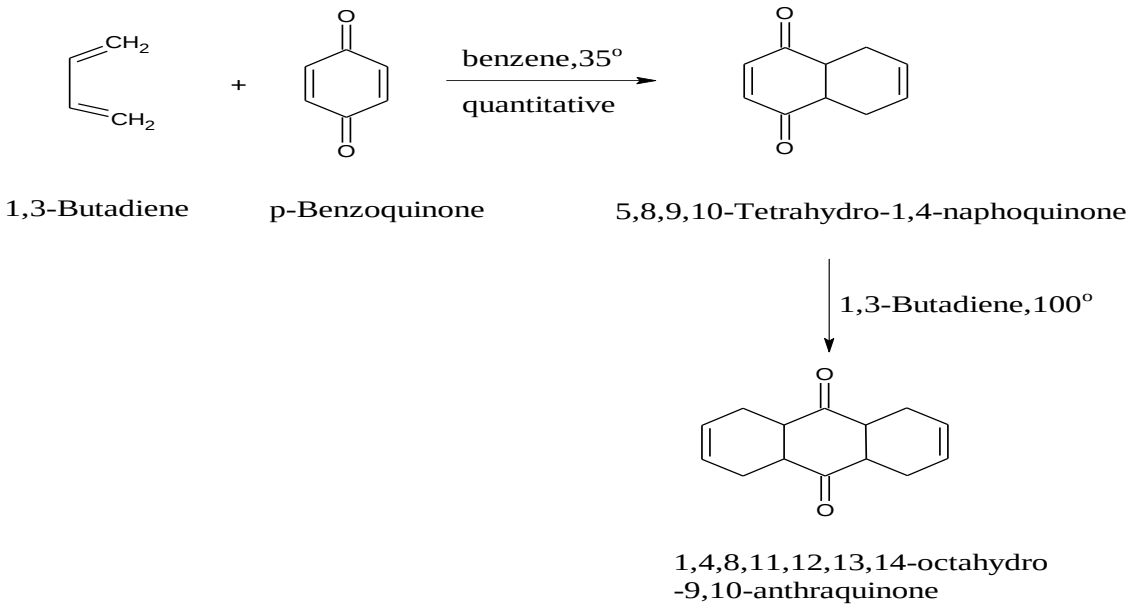
1.3.1. Diels-Alder reaction (electrocyclic addition)

α,β-unsaturated carbonyl compounds undergo an exceedingly useful reaction with conjugated dienes, known as the Diels-Alder reaction. This is an addition reaction in which C-1 and C-4 of the conjugated diene system become attached to the doubly-bonded carbons of the unsaturated carbonyl compound to form a six-membered ring:



Diene Dienophile Adduct

A concerted, single-step mechanism is almost certainly involved; both new carbon-carbon bonds are partly formed in the same transition state, although not necessarily to the same extent. The Diels-Alder reaction is the most important example of cycloaddition. The Diels-Alder reaction is useful not only because a ring is generated, but also because it takes place into readily for a wide variety of reactants. Reaction is favored by electron-withdrawing substituents in the dienophile, but even simple alkenes can react (Morrison and Boyd, 1973).

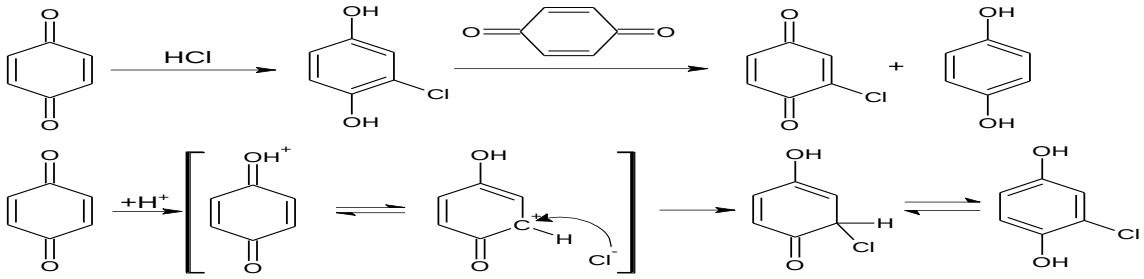


1,3-Butadiene p-Benzoquinone 5,8,9,10-Tetrahydro-1,4-naphoquinone

1,4,8,11,12,13,14-octahydro -9,10-anthraquinone

1.3.2. Electrophilic addition to quinones

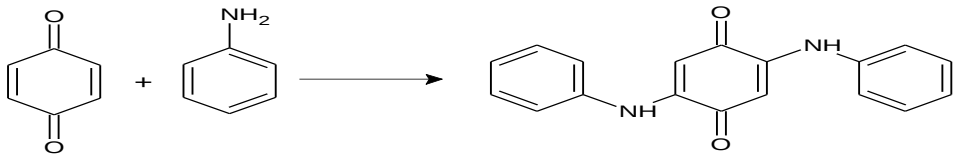
Quinones undergo the addition of hydrogen chloride. The reaction is an acid catalysed:



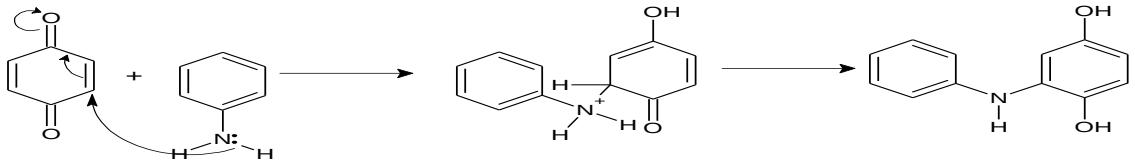
A similar reaction occurs with acetic anhydride and strong acid (Tedder and Nechvatal, 1975).

1.3.3. Nucleophilic addition to quinones

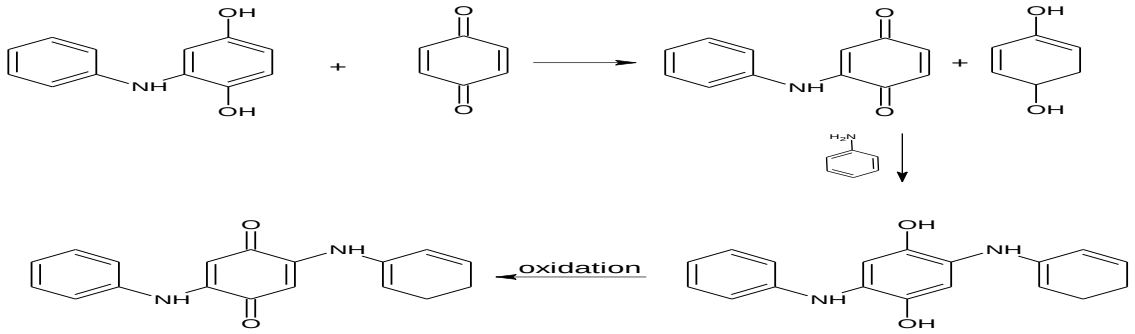
1,4-Benzoquinone reacts readily with aniline to give 2,5-dianilino-1,4-benzoquinone:



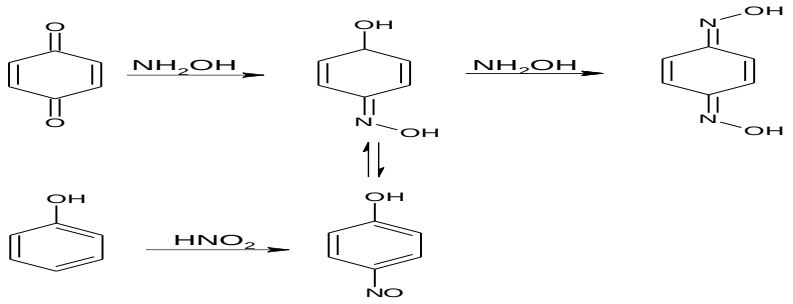
The reaction follows two steps:



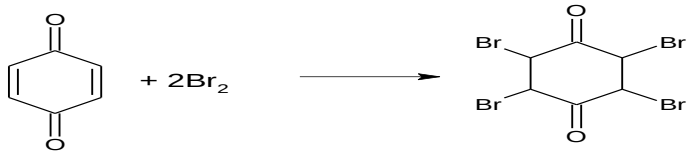
Electron-donor group lower the electrode potential, so that in the presence of an excess of quinones, the anilinoquinol will be oxidized. The resulting anilinoquinone will then react further with more aniline:



Quinones behaves like an *α,β*-unsaturated ketone. Thus, it reacts with hydroxylamine to produce, first, the quinonemonoxime and then the dioxime (Mirrison *et al*, 1969).



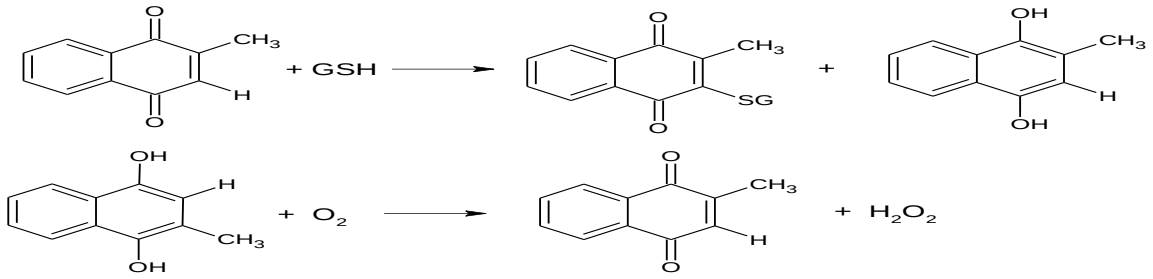
Direct addition to the carbon-carbon double bond can occur in special cases. For example, bromine reacts with quinone to give the saturated tetrabromo-diketone (Tedder and Nechvatal, 1975):



In addition of sulfhydryl derivatives to 2-methyl-1,4-naphthoquinone the alkyl substituent of 2-methyl-1,4-naphthoquinone prevents or greatly inhibit the addition of most reagents of the HA-type that add readily to substituted quinones, it does not interfere markedly with the addition of sulfhydryl compounds. This addition reaction has been utilized as a route to the synthesis of 2,3-disubstituted 1,4-naphthoquinones of types that seemed to offer some prospect of having antihemorrhagic or bacteriostatic activity or of having application in chemotherapy. The initial addition, usually conducted in alcoholic solution at room temperature, affords thio-substituted methyl-naphthoquinone that subsequently may become partially oxidized by interaction with the starting quinone. Usually it was found expedient to submit the total reaction mixture to oxidation with silver oxide in ether solution and to isolate the product in the oxidized form (Fiser and Turner, 1947, Nakai and Hase, 1968).

Formation of quinone-thioether by reaction of 2-substituted 1,4-naphthoquinone with glutathione yields derivatives containing a glutathionyl group to the 3-ring carbon via the sulfur of glutathione, thus the

reaction between menadione and glutathione (GSH) may thus be written as shown:

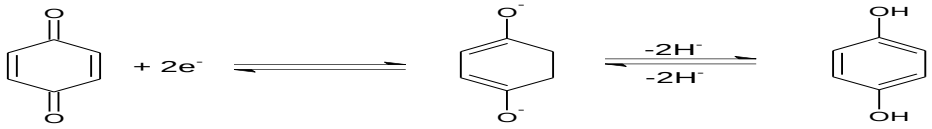


Yield and rate of thioether formation depend upon the electron-withdrawing ability of any substituent on the quinone ring. The reaction is shown to be a nucleophilic substitution (Nickerson *et al*, 1963).

In reactions with thiol nucleophiles, a number of structurally simple quinones, i.e. benzoquinone and 1,4-naphthoquinone, react with thiol nucleophiles to generate their respective semiquinone radicals. In addition, similar free radicals were observed following the reaction of benzoquinone and 1,4-naphthoquinone with the amino group of glycine and other amino acids (Gant *et al*, 1986).

1.3.4. Reduction of quinones

A characteristic and important reaction of quinones is the reduction to corresponding arendiols (Song and Jeon, 2003):



This show it is possible to add two electrons, converting it from an unsaturated diketones into the dianion of a dihydric phenol. The reaction is very similar to that of inorganic electrolytes. This is a true oxidation – reduction process. In an equilibrium of this kind, the oxidizing (or reducing) power of the solution can be measured by inserting an electrode unattacked by the solution. In a mixture solution of the quinone and hydroquinone the electrode potential is given by the Nernst equation:

$$E = E° - \frac{RT}{2F} ln \frac{a_{H2Q}}{a_Q . a_{H+}2}$$

Where E = Electrode potential under specific conditions

E^o = Electrode potential at standard conditions

F = Faraday constant

R = Gas constant

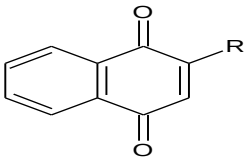
T = Temperature

a_{H2Q} = activity of hydroquinone

a_Q = activity of quinone

o-benzoquinone has a higher electrode potential than *p*-benzoquinone, suggesting that the *o*-quinonoid system is of higher energy and less stable than *p*-quinonoid system. Fused rings stabilize the quinone, making it a less powerful oxidizing agent. The following table shows the effect of substituents on the electrode potential of quinones. In table (**1.1**) the values are expressed as difference between the electrode potential of the substituted 1,4-naphthoquinones and that of substituted 1,4-naphthoquinones (Takahashi, 1993; Song and Jeon, 2003).

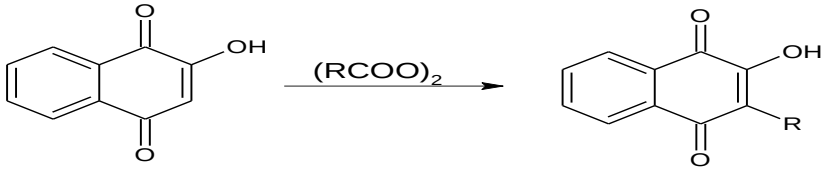
Table 1.1. Difference between the electrode potential of the substituted 1,4-naphthoquinone and substituted 1,4-naphthoquinone

	R	ΔE^omillvolt	R	ΔE^omillvolt
	$NHCH_3$	-253	CH_6H_5	-32
	NH_2	-210	$OCOCH_3$	-9
	OH	-128	Cl	+24
	OCH_3	-131	SO_3Na	+69
	CH_3	-76	$SO_2C_6H_4H_3$	+121
	H	+470		

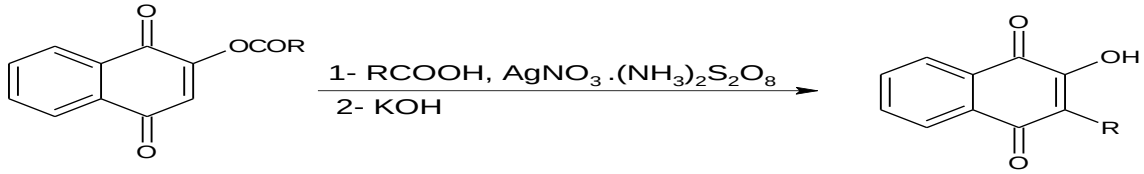
1.3.5. Carbon-Carbon bond formation

1.3.5.1. Alkyl substitution at carbon

One of the first methods was the reaction of diacyl peroxides with hydroxynaphthoquinone (lawsone) to produce a great variety of naphthoquinones possessing antimalarial activity. The reaction proceeds through a radical mechanism but usually are not satisfactory.

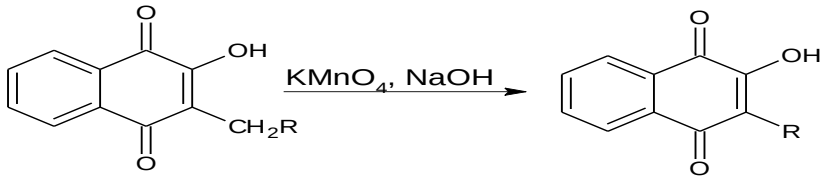


Better results obtained from the reaction of acylated lawsone, with a carboxylic acid in the presence of peroxysulfate mediated radical decarboxylation reaction (Syproudis, 2000).

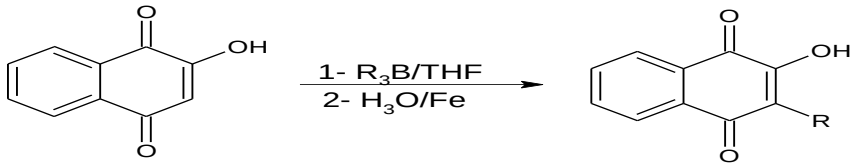


A series of allyl substituted hydroxynaphthoquinones have been prepared, from the lawsone with the corresponding allylic alcohol (Spyroudis, 2000).

The Hooker oxidation with alkaline permanganate or hydrogen peroxide was used for the preparation of alkyl homologus with one less carbon at C-1 at the side chain, exhibiting the same pesticide activity.

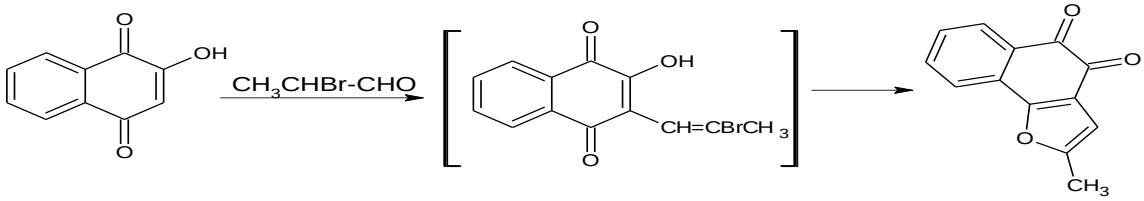


Finally, Lawsone, as well as alkoxyquinones, can be directly alkylated by alkylboranes at C-3 position.

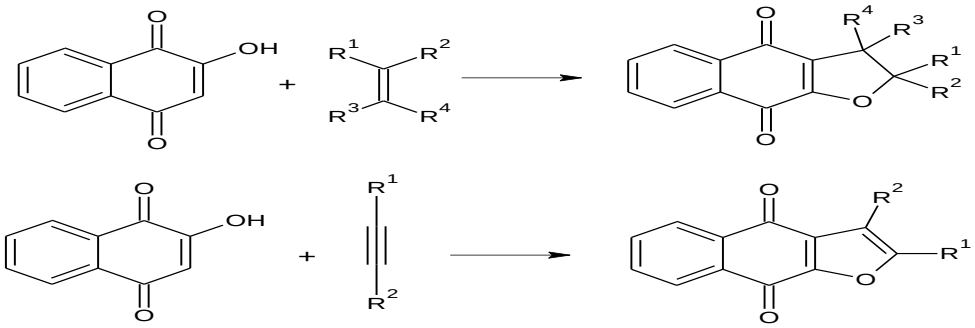


1.3.5.2. Cyclization to furan derivatives

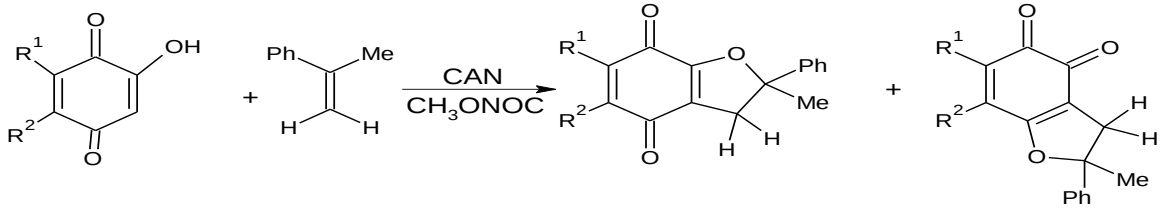
Cyclization of hydroxyquinones to the corresponding furan derivatives consists one of the most interesting features of their chemistry. The reaction of Lawsone with 2-bromopropanal afforded the *ortho*-quinone furan derivatives, through the initial alkylation of C-2 (Berger and Rieker, 1974).



An analogus reaction using 3,4-dibromo-2-butanone led to a mixture of furan and dehydrofuran derivatives. The reaction of Lowsone with a derivatives of alkenes offers an easy one-step access to dihydrofuran derivatives whereas the reaction with alkynes led to furan analogus. Similar results were obtained from the reaction with 2-hydroxybenzoquinones (Spyroudis, 2000).

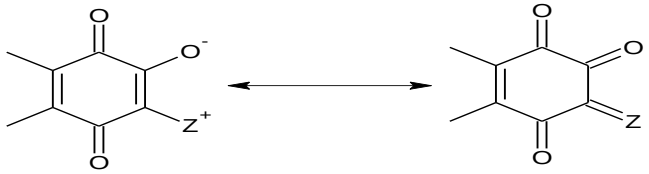


Cyclization proceeds satisfactory with substituted hydroxybenzoquinones (Spyroudis, 2000).



The above methods of cyclization involve the initial formation of free radicals. Another method is the reaction of hydroxynaphthoquinones with enamines which starts with the nucleophilic attack of quinone to enamine, afford furopara-quinones in satisfactory yields. In this case no formation of the corresponding *ortho*-quinone isomer was observed (Johnson *et al*, 1973).

Hydroxyquinones form stable zwiterionic compounds of general type:



The compounds can be described as hybrids of 1,4 or 1,2-dipoles or as ylides, whereas Z is a moiety of the elements P, S, N or I. These ylides exhibit significant stability, and hence low reactivity (Francis and Richard, 2007).

In many cases the conversion of the hydroxyl group of the quinone ring to a corresponding ester or ether group is necessary for further transformation or for monitoring the biological activity of the certain derivatives (Francis and Richard, 2007).

1.3.6. Complexes of quinones system

Electron donor-acceptor (EDA) complexes are materials of current interest since they can be utilized as organic semiconductors, photocatalysis and dendrimers. For the formation of such complexes the acceptor molecule should have an electron attracting part. A quinonoid ring has this property and it is common to many biomolecules, e.g ubiquinone and the K-vitamins. The former acts as a coenzyme and the latter occurs in blood prothrombin,

having an important but not completely understood role in blood coagulation (Pal *et al*, 2004).

With *p*-quinone derivatives, the stoichiometry of donor to acceptor (quinone) is 1:2 for acceptors stronger than *p*-chloranil. The weaker acceptors including *p*-chloranil afford non-stoichiometric products. The best fit of donor: acceptor is 1:1.7 for *p*-Iodanil and 1:1.8 for other *p*-Halonils (chloranil, bromanil). 2,5-Dichloro-*p*-benzoquinone afford 2:5 stoichiometry.

1.4. Spectroscopic properties of quinones

1.4.1. Infrared spectroscopy (IR)

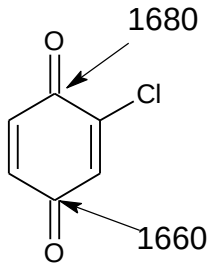
Quinones are a special case of α,β-unsaturated ketones. Characteristic frequencies in this class of compounds arise from C=O and C=C groups and lie in the range 1587-1695 cm^{-1}. The stronger, higher frequency band was assigned to the carbonyl group (Barbara Stuar, 2004).

a) **υC=O vibrations:** *p*-Quinones with two carbonyl groups in the same ring (e.g. *p*-benzoquinones) absorb in the range 1660-1680 cm^{-1}. In the large quinonoid systems (e.g. *amphi*-quinones or polycyclic quinones), the *v*CO frequency is lower, occurring at 1635-1655 cm^{-1}. In some quinones the carbonyl band is doubled. The reason for this doubling has been interpreted in several ways, namely vibrational coupling (by analogy with peroxides and anhydrides), itramolecular vibrational effect, and separation of unperturbed frequencies of *v*CO stretching vibration due to steric or electronic effects (Barbara Stuar, 2004).

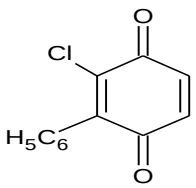
   Bezoquinone was assigned a single band in earlier works. Actually it shows a doublet which remained unnoticed because of poor experimental conditions (Barbara Stuar, 2004).

   The frequency, intensity, and splitting of the *v*CO band in substituted *p*-benzoquinones are influenced by the nature, position, and number of substituents (Barbara Stuar, 2004).

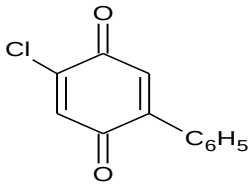
Electron-donating groups (+*I* effect, alkyl groups) or groups with a –*I* but +*E* effect (halogens, Cl) lower the frequency. The effect is enhanced by an increased number of substituents of this type. The hydroxyl group shows the most powerful effect. Electronegative substituents with –*I*, –*E* effects raise the frequency. Also in this case the shift depends on degree of substitution. *p*-Benzoquinone substituted with a chlorine atom (with strong –*I*, +*E* effect), shows two *v*CO bands. The relative intensity of the two absorptions depends on the polarity of the solvent. The distance Δv (cm^{-1}) between the two bands is 20 cm^{-1}. The higher frequency band was assigned to the carbonyl group next to the halogen atom, perturbed by a field effect as in halo-ketones. The second band corresponds to the carbonyl group adjacent to a hydrogen atom (Barbara Stuar, 2004).



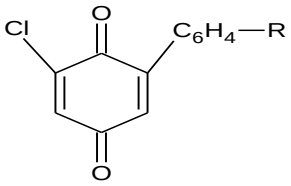
A phenyl substituent does not alter the frequency of the carbonyl group in quinones. 2-Phenyl-*p*-benzoquinone shows a band at 1671 cm^{-1} with an inflection at 1663 cm^{-1}. In phenylchloro-*p*-bezoquinones, the shift depend on the relative positions of the two substituents. Disubstituted compounds with substituents in 2- and 3-position (a) or 2- and 5-position (b) show a single *v*C=O band. Compounds with disubstitution in the 2- and 6-position (c), where substituents are adjacent to a single carbonyl group, show two bands. It is believed that in compounds (a) and (b) the opposite effect of the two substituents reduces the distance between the two bands to the extent that they overlap (Barbara Stuar, 2004).



a



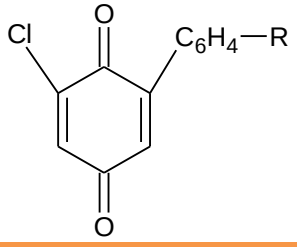
b



c

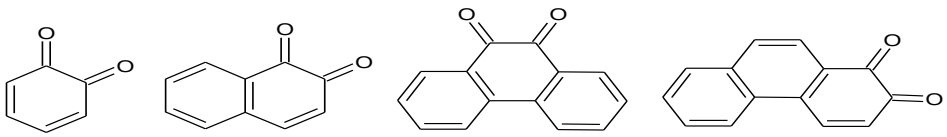
The spectrum shows a single absorption at 1683 cm^{-1}. In compound (c) the frequency and distance between the two components of the doublet are also influenced by substituents in the *para*-position of the benzene ring:

Table (1.2) *v*CO frequencies in substituted quinones



R	*v*CO, cm^{-1}	*v*CO, cm^{-1}	Δ*v*, cm^{-1}
H	1688	1659	29
Cl	1685	1658	27
NO_2	1682	1657	25

Frequencies of *o*-quinones lie in the range 1669-1684 cm^{-1} and cannot be differentiated from those of *p*-quinones (Barbara Stuar, 2004).



νCO, cm^{-1} 1669 1678 1684 1678

b) Other vibrations in quinones: out-of-plane C-H deformation vibration in *p*-benzoquinones have the following frequencies, depending on the mode of substitution:

Monosubstituted *p*-benzoquinones 825-856 and 901-916 cm^{-1}

2,3-disubstituted *p*-benzoquinones 841-846 cm^{-1}

2,5- and 2,6-disubstituted *p*-benzoquinones 897-920 cm^{-1}

c) *ν*C=C vibration: The frequency of the *ν*C=C skeletal vibration is 1600 cm^{-1}. In substituted compounds the intensity of the absorption is strongly influenced by the nature of the substituent. In methoxy quinones the band is stronger than in the corresponding methyl- or hydroxyquinones (Barbara Stuar, 2004).

1.4.2. Ultraviolet spectroscopy (UV-VIS)

The spectrum of *p*-bezoquinone is characterized by intense absorption near 240 nm (ε_{max}. 26,000), a medium band ~285 nm (ε_{max}. ~300) attributed to an electron-transfer (E.T.) transition, and much weaker absorption ($n \rightarrow \pi^*$) in the visible region (Thomson, 1971).

The diagnostic features of electronic spectrum of 1,4-naphthoquinone which is unsubstituted in the benzenoid ring are intense benzenoid and quinonoid electron-transfer (E.T.) bands in the (240-290) nm region, a benzenoid ET band at about 335 nm of medium intensity, a quinonoid ET band in the (330-450) nm region of low to medium intensity that is generally only observed for 2,3-disubstituted compounds, and finally a broad local excitation (LE) band of low intensity in the (400-500) nm region attributable to the $n \rightarrow \pi^*$ transition of the quinone carbonyls (Harmon *et al*, 1969).

In the spectrum of 1,4-naphthoquinone, the peaks at 245 and 251 nm are due to benzenoid ET processes and shift only slightly with substitution in the quinonoid ring. The quinonoid ET transitions (shoulder at 257 nm), on the other hand, are quite sensitive to substitution in the quinonoid. Benzenoid bands of 2-hydroxy-1,4-naphthoquinone appear at essentially the same position as in 1,4-naphthoquinone itself, but that the quinonoid band have shifted bathochromically to 277 and 283 nm (Novakovic *et al*, 2003).

The band at 355nm in the spectrum of 1,4-naphthoquinone is assigned to a benzenoid ET transition and as expected its position appear to be relatively independent of substitution in the quinonoid ring.

Although the quinone carbonyls insulate the aromatic portion from the quinonoidal double band and its substituent, the presence of the double bond does facilitate this excitation. The band position in 1,4-naphthoquinone is bathochromically displaced by 40 nm from the corresponding ET transition for 2,3-dihydro-1,4-naphthoquinone (295 nm in ethanol)(Ogata *et al*, 1968).

Menaphthone (K_3) react with sulfhydryl compounds to form a thioester linkage at 3-position of K_3 with an absorption maximum at 420-430 nm (Fieser and Turner, 1947; Nakai and Hase, 1968).

1.4.3. Nuclear Magnetic Resonance (NMR)

There have been numerous papers, which report on routine ^{1}H-NMR chemical shifts of the aromatic or side-chain protons of benzo-, naphtho-, anthraquinones or anthracyclines and other condensed quinones. The quinonoid protons in *p*-benzoquinone resonate at δ 6.72 ppm and in 1,4-naphthoquinone at δ 6.97 ppm. The effect of substitution (Table 1.3) is analogous to that observed in comparable *cis*-vinyl compounds, and for benzoquinones the chemical shift of Q-H is very similar to that found in cyclohex-2-ene-l,4-diones (Thomson, 1971).

Table (1.3) N.M.R. spectra (60 MHz) of some *p*-benzoquinones (δ values)

Benzoquinone	**H.2**	**H.3**	**H.5**	**H.6**	**Others**
Parent	6.72	6.72	6.72	6.72	
2-methyl-	-	6.58(m)	6.70	6.70	Me, 2.07(d)
2,6-dimethyl-	-	6.50(m)	6.50(m)	-	Me, 2.03(d)
2-Methyl-5-isopropyl-	-	6.55(q)	-	6.47(d)	Me, 2.02(d); Pr, 3.00(m)
2,6-Dimethoxy-	-	5.86(m)	5.86(m)	-	MeO, 3.84
2-Methoxy-5-methyl-	-	5.74	-	6.40(q)	Me, 1.98(d); MeO, 3.74
2,3-Dimethoxy-5-methyl-	-	-	-	6.26(q)	Me, 1.95(d); MeO, 3.90, 3.88

On reduction to a quinol the signal shifts downfield to the aromatic region, frequently with a reduction in multiplicity, and this is a useful criterion for a quinonoid structure. The signal from an alkyl substituent undergoes a corresponding shift and reduction in multiplicity. Thus in 2-methyl-1,4-naphthoquinone the quinonoid proton at C-3 gives rise to a quartet at δ 6.84 ppm (J, 1.5 Hz) coupled to a doublet from the allylie methyl protons at δ 2.19 ppm (Thomson, 1971).

Table (1.4) N.M.R. spectra (60 MHz) of some naphthaquinones (δ values)

1,4-naphthoquinone	H.2	H.3	H.5	H.6	H.7	H.8	Others
Parent	6.95	6.95	8.07(m)	7.77(m)	7.77(m)	8.07(m)	
2-methyl-	-	6.79(q)	-	-	-	-	Me, 2.13(d)
2-Hydroxy-	-	6.37	-	-	-	-	
2-Methoxy-	-	6.17	-	-	-	-	MeO, 3.89
2-Acetoxy-	-	6.76	-	-	-	-	
2-Acetyl-	-	6.06	-	-	-	-	
5-Hydroxy-	6.97	6.97	-	7.25(m)	7.60	7.70(m)	HO, 11.93
5-Hydroxy-7-methyl -	6.91	6.91	-	7.08(d)	-	7.41(d)	HO, 11.83; Me, 2.42
5-Hydroxy-3,7-dimethoxy-	6.08	-	-	6.60(d)	-	6.08(d)	HO, 11.97; MeO, 6.09
5,8-Dihydroxy-	7.13	7.13	-	7.13	7.13	-	HO, 12.43
5,8-Dihydroxy-2-methoxy-	-	6.17	-	7.23	7.23	-	HO, 12.63, 12.17; MeO, 3.92
5,8-Dihydroxy-2-ethyl-	-	6.84(t)	-	7.20	7.20	-	HO, 12.45, 12.60
5,8-Dihydroxy-2,7-dimethoxy	-	6.40	-	6.40	-	-	HO, 13.12, 12.70; MeO, 3.94

Note that in unsymmetrical di-substituted 1,4-naphthoquinones (Table 1.4) the adjacent protons at C-2 and C-3 frequently give a singlet rather than an AB quartet, and this is also true for some monosubstituted benzoquinones. The nuclear protons in simple benzoquinones give rise to multiplets which originate from long range interactions. The following coupling constants have been observed: $J_{allylic}$ (CH_3-*C=C-H)* 1.5-1.7 Hz, $J_{homo\text{-}allylic}$(CH_3-C=C-CH_3) 1.3 Hz, J(H-C-C-C-H) 2.2-2.5 Hz. Other long range spin-spin couplings, if present, are much smaller, and the coupling constants for allylic and homo-allylic systems

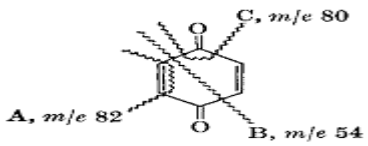
vary with the angle between the C=C double bond and the relevant C-H bonds (Pinhey and Sternhell, 1963). The other signals observed in the n.m.r. spectra of quinones, arising from aromatic and side chain protons, are not peculiar to these compounds and little comment is needed. In 1,4-naphthoquinone and 9,10-anthraquinone the α- and β-protons give A_2B_2 multiplets centered at δ 8.07 ppm and 7.67 ppm respectively, and these are modified by substitution in the normal way. In naphthoquinones the benzenoid substitution pattern can usually be deduced from the aromatic proton signals without difficulty but the situation is more complex in complex in anthraquinone (Thomson, 1971).

1.4.4. Mass Spectra (MS)

The positive-ion electron impact spectra of quinones exhibit two characteristic features, namely (1) the stepwise loss of two molecules of carbon monoxide, and (2) the formation of peaks two mass units higher than the molecular mass due to partial reduction before the ionization step. Benzoquinones and naphthaquinones also eliminate an acetylenic fragment from the quinone ring, and if the latter is hydroxylated breakdown is accompanied by a characteristic hydrogen rearrangement (Zeller and Roland, 1988).

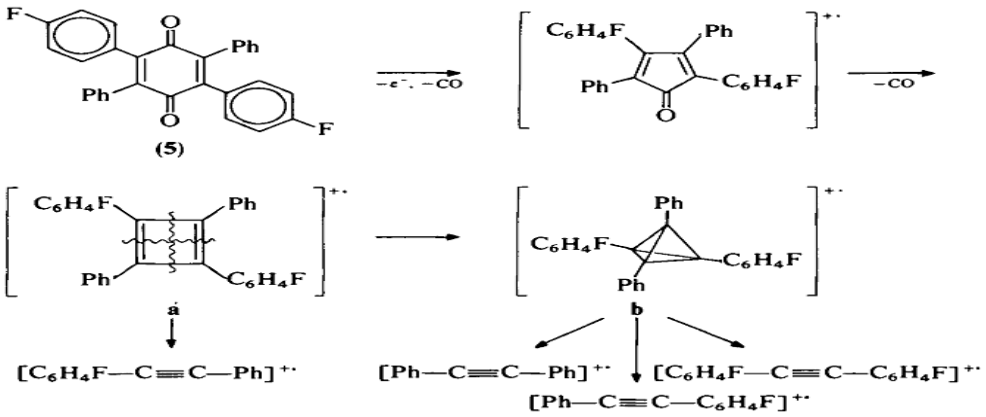
Benzoquinones:

These compounds normally form abundant molecular ions which frequently give rise to the base peak. The principal fragmentation processes are shown in below for the parent compound (Bowie *et al*, 1970).

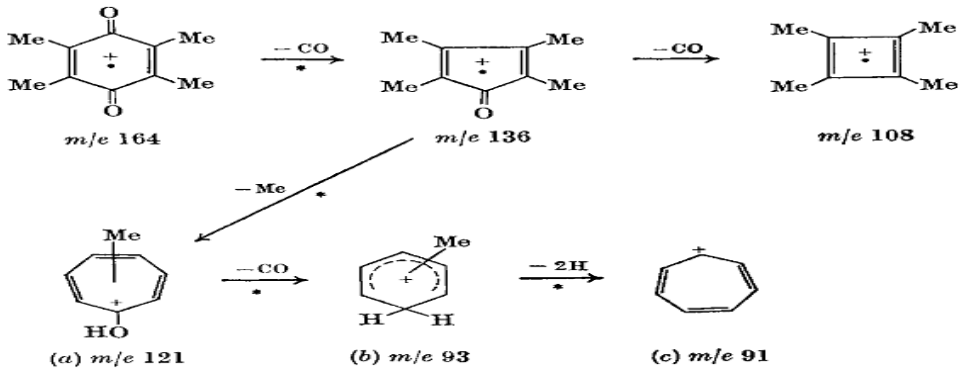


In addition loss of two molecules of carbon monoxide gives an important peak at *m/e* 52. This necessarily requires the formation of at least one carbon-carbon bond and the fragment is most simply represented as ionized cyclobutadiene. A cyclobutadiene structure (a) would only predict monofluoro-labelled product ions. Therefore, Bursey *et al* concluded that

the $[M-2CO]^+$ ions either decompose as a tetrahedrane-like structure (b) or the decomposing species consist of isomeric substituted tetraphenylcyclobutadiene cation radicals undergoing inter-conversions via (b). If the tetrahedrane intermediates (or transition states) are undistorted, the intensity ratio of unlabeled, singly labeled, and doubly labeled product ions should be 1:4:1. The experimental ratio obtained by measurement of conventional metastable ion intensities in the spectrum of (5**)** generated by a single focusing magnetic deflection instrument was 1: 4.8: 0.84. The divergence between the experimental and the theoretically predicted ratio was rationalized by a distorted tetrahedrane structure (Szulejko and Bursey, 1985).



Similarly in fragmentation (5), the most highly substituted neutral moiety is eliminated. Appropriate metastable peaks show that this breakdown is frequently a two-step process, elimination of an acetylene being followed by loss of carbon monoxide. Scheme below shows the postulated fragmentation path for tetramethylbenzoquinone (Thomson, 1971).

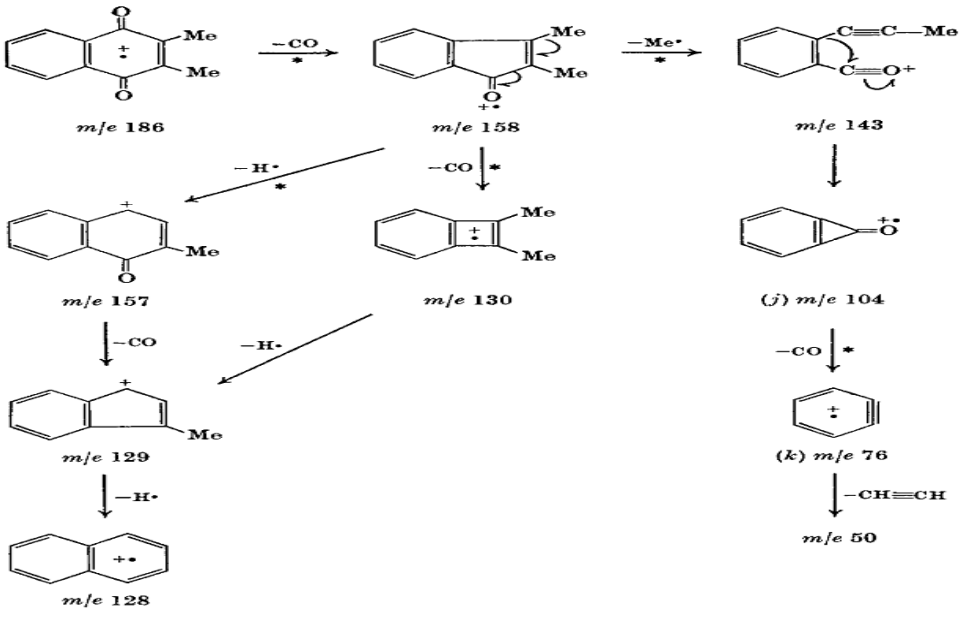


The formation of a hydroxytropylium ion (a) is supported by evidence from other spectra which indicates that the presence of at least two methyl (or larger) groups is necessary to allow an M-CO ion to break down by loss of a radical with formation of a relatively stable carbonium ion, and also by the subsequent decomposition of (a) into (b) and (c) which is exactly analogous to the fragmentation of the hydroxytropylium ion in the spectrum of benzyl alcohol (Thomson, 1971).

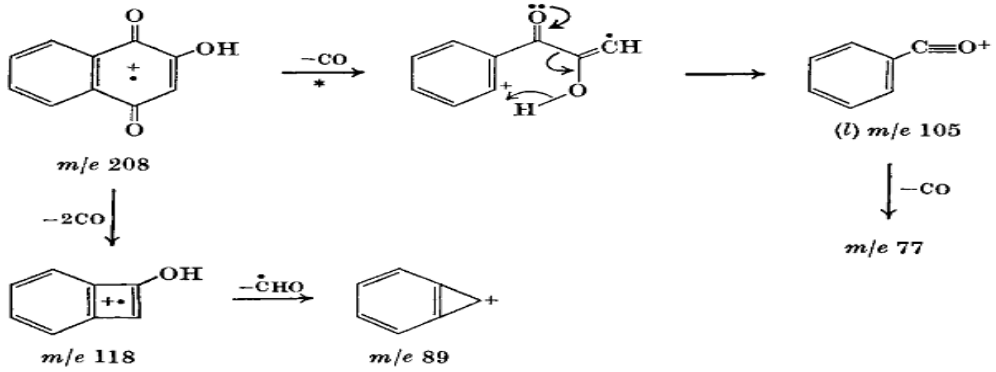
Significant M+2 peaks are frequently observed in the mass spectra of benzoquinones, sometimes increasing in intensity with time. Introduction of deuterium oxide into the ionisation chamber along with a quinone results in the appearance of M+3 and M+4 peaks in the mass spectrum, indicating that the M+2 peaks originate from a reaction involving water (Silverstein and Bassler, 1964). The intensity of the M+2 peak can be correlated with the redox potential of the quinone. However in some cases the M+2 ion may arise by hydrogen transfer from a side chain (Heiss *et al*, 1969).

Naphthoquinone:

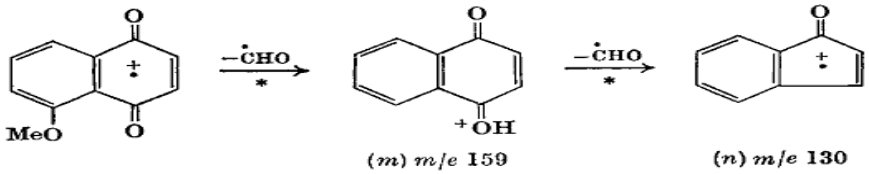
The fragmentation processes of 1,4-naphthaquinone and its simple derivatives are essentially similar to those of the benzoquinones (Beynon and Williams,1960).



Usually the molecular ion forms the base peak. The appearance of an abundant ion *m/e* 104 (j) and its decomposition products *m/e* 76 (k) and *m/e* 50 are characteristic for naphthaquinones with no benzenoid substituents. On the other hand substitution in the benzenoid ring causes these peaks to shift to the appropriate higher *m/e* values. Again, as in the benzoquinone series, a 2-hydroxynaphthaquinone undergoes a characteristic hydrogen rearrangement which results in a partial or almost complete replacement of the ion *m/e* 104 (j) by the benzoyl ion (I) at *m/e* 105 in the case of lawsone (Bowie *et al*, 1965):

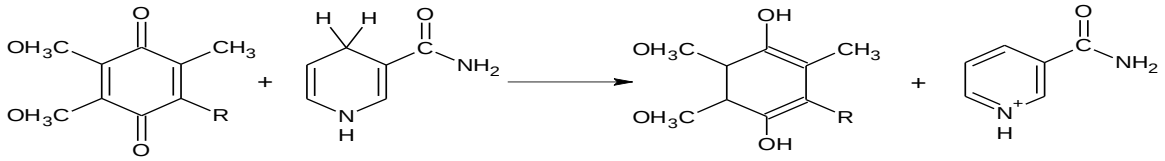


However, in hydroxynaphthazarins this rearrangement may be suppressed. In methoxynaphthaquinones the initial fragmentation tends to involve the methoxyl groups, the naphthaquinone skeleton being broken subsequently. 2-Methoxy-1,4-naphthaquinone affords abundant M-Me and M-CH_2O ions while the 5-methoxy isomer shows an M-CHO peak at *m/e* 159 represented as (m). Elimination of a second formyl radical leads to *m/e* 130 (n) which breaks down in the usual way. The same spectrum contains an M-H_2O peak (11%) which is characteristic of *peri*-methoxyquinones, the water originating from the carbonyl oxygen and the hydrogen atoms of the methoxyl group (Bowie and White, 1969). (A *peri*-ethoxyquinone fragments initially by loss of Me followed by CHO)(Bowie and White, 1969).



1.5. Biological importance of quinones

Benzoquinone and naphthoquinone derivatives are biologically important compounds, such as vitamin K group and co-enzyme Q. These compounds play an important role in cell metabolism, especially as electron carriers (Ambrogi *et al*, 1970). The quinone co-enzyme Q is also called ubiquinone because it is ubiquitous (found everywhere) in oxygen-consuming organism. Co-enzyme Q serves as an oxidizing agent within the mitochondria of cells behaving as a carrier in the electron transport sequence system (Tremblay and Sames, 2005). The following reaction shows the reduction of co-enzyme Q by NADH (the reduced form of nicotainamide adenine dinucleotide), which becomes oxidized to NAD^+.



Co-enzyme Q oxidized form | NADH reduced form | Co-enzyme Q reduced form

$$R = \left(CH_2CH\ C\ CH_3CH_2\right)_{10}$$

Quinones were found to possess a wide range of biological activities. 2-Sulphanilamido menadion and 2,5-disulphanilamido-1,4-benzoquinone were found to possess antituberculostatic activity (Roushdi *et al*, 1976 and 1977; Osman *et al*, 1983). 2-Alkyl mercapto-1,4-naphthoquinone can be used as antitumor (Porter *et al*, 1978).

A number of 1,4-naphthoquinone derivatives are active against bacteria and fungi, their activity being increased through halogenation in the nucleus. Naphthoquinones substituted with chlorine in the nucleus and side chain show a particularly marked activity against bacteria and fungi (Ambrogi *et al*, 1970; Gershon and Shanks, 1975; Paulino *et al*, 2005).

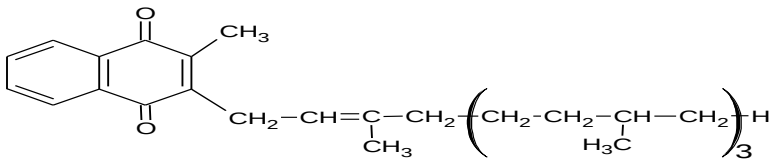
One class of compounds extensively investigated for anti-plasmodial activity is the hydroxynaphthoquinones. These anti-malarias are powerful

inhibitors of respiration and act in the region of cytochrome C/cytochrome B in the respiratory enzyme chain. A number of such quinones, e.glapinone and menactone, have been evaluated in malaria-infected patients (Ball *et al*, 1947; Hudson *et al*, 1985).

A great number of furoquinones, especially naphthoquinones, are naturally exhibiting broad spectrum of biological activity.

The naphthoquinone moiety was proven to be essential to the biological activities of sakymicin A using various naphthoquinone derivatives. Among the naphthoquinones tested, juglone (5-hydroxy-1,4-naphthoquinone) which resembles the partial structure of sakyomicin A was the most active in cytotoxicity against murine lymphosarcoma L5178Y cell electron acceptor function in the oxidation of NADH by clostridium kluyveridiaphorase or rat liver mitochondria and inhibition against avian myeloblastosis virus reverse transcriptase. The significantly lower cytotoxicity of sakyomicin A as compared with juglone was attributed to it's poor membrane transport. The inhibition of reverse transcriptase activity may result from the interaction between a sulfhydryl group in the active centre of the enzyme and quinone groups of the naphthoquinones and sakyomicinA (Take *et al*, 1985).

One of the most important naturally occurring substance having quinone-type structure, is the blood anti-hemorrnagic factor, vitamin K_1 that occurs in green plants and is a substituted 1,4-naphthoquinone.



Quinones, being structurally related to phthiocol, the yellow pigment isolated from the human tubercle fats, may help in penetration of the sulfa drugs through the fatty tissues surrounding the tubercle bacilli (Roushdi *et al*, 1976). The concept of masked quinones was cited (David and Wong, 1977).

1.6. Molecular modeling

The Oxford English Dictionary defines ‘model’ as a simplified or idealized description of a system or process, often in mathematical terms, devised to facilitate calculations and predictions. Molecular modeling would therefore appear to be concerned with ways to mimic the behavior of molecules and molecular systems. Today, molecular modeling is invariable associated with computer modeling, but is quite feasible to perform some simple molecular modeling studies using mechanical models or a pencil, paper and hand calculator. Nevertheless, computational techniques have revolutionized molecular modeling to the extent that most calculations could not be performed without use of a computer. This is not imply that a more sophisticated model is necessarily any better than simple one, but computers have certainly extended the range of models that can be considered and the systems to which they can be applied (Andrew, 1996).

Most molecular modeling studies involve three stages. In the first stage a model is selected to describe the intra-and inter-molecular interaction system. The two most common models that are used in molecular modeling are quantum mechanics and molecular mechanics. These models enable the energy of any arrangement of atoms and molecules in the system to be calculated, and allow the modeler to determine how the energy of the system varies as the positions of the atoms and molecules change. The second stage of a molecular modeling study is the calculation itself, such as an energy minimization, a molecular dynamics or Monte Carlo simulation, or a conformational search. Finally, the calculation must be analyzed, not only to calculate properties but also to check that it has been performed properly (Andrew, 1996).

1.7. QSAR

QSARs, quantitative structure–activity relationship, or quantitative structure–property relationships (QSPRs), are mathematical models that attempt to relate the structure-derived features of a compound to its biological or physicochemical activity (Worth *et al*, 2007).

1.7.1. Modeling methods

In general, methods for constructing QSAR can be divided into two groups **(**Fernandez and Caballero, 2007**)**:

1.7.1.1. Methods for Regression Problems

- Multiple Linear Regression
- Partial Least Squares
- Feedforward Backpropagation Neural Network
- General Regression Neural Network
- Gaussian Processes

1.7.1.2. Methods for Classification Problems

- Logistic Regression
- Linear Discriminant Analysis
- Decision Tree and Random Forest
- k-Nearest Neighbor
- Probabilistic Neural Network
- Support Vector Machine

1.7.2. Purpose of QSAR **(**Mark, 2009**)**

- To predict biological activity and physicochemical properties by rational means.
- To comprehend and rationalize the mechanisms of action within a series of chemicals.
- Savings in the cost of product development (e.g. in the pharmaceutical, pesticide, personal products, etc.).
- Predictions could reduce the requirement for lengthy and expensive animal tests.
- Other areas of promoting green and greener chemistry to increase efficiency and eliminate waste by not following leads unlikely to be successful.

1.7.3. Applications of QSAR **(**Mark, 2009**)**

- The rational identification of new leads with pharmacological, biocidal or pesticidal activity.

- The optimization of pharmacological, biocidal or pesticidal activity.
- The rational design of numerous other products such as surface-active agents, perfumes, dyes, and fine chemicals.
- The identification of hazardous compounds at early stages of product development or the screening of inventories of existing compounds.
- The designing out of toxicity and side-effects in new compounds.
- The prediction of toxicity to humans through deliberate, occasional and occupational exposure.
- The prediction of toxicity to environmental species.
- The selection of compounds with optimal pharmacokinetic properties, whether it be stability or availability in biological systems.
- The prediction of a variety of physicochemical properties of molecules.
- The prediction of the fate of molecules which are released into the environment.
- The rationalization and prediction of the combined effects of molecules, whether it be in mixtures or formulations.

1.7.4. Software for QSAR Development

There are many commercial or free software available for QSAR development. A good website for QSAR resources is the Cheminformatics and QSAR Society website (http://www.qsar.org/). There are lists of software, data sets, and resources pertaining to QSAR in the website (Matthias *et al*, 2012).

1.7.4.1. Structure Drawing or File Conversion

- ChemDraw
- ACD/ChemSketch
- Open Babel

1.7.4.2. 3D Structure Generation

- CORINA
- Concord
- Frog
- Smi23d

1.7.4.3. Descriptor Calculation

- ADRIANA.Code
- Dragon
- Molconn-Z
- PaDEL-Descriptor

1.7.4.4. Modeling

- KNIME
- RapidMiner
- WEKA
- ORANGE
- TANAGRA
- MATLAB
- R

1.7.4.5 General purpose

- SYBYL
- Discovery Studio
- MOE: Molecular Operating Environment
- CODESSA

All QSAR models developed should be presented with the following information (OECD, 2007):

- a defined endpoint
- an unambiguous algorithm
- a defined domain of applicability
- appropriate measures of goodness-of-fit, robustness and predictivity
- a mechanistic interpretation if possible

1.8. Aim of the project

p-quinones being *α,β*-unsaturated diketones were one of the most important naturally occurring or synthetic group of compounds through their role in different biological processes.

One of the aims of this study is to prepare some derivatives of *p*-quinone compounds. Different types of *p*-quinone may be studied and reacted with selected amines which satisfied a certain structural requirement. The synthetic procedure, mechanistic explanations and retro synthetic analysis of the target amino-*p*-quinones is one of the objectives of this study.

The main aim of this work is the study of QSAR of some *p*-quinone compounds and select some of them to be synthesized depending upon the calculated physiochemical values especially (log P) when correlated with substituted groups. Which give us prediction and an indication of what expected to be more biologically active derivatives.

The chromatography behavior especially thin layer chromatography (TLC) of the *p*-quinone and their amines coupled products may be investigated and compared. The study may highlight upon a certain vibrational and electronic spectral pattern of quinones. Deep insight into benzenoid and quinonoid rings spectral properties could be summarized from this work.

Chapter Two

2. Materials and Methods

2.1. Materials

2.1.1. Chemicals

Aniline (93.13, 1.02 g/cm^3, 99% Scharlau Chemie S.A), Chromium trioxide (99.9, 99%, Labtech Chemicals), Hydroquinone (99.5%, B.D.H chemical LTD Poole England), Naphthalene (98%, B.D.H chemical LTD Poole England), Sodium acetate (82.03, 98%, Tchno pharmchem Bahadurgarh, India), Sulphadoxine (99%, B.D.H chemical LTD Poole, England), Sulphamethoxazole (99%, B.D.H chemical LTD Poole England), Sulphanilamide (172.20, 99%, Techno Pharmchem, India).

All chemicals were used without further purification.

2.1.2. Solvents

Chloroform (119.38, [1.474-1.480] g/cm^3, 99%, Qualikems Fine Chemicals, India), Ethanol absolute (46, [0.7893-0.7899] g/cm^3, 99.9%, Carlo Erba reagents), Glacial acetic acid (60.05, 99.5%, Breckland Scientific Supplies), Methanol (32.04, 0.97 g/cm^3, 99.8%, Chem Lab NV, Belgium), Petroleum ether (74.12, 0.71 g/cm^3, 99.8%, ROMIL LTD, UK).

2.2. Thin- layer chromatography (TLC)

Thin-layer chromatography (**TLC**) was carried out using pre-coated LK5DF silica gel 150A plate (size 5×20 cm, 250 µm layer) obtained from Whatman lnc, New Jersey, USA using 98% chloroform and 2% methanol as an eluent and the spots were visualized by iodine vapors/ultraviolet light as visualizing agents.

2.3. Infra-red spectrophotometer (IR)

IR spectral analysis were carried out using **FTIR** spectrophotometer obtained from SHIMADZU (model No.3116465) in KBr pellets.

2.4. Ultraviolet-visible spectrophotometer (UV-VIS)

Ultraviolet spectral data analysis were carried out using 6505 **UV-VIS** spectrophotometer Jenway, England.

2.5. Proton-Nuclear Magnetic Resonance spectrophotometer (^{1}H-NMR)

The NMR spectra were recorded on a Varian Mercury VX-300 **NMR** spectrometer. ^{1}**H** spectra were run at 300 MHz in dimethylsulphoxide (DMSO).

2.6. Gas Chromatography/ Mass Spectrometer (GC-MS)

Chromatograms and mass spectra were recorded on Shimadzu QP 2010 plus **GC/MS** spectrometer using electron ionization (EI) mode, electron voltage 70 eV and ion source temperature 250 ^{o}C.

2.7. General equipment

Sensitive balance (A&D CO, LTD, Japan).

Magnetic stirrer with hot plate (stuart, Bibby sterilin LTD, UK).

Melting point instrument (Gallenkamp, England).

Thermometer (Hallenkamp, England).

Water bath (stuart, Bibby sterilin LTD, UK).

All of the glasses used were of Pyrex type.

2.8. ACD lab program

ACD/lab free ware 2012 downloaded from www.acdlabs.com.

2.9. General method of ACD/lab program and physiochemical property calculation

There were two modes to ACD/ChemSketch, namely Structure and Draw. Structure mode was used to draw chemical molecules, while Draw mode used to create and edit graphical objects. Upon startup, the Draw Normal mode and Carbon were automatically selected. By clicking and dragging the cursor in the window, C-C bonds were created. Clicking on a carbon atom produces a branched structure. The change was made by

selecting a heteroatom from the element list in the left toolbar and clicking on an atom in the structure to replace it. Radicals were made by selecting it from table which including carbon rings, carbon-based side chains and functional groups. A reaction requires were drawing by using the reaction arrow and reaction plus icons. Bond lengths and bond angle standardized by clicking on Clean Structure. The calculated properties were inserted into the ChemSketch window as a text field; on the tools menu, point to calculate, and choose the desired property. By selecting a structure and clicking on generate Name for structure, the IUPAC name was generated as a text field underneath the structure (Tables No [2.1.1], [2.1.2] and [2.1.3]).

2.10. Synthetic methods

2.10.1. Preparation of *p*-benzoquinone (I)

A solution of 33 g (0.3 mole) of hydroquinone was cooled in 150 ml of 60 per cent acetic acid contained in a 600 ml beaker to below 5° in an ice bath. 42 g (0.42 mole) of chromic trioxide was dissolved in 70 ml of water, and 30 ml of glacial acetic acid was added. By means of a separatory funnel over the beaker, the chromic trioxide was added to the mechanically-stirred solution of hydroquinone at such a rate that the temperature was not raised above 10°C; the addition was taken about 2 hours. The mixture was filtered at once and washed the quinone several times with 10 ml portions of ice cold water. The material was spreaded upon filter paper until dry, but no longer or the quinone will be lost through sublimation. The yield of quinone (a bright yellow crystalline solid), m.p. =115°C, is 21 g (66%); it darkens when exposed to light**.**

2.10.2. Preparation of 2,3,5,6- tertrabromo-1,4-Benzoquinone (II)

To a stirred solution of hydroquinone 6 g (0.055 mole) in 60 ml glacial acetic acid was added 10 ml of concentrated nitric acid and the solution was further stirred for 30 min. Bromine (20 ml, 62 g, 0.38.mole) was added over a period of 30 min. The reaction mixture was stirred at room temperature for one hour. The precipitated product was filtered and washed with cold water (Rec. GAA, Y = 93%, m.p. = 299 - 300°C).

2.10.3. Preparation of 1,4-naphthoquinone (III)

A solution of 60 g (0.6 mole) of pure chromium trioxide was placed in 150 ml of 80 per cent aqueous acetic acid in a 1-litre three necked flask, fitted with a thermometer, mechanical stirrer and 250 ml dropping funnel. The flask was surrounded by a mixture of ice and salt and, when the temperature has fallen to 0°, a solution of 32 g (0.25 mole) of pure naphthalene was added in 300 ml of glacial acetic acid, with constant stirring, over a period of 2-3 hours whilst maintaining the internal temperature at 10-15°. The stirring was continued overnight, during which time the reaction mixture and bath attain room temperature has allowed the dark green solution to stand for 3 days and stirred occasionally. The reaction mixture was poured into 2-3 litres of water, the crude naphthoquinone was collected by suction filtration, washed with 100 ml of water and dried in a desiccator. Recrystallized from 250 ml of petroleum ether (b.p. = 80-100°). The yield of pure 1: 4-naphthoquinone, m.p. = 124-125 °C, is 8.5 g (22%).

2.10.4. Preparation of 2,5-diamino-1,4-benzoquinones (Ia-Id) and 3,6-dibromo-2,5-diamino-1,4-benzoquinones (IIa-IId)

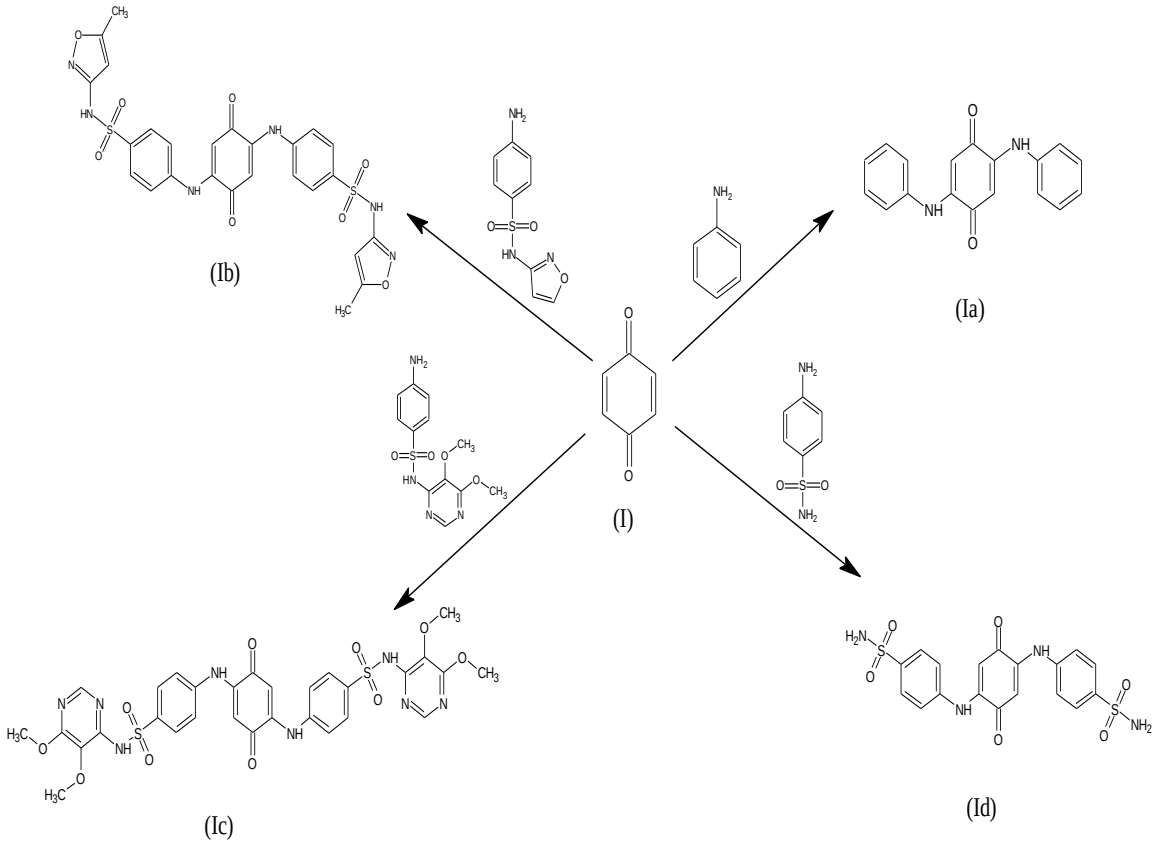
In a 250ml one neck round bottom flask, fitted with a reflux condenser and maintained over a magnetic stirrer were placed the following: 0.03 mole of 1,4-benzoquinone, 5ml ethanol, 5ml glacial acetic acid, 0.5g sodium acetate and 1ml water, The mixture was stirred for three minutes . A solution of 0.02 mole of the required amine in 3ml ethanol, 3ml glacial acetic acid was added to the reaction mixture and then refluxed for three hours with continuous stirring. The solution was poured into 250ml beaker containing 100ml water, the precipitated was filtered, air dried, and recrystallized from ethanol or glacial acetic acid.

2.10.5. Preparation of 2-amino-*p*-naphtoquinones (IIIa-IIId)

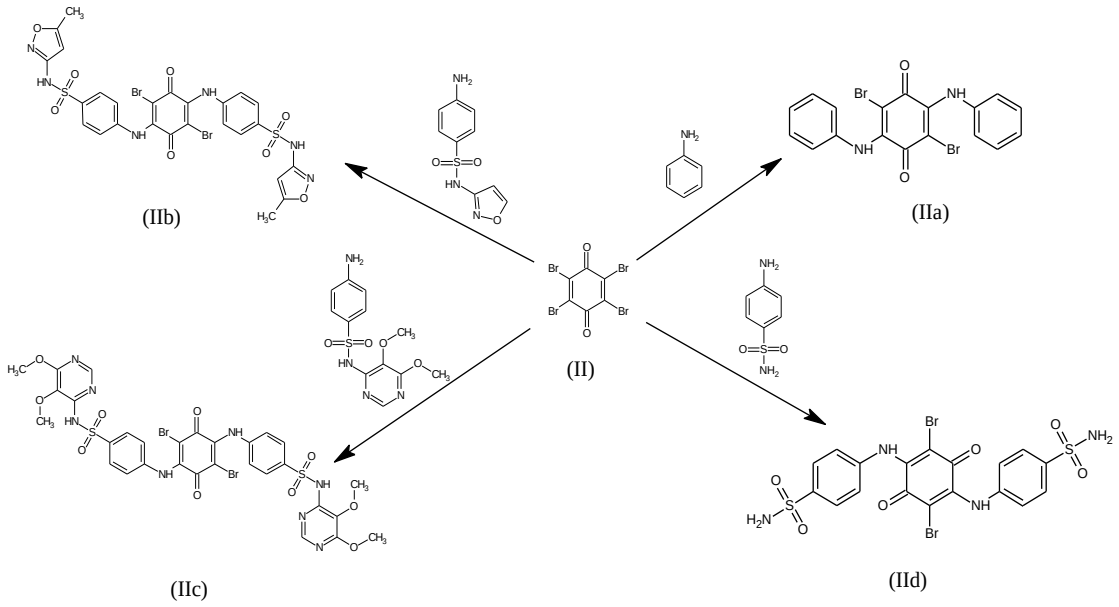
In 50 ml round bottom flask equipped with reflux condenser and magnetic stirrer were placed the following: 0.02 mole of 1,4-naphthoquinone, 5ml ethanol, 5ml glacial acetic acid, 0.5g of sodium acetate and 1ml water, The mixture was stirred for three minutes. A solution of 0.01 mole of the required amine in 3ml of glacial acetic acid, 3ml of ethanol was added to the reaction mixture and then refluxed for three hours

with continuous stirring. The solution was poured into beaker containing 100ml of distilled water. The precipitate product was filtered and air dried, and recrystallized from ethanol or glacial acetic acid.

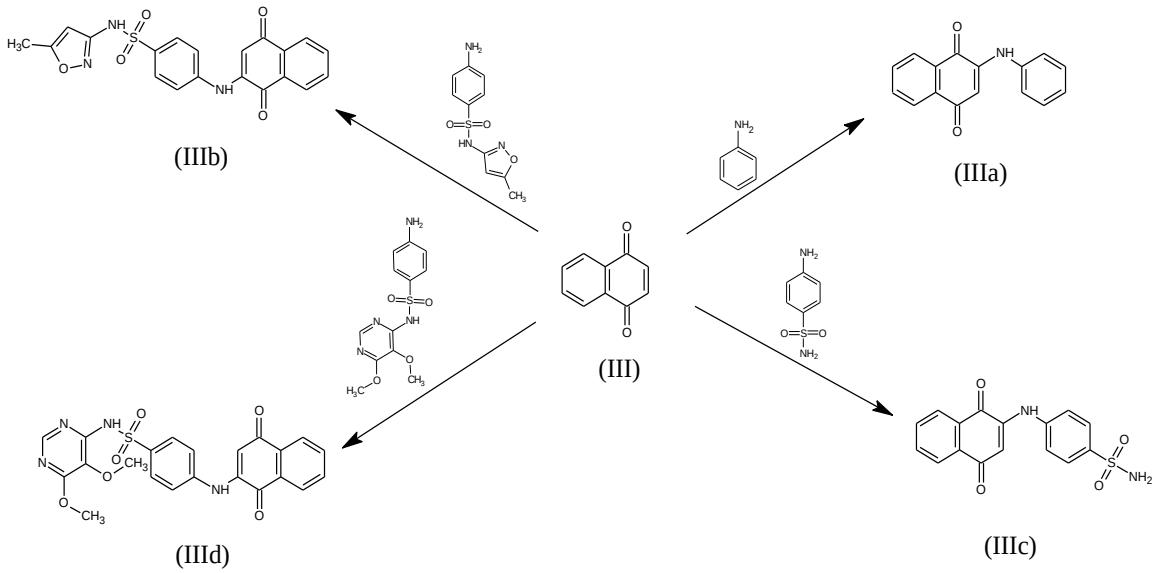
2.11. Reaction schemes



Scheme 2.1 Chemical structure of the prepared 2,5-diamino-1,4-benzoquinones



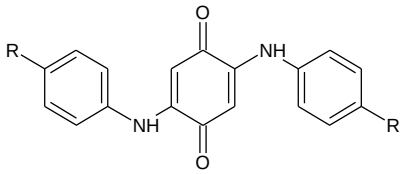
Scheme 2.2 Chemical structure of the prepared 3,6-dibromo-2,5-diamino-1,4-bezoquinones



Scheme 2.3 Chemical structure of the prepared 2-amino-*p*-naphthoquinones

Tables (2.1) Chemical names of the synthesized compounds

Table (2.1.1) Chemical name of the synthesized 2,5-diamino-1,4-benzoquinones



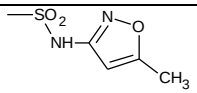
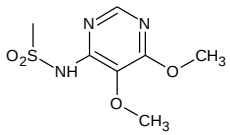
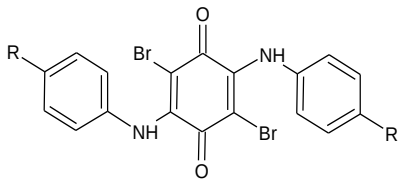
Comp No	R	Chemical name
Ia	H-	2,5-dianilino-1,4-benzoquinone
Ib		2,5-disulphamethoxazolyl-1,4-benzoquinone
Ic		2,5-disulphadoxinyl-1,4-benzoquinone
Id	$H_2N\text{-}SO_2\text{-}$	2,5-disulphanil amidyl-1,4-benzoquinone

Table (2.1.2) Chemical name of the synthesized 3,6-dibromo-2,5-diamino-1,4-benzoquinones



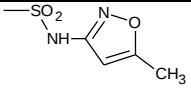
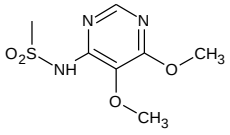
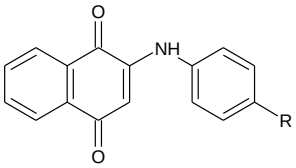
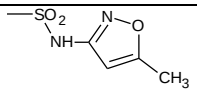
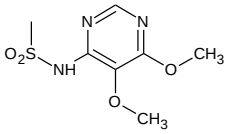
Comp No	R	Chemical name
IIa	-H	3,6-dibromo-2,5-dianilino-1,4-benzoquinone
IIb		3,6-dibromo-2,5-disulphamethoxazolyl-1,4-benzoquinone
IIc		3,6-dibromo-2,5-disulphadoxinyl-1,4-benzoquinone
IId	$H_2N\text{-}SO_2\text{-}$	3,6-dibromo-2,5-disulphanilamidyl-1,4-benzoquinone

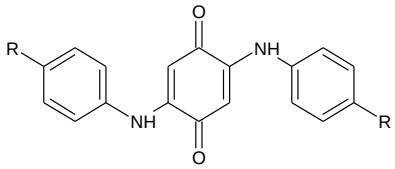
Table (2.1.3) Chemical name of the synthesized 2-amino-*p*-naphthoquinones



Comp No	R	Chemical name
IIIa	-H	2-anilino-1,4-naphthoquinone
IIIb		2-sulphamethoxazolyl-1,4-naphthoquinone
IIIc		2-sulphadoxinyl-1,4-naphthoquinone
IIId	$H_2N\text{-}SO_2\text{-}$	2-sulphanil amidyl-1,4-naphthoquinone

Tables (2.2) Reaction conditions

Table (2.2.1) Reaction conditions of 2,5-diamino-1,4-benzoquinone compounds



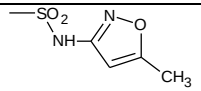
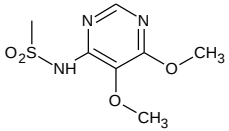
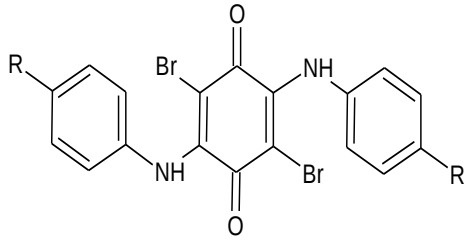
Comp No	R	Re. Time	Re. Temp	Y %	Rec. solv	Molecular formula	m.p °C	M.wt
Ia	-H	3 hours	Reflux temperature	68	Water / ethanol	$C_{18}H_{14}N_2O_2$	188-198	290.316
Ib		3 hours and 30 minutes	Reflux temperature	67	Water / ethanol	$C_{26}H_{22}N_6O_8S_2$	268-280	610.618
Ic		4 hours	Reflux temperature	65	Water / ethanol	$C_{30}H_{28}N_8O_{10}S_2$	316-317	724.721
Id	$H_2N\text{-}SO_2\text{-}$	3 hours and 40 minutes	Reflux temperature	68	Water / ethanol	$C_{18}H_{16}N_4O_6S_2$	> 300	448.473

Table (2.2.2) Reaction conditions of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds



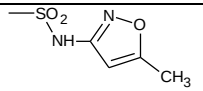
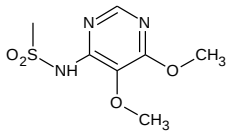
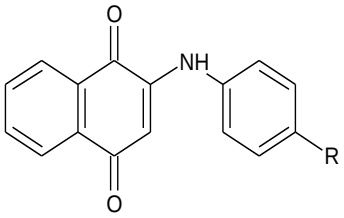
Comp No	R	Re. Time	Re. Temp	Y %	Rec. solv	Molecular formula	m.p ^{o}C	M.wt
IIa	-H	3 hours	Reflux temperature	72	Water / ethanol	$C_{18}H_{12}Br_2N_2O_2$	275-285	448.108
IIb		3 hours	Reflux temperature	64	Water / ethanol	$C_{26}H_{20}Br_2N_6O_8S_2$	247-257	768.410
IIc		3 hours	Reflux temperature	63	Water / ethanol	$C_{30}H_{26}Br_2N_8O_{10}S_2$	> 300	882.513
IId	H_2N-SO_2-	3 hours	Reflux temperature	70	Water / ethanol	$C_{18}H_{14}Br_2N_4O_6S_2$	274-280	606.265

Table (2.2.3) Reaction conditions of 2-amino-*p*-naphthoquinone compounds



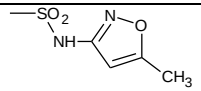
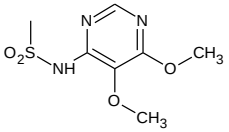
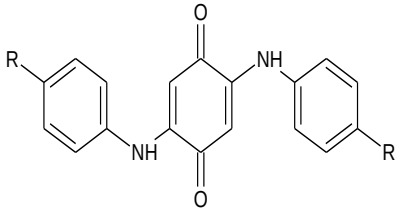
Comp No	R	Re. Time	Re. Temp	Y %	Rec. solv	Molecular formula	m.p °C	M.wt
IIIa	-H	3 hours	Reflux temperature	88	Water / ethanol	$C_{16}H_{11}NO_2$	194-196	249.264
IIIb		3 hours	Reflux temperature	80	Water / ethanol	$C_{20}H_{15}N_3O_5S$	291-295	409.415
IIIc		3 hours	Reflux temperature	78	Water / ethanol	$C_{22}H_{18}N_4O_6S$	280-288	466.467
IIId	H_2N-SO_2-	3 hours	Reflux temperature	87	Water / ethanol	$C_{16}H_{12}N_2O_4S$	290-305	328.342

Table (2.3) Infrared spectral data of the synthesized compounds

Table (2.3.1) Infrared spectral data of 2,5-diamino-1,4-benzoquinone compounds



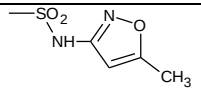
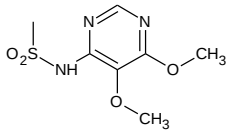
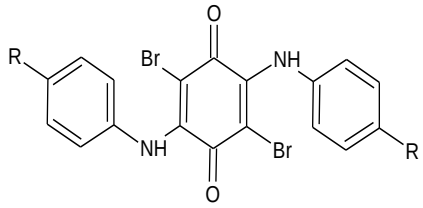
Comp No	R	C=O st.vib	N-H	C=C St.vib	SO_2 st.vib	C-H st.vib	Ring subs
Ia	-H	1639	st.vib 3236 Ben 1504	1504, 1490, 1442	----------	3053	mono 740, 694
Ib		1643	st.vib 3292, 3271 Ben 1606, 1535	1535, 1510, 1469	asym 1388, sym 1163	3139	para 827
Ic		1639	st.vib 3402, 3274 Ben 1573, 1504	1504, 1461, 1409	asym 1342, sym 1161	3101, 3020, 2941, 2860	para 835
Id	H_2N-SO_2-	1637	st.vib 3359, 3246, 3234 ben 1562, 1504, 1485	1504, 1485, 1406	asym 1334, sym 1159	3089	para 827

Table (2.3.2) Infrared spectral data of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds



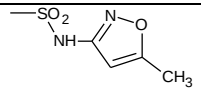
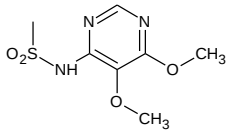
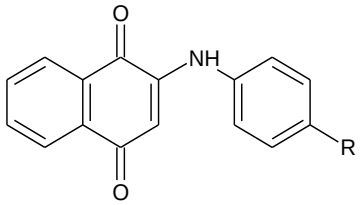
Comp No	R	C=O st.vib	N-H	C=C St.vib	SO_2 st.vib	C-H st.vib	Ring subs	C-Br st.vib
IIa	-H	1647	st.vib 3234 ben 1566	1498, 1477, 1442	----------	3055	mono 690, 729	1020
IIb		1658	st.vib 3244, 3753 ben 1610,1569	1490, 1406	asym 1328 sym 1166	2925, 2854	para 877	1091
IIc		1656	st.vib 3394, 3226 bed 1614, 1583	1483, 1454, 1407	asym 1330 sym 1159	2948, 2856	para 648	1081
IId	H_2N-SO_2-	1654	st.vib 3346, 3313, 3247 ben 1608, 1583	1502, 1402	asym 1326 sym 1155	3100	para 837	1016

Table (2.3.3) Infrared spectral data of 2-amino-*p*-naphthoquinone compounds



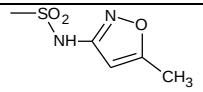
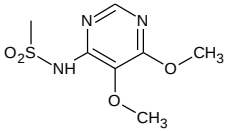
Comp No	R	C=O st.vib	N-H	C=C St.vib	SO_2 st.vib	C-H st.vib	Ring subs
IIIa	-H	1668, 1635	st.vib 3315 ben 1525	1569, 1525, 1444	----------	3053	mono 715, 621
IIIb		1672, 1620	st.vib 3299 ben 1535, 1469	1535, 1469, 1406	asym 1334 sym 1166	3078, 2997, 2846	mono 690, 576
IIIc		1677, 1635	st.vib 3299 ben 1539, 1483	1539, 1483, 1446, 1411	asym 1296 sym 1163	3174, 2939, 2854	mono 723, 694
IIId	H_2N-SO_2-	1677, 1627	st.vib 3367, 3259, 3234 ben 1531, 1479	1573, 1479, 1413	asym 1305 sym 1149	3105, 2923	mono 754, 692

Table (2.3.4) Infrared spectral data of *p*-quinones

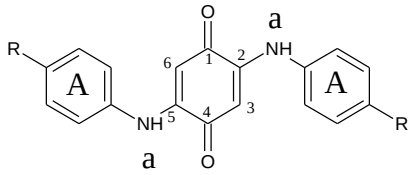
Comp. name	C=O st.vib	C=C st.vib	C-H st.vib	Ring subs	C-Br st.vib
1,4-benzoquinone (I)	1647	1589, 1537, 1479	3056	-------	-----
2,3,5,6-tetrabromo-benzoquinone (II)	1676	1588, 1544, 1450	------	tetra 865, 703, 642	1053
1,4-naphthoquinone (III)	1660	1589, 1566, 1504	3049	ortho 783	-----

Table (2.3.5) Infrared spectral data of amines

Comp. name	N-H	C=C	C-H st.vib	SO_2 st.vib	Ring subs
Aniline (A)	st.vib 3430, 3350 ben 1620	1600, 1502	3060	----------	para 879
Sulphanilamide (B)	st.vib 3470, 3365, 3232 ben 1630, 1589	1592, 1502, 1424	3087	asym 1350 sym1145	para 834
Sulphamethoxazole (C)	3379, 3300,3242	1619, 1575, 1502	3114	asym 1315 sym 1146	para 830
Sulphadoxine (D)	3379, 3300, 3242	1622, 1583, 1448	3076	asym 1315 sym 1091	para 838

Table (2.4) ^{1}H-NMR Chemical shift of the synthesized compounds

Table (2.4.1) ^{1}H-NMR Chemical shift of 2,5-diamino-1,4-benzoquinone compounds



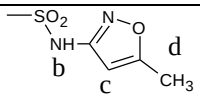
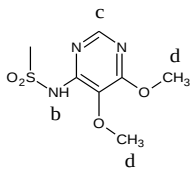
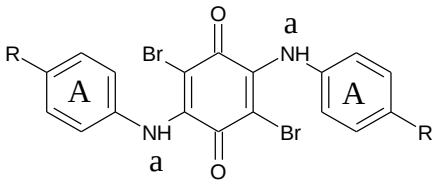
Comp. No	R	Chemical shift ppm (intensity, multiplicity, J constant Hz)					
		H-3 & H-6	Others				
			A	a	b	c	d
Ia	-H	5.95(s, 2)	7.45-6.36 (m, 10)	9.27(s, 2)	-	-	-
Ib		6.15(s, 2)	7.87 (4, d, 1.0 Hz) 7.61 (4, d, 1.0 Hz)	9.54(s, 2)	11.45(s, 2)	6.09(s, 2)	2.30(s, 6)
Ic		6.08(s, 2)	8.01 (4, d, 1.0 Hz) 7.58 (4, d, 1.0 Hz)	9.52(s, 2)	11.17(s, 2)	8.13(s, 2)	3.91(s, 6) 3.71(s, 6)
Id	b H_2N-SO_2-	6.03(s, 2)	7.86 (4, d, 1.0 Hz) 7.57 (4, d, 1.0 Hz)	9.52(s, 2)	7.37(s, 4)	-	-

Table (2.4.2) ^{1}H-NMR Chemical shift of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds



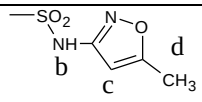
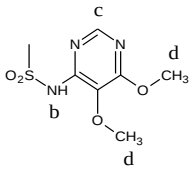
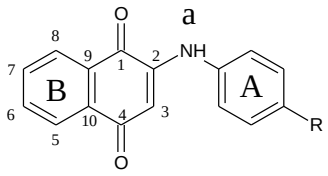
Comp. No	R	Chemical shift ppm (intensity, multiplicity, J constant Hz)				
		Others				
		A	a	b	c	D
IIa	-H	7.36-7.16 (m, 10)	9.69(s, 2)	-	-	-
IIb		7.78 (4, d, 1.0 Hz) 7.24 (4, d, 1.0 Hz)	9.77(s, 2)	11.35(s, 2)	6.14(s, 2)	2.29 (s, 6)
IIc		7.93 (4, d, 1.0 Hz) 7.23 (4, d, 1.0 Hz)	9.78(s, 2)	11.07(s, 2)	8.12(s, 2)	3.91 (s, 6) 3.70 (s, 6)
IId	b H_2N-SO_2-	7.76 (4, d, 1.0 Hz) 7.26 (4, d, 1.0 Hz)	9.80(s, 2)	4.70 (bs, 4)	-	-

Table (2.4.3) ^{1}H-NMR Chemical shift of 2-amino-*p*-naphthoquinone compounds



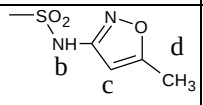
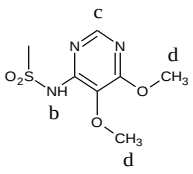
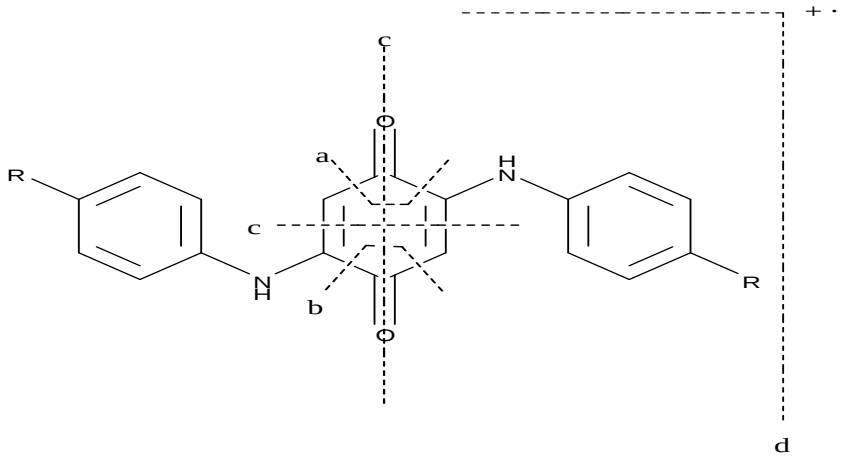
Comp. No	R	Chemical shift ppm (intensity, multiplicity, J constant Hz)						
		H-3	H-B	Others				
				A	a	b	c	d
IIIa	-H	6.10(s, 1)	7.78-8.06 (m, 4)	7.47-7.22(m, 5)	9.25(s, 1)	-	-	-
IIIb		6.14(s, 1)	8.06-7.90 (m, 4)	7.95(2, d, 1.0 Hz) 7.60(2, d, 1.0 Hz)	9.46(s, 1)	11.42(s, 1)	6.38(s, 1)	2.30(s, 3)
IIIc		6.37(s, 1)	7.8-8.09 (m, 4)	7.61(2, d, 1.0 Hz) 7.43(2, d, 1.0 Hz)	9.45(s, 1)	11.19(s, 1)	8.13(s, 1)	3.90(s, 3) 3.70(s, 3)
IIId	b H_2N-SO_2-	6.28(s, 1)	7.77-8.08 (m, 4)	7.87(2, d, 1.0 Hz) 7.34(2, d, 1.0 Hz)	7.34(s, 1)	3.34(s, 2)	-	-

Table (2.5) Mass spectral data of the synthesized compounds

Table (2.5.1) Mass spectral data of 2,5-diamino-1,4-benzoquinone compounds



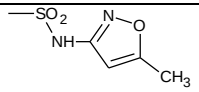
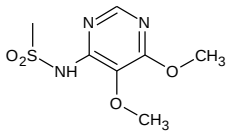
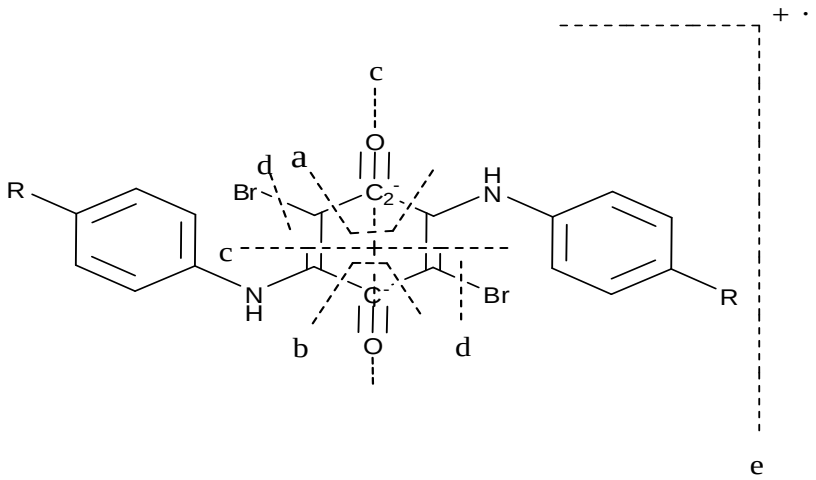
Comp No	R	Mw(calc)	Mw(obs)	m/z (Relative intensity %)			
				a	b	c	d
Ia	-H	290.316	290.10	261(6.31)	234(4.14)	117(22.91)	290.10(17.81)
Ib		610.618	610.10	585(5.41)	554(5.14)	278(0.13)	610.10(15.22)
Ic		724.721	724.10	696(7.16)	668(8.35)	338(23.13)	724.10(16.24)
Id	H_2N-SO_2-	448.473	448.10	420(0.89)	392(6.89)	196(1.22)	448.10(20.12)

Table (2.5.2) Mass spectral data of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds



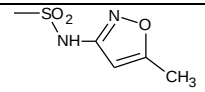
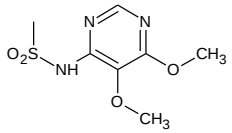
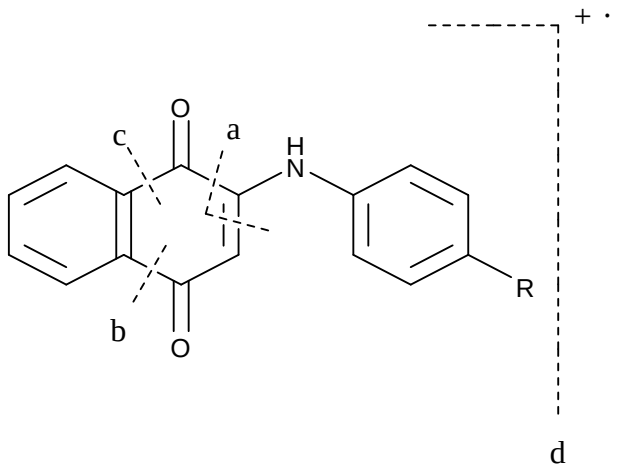
Comp No	R	Mw(calc)	Mw(obs)	m/z (Relative intensity %)				
				a	b	c	d	e
IIa	-H	448.108	448.85	420.8(0.24)	392.8(0.01)	195.90(3.16)	367.95(9.32) 288.95(5.44)	448.85(16.96)
IIb		768.410	768.00	740.0(0.89)	714(9.95)	352.0(13.38)	669.0(8.92) 611.0(9.43)	768.0(13.55)
IIc		882.513	882.00	854.0(0.60)	826.10(0.80)	413.10(0.81)	803.10(5.30) 724.10(0.98)	882.0(17.69)
IId	H_2N-SO_2-	606.265	606.00	578.0(1.67)	550.0(2.09)	272.10(0.49)	527.10(7.12) 448.10(5.24)	606.0(19.40)

Table (2.5.3) Mass spectral data of 2-amino-*p*-naphthoquinone compounds



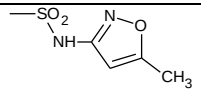
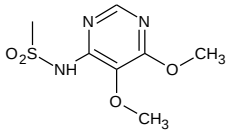
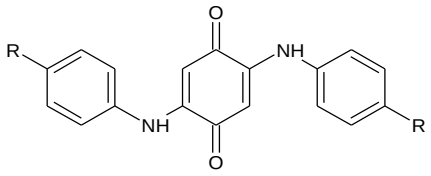
Comp No	R	Mw(calc)	Mw(obs)	m/z (Relative intensity %)			
				a	b	c	d
IIIa	-H	249.264	249.10	147.00(0.75)	105.00(3.96)	77.05(14.26)	249.10(2.02)
IIIb		409.415	408.10	146.10(3.58)	105.10(23.22)	77.05(39.39)	408.10(1.03)
IIIc		466.467	466.10	146.10(0.57)	105.10(3.44)	77.05(4.38)	466.10(0.42)
IIId	H_2N-SO_2-	328.342	328.10	146.10(10.51)	105.10(28.21)	76.10(81.91)	328.10(20.04)

Table (2.6) Ultraviolet-Visible spectral data of the synthesized compounds

Table (2.6.1) Ultraviolet-Visible spectral data of 2,5-diamino-1,4-benzoquinone compounds



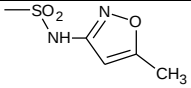
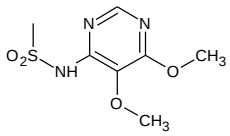
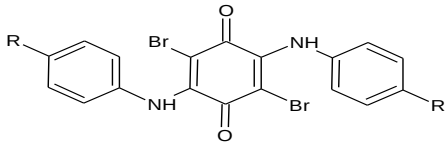
Comp. No	R	Solvent	λ_{max} nm
Ia	-H	Ethanol	380, 268
Ib		Ethanol	387.5, 286.5
Ic		Ethanol	387, 266
Id	H_2N-SO_2-	Ethanol	373, 277.5

Table (2.6.2) Ultraviolet-Visible spectral data of 3,6-dibromo-2,5-diamino-1,4-benzoquinone compounds



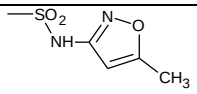
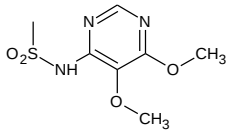
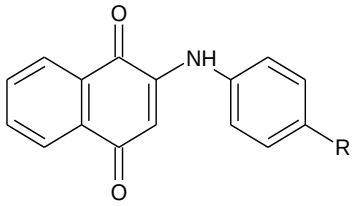
Comp. No	R	Solvent	λ_{max}
IIa	-H	Ethanol	597.5, 391.5, 247.5
IIb		Ethanol	352, 285
IIc		Ethanol	339.5, 263
IId	H_2N-SO_2-	Ethanol	358.5, 259

Table (2.6.3) Ultraviolet-Visible spectral data of 2,-amino-*p*-naphthoquinone compounds



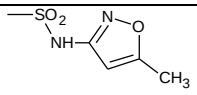
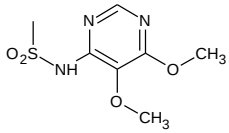
Comp. No	R	Solvent	λ_{max}
IIIa	-H	Ethanol	468, 272
IIIb		Ethanol	458, 281.5
IIIc		Ethanol	451, 276.5, 220
IIId	$H_2N\text{-}SO_2\text{-}$	Ethanol	460, 281

Table (2.6.4) Ultraviolet-Visible spectral data of *p*-quinones

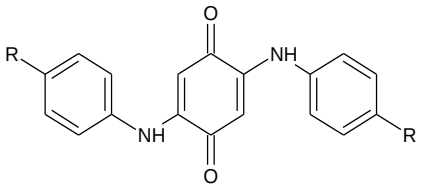
Comp. name	Solvent	λ_{max}
1,4-benzoquinone (X)	Ethanol	245, 335
2,3,5,6-tetrabromo-benzoquinone (Y)	Ethanol	308
1,4-naphthoquinone (Z)	Ethanol	417, 335.5, 246, 220.5

Table (2.6.5) Ultraviolet-Visible spectral data of amines

Comp. name	Solvent	λ_{max}
Aniline (A)	Ethanol	240, 285
Sulphanilamide (B)	Ethanol	215, 260
Sulphamethoxazole (C)	Ethanol	235, 304
Sulphadoxine (D)	Ethanol	235, 304

Table (2.7) Thin layer chromatography of the synthesized compounds

Table (2.7.1) Thin layer chromatography of 2,5-diamino-1,4-benzoquinone compounds



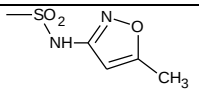
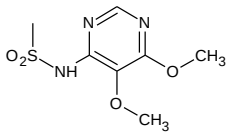
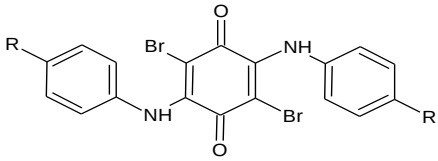
Comp. No	R	Developing solvent	R_f
Ia	-H	Chloroform:Methanol 9.8 : 0.2	0.92
Ib		Chloroform:Methanol 9.8 : 0.2	0.72
Ic		Chloroform:Methanol 9.8 : 0.2	0.86
Id	H_2N-SO_2-	Chloroform:Methanol 9.8 : 0.2	091

Table (2.7.2) Thin layer chromatography of 3,6-dibromo-2,5-diamino--1,4-benzoquinone compounds



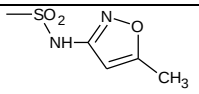
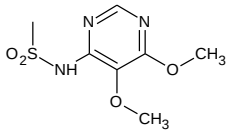
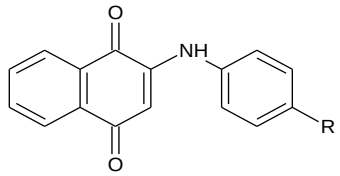
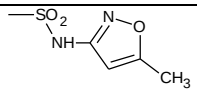
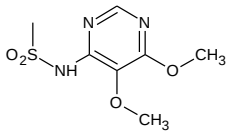
Comp. No	R	Developing solvent	R_f
IIa	-H	Chloroform:Methanol 9.8 : 0.2	0.95
IIb		Chloroform:Methanol 9.8 : 0.2	0.94
IIc		Chloroform:Methanol 9.8 : 0.2	0.93
IId	H_2N-SO_2-	Chloroform:Methanol 9.8 : 0.2	0.94

Table (2.7.3) Thin layer chromatography of 2-amino-*p*-naphthoquinone compounds



Comp. No	R	Developing solvent	R_f
IIIa	-H	Chloroform:Methanol 9.8 : 0.2	0.89
IIIb		Chloroform:Methanol 9.8 : 0.2	0.73
IIIc		Chloroform:Methanol 9.8 : 0.2	0.81
IIId	$H_2N\text{-}SO_2\text{-}$	Chloroform:Methanol 9.8 : 0.2	0.87

Chapter Three

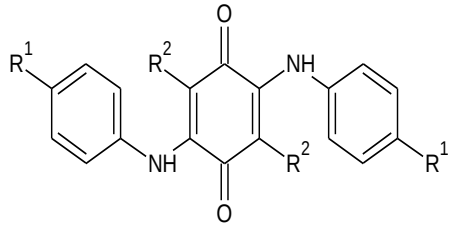
3. Results and Discussion

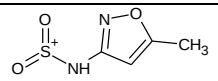
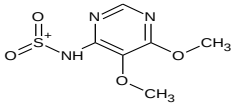
Molecules with the quinonoid structure constitute one of the most interesting classes of compounds in organic chemistry. The term ‘‘Quinones’’ refers generally to a 1,4-diketone formally derived from dihydro-aromatic compounds in which the two carbonyl groups are connected by a system of conjugated double bonds; which are usually a coloured compounds. The quinone-hydroquinone pair form an oxidation-reduction system of chemical and electrochemical interest. Quinones were reported to possess a wide range of biological activities. The chemistry of quinones is largely dependent on the substituents being either on the quinonoid or on adjacent rings.

Amino quinones are used as medicines, herbicides and they also show interesting redox switching properties. Amino quinones are formed in the reactions of different amines with quinones. For example 1,4-benzoquinone reacts with primary amines to give 2,5-diamino-1,4-benzoquinone; similar reaction of 1,4-naphthoquinone with primary amines results in the formation of 2-amino-1,4-naphthoquinone. However, the product formed from such simple reaction of amine with various quinones has much scope for exploration, especially in terms of synthesis of electro/photoactive supra-molecular assemblies or polymers.

ACD/ChemSketch Freeware was used to draw chemical structures, calculation of molecular properties molecular weight, density, molar volume, polarizability, parachor, Index of Refraction, naming structures and prediction of logP Table (3.1) and (3.2). From a group of 36 compounds and based upon the calculated values especially (log P); the highest (log P) values were selected: it describe hydrophobicity of compounds; when correlated with the substituted groups, twelve compounds were selected to synthesized and investigated.

Table (3.1) ACD/Lab results of some amino-*p*-benzoquinone derivatives



Co.No	R^1	R^2	Log P	Molar volume ±3.0cm3	Density ±0.06g/cm3	Polarizability ±0.5 10-24cm3	Parachor ± 6.0 cm3	Index of Refraction ± 0.02
1.	H	H	2.47+/- 0.75	211.9	1.370	33.92	622.9	1.741
2.	SO_2NH_2	H	0.09+/- 0.75	269.7	1.662	43.20	838.2	1.741
3.		H	3.26+/- 0.75	374.7	1.629	58.77	1161.0	1.721
4.		H	2.17+/- 0.76	459.0	1.578	69.42	1399.6	1.688
5.	COOH	H	2.68+/- 0.75	236.9	1.596	39.42	743.9	1.780
6.	$CO_2CH_2CH_3$	H	4.35+/- 0.75	320.7	1.354	46.93	910.8	1.660
7.	Br	H	4.80+/- 0.75	244.2	1.834	40.02	725.1	1.764
8.	OCH_3	H	2.36+/- 0.75	259.9	1.348	39.22	740.2	1.686
9.	NO_2	H	3.38+/- 0.75	235.5	1.614	39.11	737.1	1.778

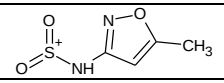
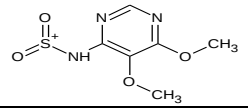
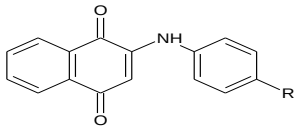
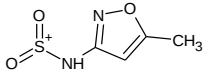
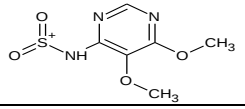
10.	Pyridine-2-$NHSO_2$	H	1.55+/- 0.75	376.5	1.600	61.07	1174.0	1.754
11.	1,3-thiazol-2-$NHSO_2$	H	2.05+/- 0.75	355.5	1.728	59.59	1143.8	1.788
12.	SO_3H	H	0.37+/- 0.75	257.4	1.749	41.54	812.7	1.749
13.	H	Br	3.18+/- 0.75	236.6	1.893	40.09	721.2	1.800
14.	SO_2NH_2	Br	0.80+/- 0.75	294.5	2.058	49.14	936.4	1.783
15.		Br	3.97+/- 0.75	399.4	1.923	64.72	1259.3	1.753
16.		Br	2.88+/- 0.81	483.7	1.824	75.36	1497.8	1.715
17.	COOH	Br	3.40+/- 0.75	261.6	2.048	45.59	842.1	1.831
18.	$CO_2CH_2CH_3$	Br	5.06+/- 0.75	345.4	1.714	53.10	1009.0	1.703
19	Br	Br	5.51+/- 0.75	268.9	2.252	46.19	823.3	1.814
20.	OCH_3	Br						
21.	NO_2	Br	4.09+/- 0.75	260.2	2.067	45.28	835.3	1.829
22.	Pyridine-2-$NHSO_2$	Br	2.26+/- 0.75	401.2	1.894	67.01	1272.3	1.784
23.	1,3-thiazol-2-$NHSO_2$	Br	2.76+/- 0.75	380.2	2.031	65.54	1242.0	1.818
24.	SO_3H	Br	1.09+/- 0.75	282.1	2.155	47.49	911.0	1.792

Table No. (3.2) ACD/Lab results of some 2-amino-*p*-naphthoquinone derivatives



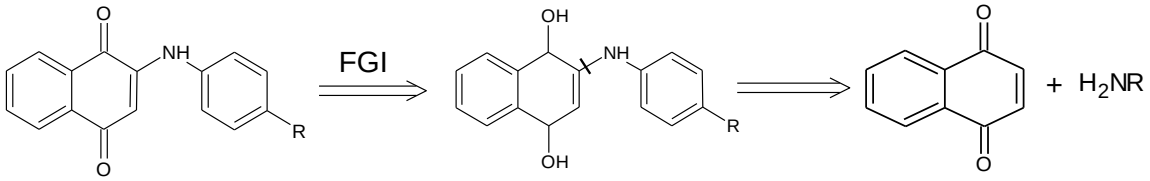
Co.No	R	Log P	Molar volume ±3.0cm3	Density ±0.06g/cm3	Polarizability ±0.5 10-24cm3	Parachor ± 6.0 cm3	Index of Refraction ± 0.02
25.	H	2.89+/- 0.75	185.4	1.343	28.59	528.9	1.705
26.	SO_2NH_2	1.70+/- 0.75	214.4	1.531	33.27	636.5	1.711
27.		3.29+/- 0.75	266.8	1.533	41.06	797.9	1.703
28.		2.74+/- 0.75	309.0	1.509	46.38	917.2	1.681
29.	COOH	3.00+/- 0.75	198.0	1.481	31.34	589.3	1.730
30.	$CO_2CH_2CH_3$	3.83+/- 0.75	239.8	1.339	35.09	672.8	1.659
31.	Br	4.06+/- 0.75	201.6	1.627	31.64	579.9	1.721
32	OCH_3	2.84+/- 0.75	209.4	1.333	31.24	587.5	1.676
33.	NO_2	3.35+/- 0.75	197.3	1.491	31.18	585.9	1.728
34.	Pyridine-2-$NHSO_2$	2.43+/- 0.75	267.8	1.513	42.21	804.4	1.726
35.	1,3-thiazol-2-$NHSO_2$	2.68+/- 0.75	257.3	1.599	41.47	789.3	1.748
36.	SO_3H	1.84+/- 0.75	208.2	1.581	32.44	623.8	1.715

The selection of these compounds is depended upon examination of their log P with standard range for logP and other variables. The identity of the prepared compounds were confirmed by spectral (IR, UV and ^{1}H-NMR), chromatographic (TLC) and classical data (m.p, colour).

3.1. Analysis of 2-amino-*p*-naphthoquinone

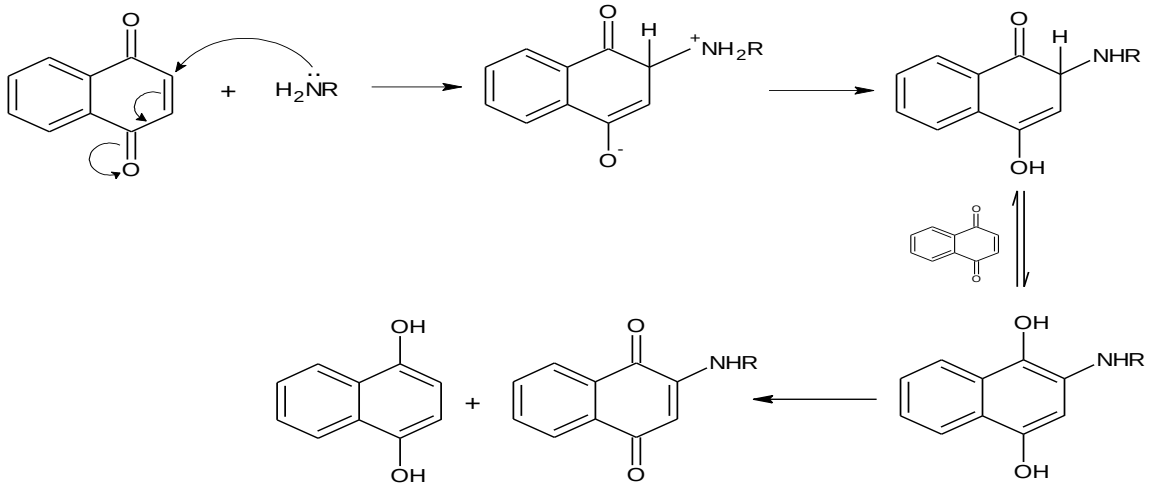
3.1.1. Retro-synthetic disconnection of 2-amino-*p*-naphthoquinone

The synthetic designing of the 2-amino-1,4-naphthoquinone in this work was adopted through the disconnection approach. The retro-synthetic analysis of these compounds can be shown below:



3.1.2. Mechanism formation of 2-amino-*p*-naphthoquinone

Therefore a reaction of 2:1 molar ratio of the required 1,4-naphthoqinone and the amine can produce the mono substituted product. The mechanism of such reaction can be illustrated below:



3.1.3. Spectral data of 2-amino-*p*-naphthoquinone interpretation

3.1.3.1. The IR spectrum of 2-amino-*p*-naphthoquinone

- The *IR* spectrum of these compounds showed a characteristic bands of the carbonyl groups at (1668 & 1635), (1672 & 1620), (1677 & 1635) and (1677 & 1627) cm^{-1} for compounds IIIa, IIIb, IIIc and IIId respectively. It appears in two bands as indication of mono substituted *p*-naphthoquinone in position 2 or 3. The lower band frequency is resulting from neighboring the electron donating group (-NHR) with (+*I* & +*E*) effect.
- The *IR* spectrum showed bands at 3315, 3299, 3299 and (3367 & 3232) cm^{-1} for compounds IIIa, IIIb, IIIc and IIId respectively as indication of N-H stretching vibration of secondary aromatic amines. The N-H bending (scissoring) mode occur at 1525, (1535 & 1469), (1539 & 1438) and (1531 & 1479) cm^{-1} respectively. All N-H vibrations (stretching & bending) are shifted to lower frequencies because of nitrogen lone pair resonance with the benzene and quinone double bonds (conjugation effect).
- The *IR* spectrum showed bands at 1600-1440 cm^{-1} for C=C stretching vibration of prepared compounds. It occurs lower than usual because of extended conjugation.
- The *IR* spectrum showed bands at 1334, 1296 and 1305 cm^{-1} for compounds IIIb, IIIc and IIId respectively resulting from sulfonamide group S=O asymmetry stretching vibration and 1166, 1163 and 1149 cm^{-1} for symmetry stretching vibration for prepared compounds respectively.

3.1.3.2. The ^{1}H-NMR spectrum of 2-amino-*p*-naphthoquinone

- The *NMR* spectrum of these compounds showed a characteristic peaks of the quinonoid hydrogen approximately downfield at 6.10, 6.14, 6.37 and 6.28 ppm (s, 1) for compounds IIIa, IIIb, IIIc and IIId.
- Hydrogens attached to an aromatic (benzenoid) ring of naphthoquinone (**H-B**) chemical shift appear downfield usually between (7.78 - 8.06) ppm with a different splitting batten.
- Hydrogens attached to an aromatic (benzenoid) ring of aromatic amines (**H-A**) chemical shift appear downfield usually between (7.47 - 7.22) ppm with a different splitting batten.

- The aniline hydrogen, hydrogen **a**, located downfield at 9.25 ppm (s, 1), 9.46 ppm (s, 1), 9.45 ppm (s, 1) and 9.34 ppm (s, 1) for compounds IIIa,II Ib, IIIc and IIId respectively. This high deshielding chemical shift because of changing the hybridization of nitrogen atom and hydrogen bonding between hydrogen and neighboring carbonyl oxygen.
- The sulphnil-amine hydrogen if present, hydrogen **b**, appear downfield at 11.42 ppm (s, 1), 11.19 ppm (s, 1) and 3.34 ppm (s, 2) for compounds Ib, Ic and Id respectively. The higher chemical shift of (**b**) hydrogen because of anisotropy and electronegativity of sulphnil group, but compound Id appear at up-filed as a result of absence of aromatic side-chain.
- Other hydrogen atoms appear downfield at the *NMR* spectrums are **H-c** at 6.38 ppm (s, 1) and 8.13 ppm (s, 1) for compounds IIIb and IIIc respectively. **H-d** resonate upfield at 2.30 ppm (s, 3) and [3.90ppm (s, 3) & 3.70 ppm (s, 3)] for compounds Ib and Ic respectively.

3.1.3.3. Mass spectrum of 2-amino-*p*-naphthoquinone compounds

- The $M^{+\cdot}$ peaks appeared in the mass spectra of compounds IIIa-IIId with reasonable intensity.
- Compounds IIIa-IIId showed a peak at m/e 146 which can be attributed to $[M\text{-}CNR]^+$ and at m/e 105 for $[M\text{-}CNR\text{-}C_2HO]^+$ which further lost CO to give m/e 77.
- The fragmentation pattern observed was in accordance with the literature proposed (Bowie *et al*, 1965).

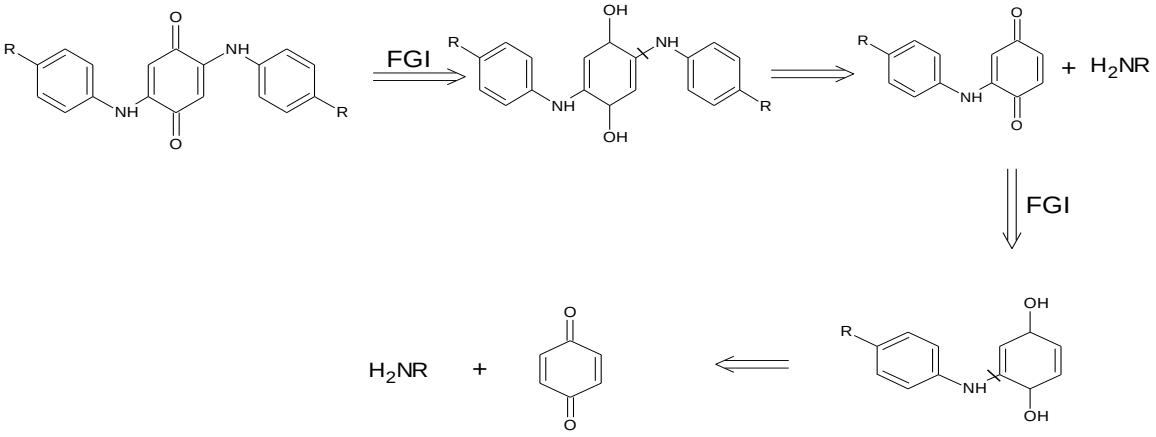
3.1.3.4. UV spectrum of 2-amino-*p*-naphthoquinone

- The UV spectrums showed a benzenoid ET band at 272, 281.5, 276.5 and 281.5 nm of medium intensity for compounds IIIa, IIIb, IIIc and IIId respectively.
- The UV spectrums showed a quinoid ET band at 468, 458, 451 and 460 nm of low to medium intensity for compounds IIIa, IIIb, IIIc and IIId respectively.

3.2. Analysis of 2,5-diamino-1,4-benzoquinone and 3,6-dibromo-2,5-diamino-1,4-benzoquinone

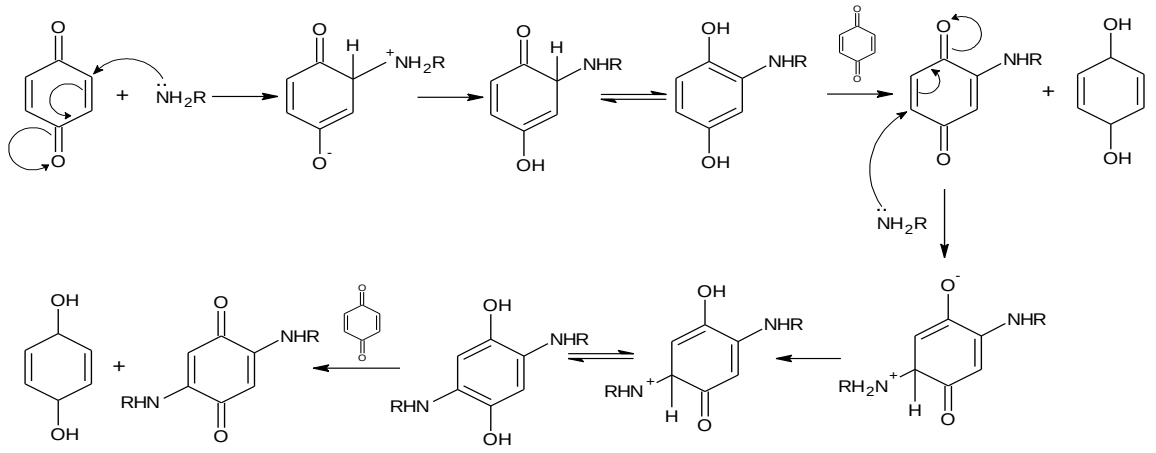
3.2.1. Retro-synthetic disconnection of 2,5-diamino-1,4-benzoquinone and 3,6-dibromo-2,5-diamino-1,4-benzoquinone

The same approach was adopted for the 2,5-diamino-1,4-benzoquinone



3.2.2. Mechanism formation of 2,5-diamino-1,4-benzoquinone and 3,6-dibromo-2,5-diamino-1,4-benzoquinone

In the case of the 2,5-diamino-1,4-benzoquinone, the same mechanism worked, a reaction of 3:2 molar ratio of the required 1,4-benzoquinone and the amine respectively, whereby after the formation of the mono amino benzoquinone a second amino group was added:



3.2.3.a. Spectral data of 2,5-diamino-1,4-benzoquinone interpretation

3.2.3.a.1. The IR spectrum of 2,5-diamino-1,4-benzoquinone

- The *IR* spectrum of these compounds showed a characteristic beaks of the carbonyl groups at 1639, 1643, 1639 and 1637 cm^{-1} for compounds Ia, Ib, Ic and Id respectively. It appears as one band as indication of high symmetry by disubstituted *p*-benzoquinone in position (2 & 5) or (3 & 6) with the same substituted group. The carbonyl group frequencies occur at lower than usual because of large quinoid systems and disubstituted electron donating group (-NHR) with (+*I* & +*E*) effect.
- The *IR* spectrum showed bands at 3236, (3292 & 3271), (3402 & 3274) and (3359 & 3234) cm^{-1} for compounds Ia, Ib, Ic and Id respectively as indication of N-H stretching vibration of secondary aromatic amines. The N-H bending (scissoring) mode occur at 1504, (1606 & 1535), (1573 & 1504) and (1562, 1504) cm^{-1} respectively. All N-H vibrations (stretching & bending) are shifted to lower frequencies because of nitrogen lone pair resonance with the benzene and quinone double bonds (conjugation effect) and the higher frequencies resulting from N-H adjacent to sulfonamide group.
- The *IR* spectrum showed bands at 1600-1440 cm^{-1} for C=C stretching vibration of prepared compounds. And it occurs lower than usual because of extended conjugation.
- The *IR* spectrum showed bands at 1388, 1342 and 1334 cm^{-1} for compounds Ib, Ic and Id respectively resulting from sulfonamide group S=O asymmetry stretching vibration. 1163, 1161 and 1159 cm^{-1} for symmetry stretching vibration for prepared compounds respectively.
- The *IR* spectrum showed beaks at 894, 929, 904 and 891 cm^{-1} for compounds Ia, Ib, Ic and Id respectively resulting from disubstitution in the *p*-quinone ring at 2 and 5 position.

3.2.3.a.2. The ^{1}H-NMR spectrum of 2,5-diamino-1,4-benzoquinone

- The *NMR* spectrum of these compounds showed a characteristic peaks of the quinonoid hydrogen downfield at [5.79, 5.95] ppm (s, 1), 6.15 ppm (s, 1), 6.08 ppm (s, 1) and 6.03 ppm (s, 1) for compounds Ia, Ib, Ic and Id respectively.
- Hydrogens attached to an aromatic (benzenoid) ring of aromatic amines (**H-A**) appear usually downfield between (7.3 - 8.0) ppm with a different splitting batten.
- The aniline hydrogen, hydrogen **a**, located downfield at 9.27 ppm (s, 2), 9.54 ppm (s, 2), 9.52 ppm (s, 2) and 9.52 ppm (s, 2) for compounds Ia, Ib, Ic and Id respectively. This high deshielding chemical shift because of changing the hybridization of nitrogen atom and hydrogen bonding between hydrogen and neighboring carbonyl oxygen.
- The sulphnil-amine hydrogen if present, hydrogen **b**, appear downfield at 11.45 ppm (s, 2), 11.17 ppm (s, 2) and [7.37 ppm (s, 2) & 6.03 ppm (s, 2)] for compounds Ib, Ic and Id respectively. The higher chemical shift of (**b**) hydrogen because of anisotropy and electronegativity of sulphnil group, but compound Id appear at up-filed and in two peaks as a result of absence of aromatic side and unequivalence of the two hydrogen.
- Other hydrogen atoms appear at the *NMR* spectrums are **H-c** downfield at 6.09 (s, 2) and 8.13 ppm (s, 2) for compounds Ib and Ic respectively. **H-d** resonate upfield at 2.30 ppm (s, 6) and [3.91ppm (s, 6) & 3.71 ppm (s, 6)] for compounds Ib and Ic respectively.

3.1.3.a.3. Mass spectrum of 2,5-diamino-1,4-benzoquinone

- The $M^{+\cdot}$ peaks appear in the mass spectra of compounds Ia-Id with reasonable intensity.
- Compounds Ia showed a peak at m/e 261 which can be attributed to $[M\text{-}CO]^{+}$ and at m/e 106 for $[M\text{-}2CO]^{+}$ which further lost $[M\text{-}2CO\text{-}H_2C_2NAr]^{+}$ to give m/e 117. Compounds Ib-Id follows the same fragmentation pattern.
- The fragmentation pattern observed was in accordance with the literature proposed.

3.1.3.a.4. UV spectrum of 2,5-diamino-1,4-benzoquinone

- The UV spectrums showed λ_{max} at 268, 286.5, 266 and 277.5 nm for compounds Ia, Ib, Ic and Id respectively due to $\pi \rightarrow \pi^*$ transition. This absorptions are shifted bathochromically to higher values in compare to corresponding amines Table (2.4.5) which appear in lower values as a result of participation of nitrogen lone pair of electrons in the resonance with C=C.
- The UV spectrums showed λ_{max} at 380, 387.5, 387 and 373 nm for compounds Ia, Ib, Ic and Id respectively due to $n \rightarrow \pi^*$ transition. This absorption absorptions are shifted bathochromically to higher values in compare to corresponding amines Table (2.4.5) which appear in lower values due to the same reason.

3.2.3.b. Spectral data of 3,6-dibromo-2,5-diamino-1,4-benzoquinone

interpretation

3.2.3.b.1. The IR spectrum of 3,6-dibromo-2,5-diamino-1,4-benzoquinone

- The spectrum of these compounds has the same characteristics peaks as 2,5-diamino-1,4-benzoquinone but they are occur at lower frequencies because of the (*-I* & *+E*) effect of the disubstituted halogen (Br) in the quinonoid system at 3 and 6 position.

3.2.3.b.2. The ^{1}H-NMR spectrum of 3,6-dibromo-2,5-diamino-1,4-benzoquinone

- Hydrogens attached to an aromatic (benzenoid) ring of aromatic amines (**H-A**) appear downfield usually between (7.0 – 8.0) ppm with a different splitting batten.
- The aniline hydrogen, hydrogen **a**, located downfield approximately at 9.77 ppm (s, 2) for compounds IIa, IIb, IIc and IId. This high deshielding chemical shift because of changing the hybridization of nitrogen atom and hydrogen bonding between hydrogen and neighboring carbonyl oxygen.

- The sulphnil-amine hydrogen if present, hydrogen **b**, appear downfield at 11.35 ppm (s, 2), 11.07 ppm (s, 2) and 4.70 ppm (bs, 4) for compounds IIb, IIc and IId respectively. The higher chemical shift of (**b**) hydrogen because of anisotropy and electronegativity of sulphnil group, but compound Id appear at up-filed and broad singlet a result of absence of aromatic side and quadrupole broadening ; chemical exchange of N-H proton with solvent proton;.
- Other hydrogen atoms appear at the *NMR* spectrums are **H-c** downfield at 6.14 ppm (s, 2) and 8.12 ppm (s, 2) for compounds Ib and Ic respectively. **H-d** upfield resonate at 2.29 ppm (s, 6) and [3.91ppm (s, 6) & 3.70 ppm (s, 6)] for compounds Ib and Ic respectively.

3.2.3.b.3 Mass spectrum of 3,6-dibromo-2,5-diamino-1,4-benzoquinone

- The $M^{+\cdot}$, M+2 and M+4 peaks appear in the mass spectrums of compounds IIa-IId with reasonable intensity.
- Compounds IIa showed a peak at m/e 420 which can be attributed to $[M\text{-}CO]^+$ and at m/e 392 for $[M\text{-}2CO]^+$ which further lost $[M\text{-}2CO\text{-}Br\text{-}HC_2NAr]^+$ to give m/e 197. Compounds Ib-Id follows the same fragmentation pattern.
- The fragmentation pattern observed was in accordance with the literature proposed (Szulejko and Bursey, 1985).

3.2.3.b.4. UV spectrum of 3,6-dibromo-2,5-diamino-1,4-benzoquinone

- The UV spectrums showed λ_{max} at 247.5, 285, 263 and 259 nm for compounds IIa, IIb, IIc and IId respectively due to $\pi \rightarrow \pi^*$ transition. And $n \rightarrow \pi^*$ transition at λ_{max} 391.5, 352, 339.5 and 358 respectively. All This absorptions are bathochromically shifted but it is not too high values compared to 2,5-diamino-*p*-quinone due to hypsochromic effect of the disubstituted bromide atoms.

3.3. Analysis TLC data of prepared *p*-amino quinones

TLC was used to confirm and verified that the coupling between amines and *p*-quinones was completed and accomplished correctly. As

expected, Rf values of amine was the lowest one and Rf values of *p*-quinones was the highest, where Rf values of the reaction product was in the middle. This result was explained by the polarity factor of amine most polar, *p*-quinone least polar and reaction product medium polar tables (2.7.1), (2.7.2) and (2.7.3).

Conclusion and recommendation

In the present study 12 compounds of amino-*p*-quinone were confirmed and verified to synthesized by refluxing *p*-quinone with different aromatic amines in acetic acid, ethanol and water medium.

The structure and identity of the prepared compounds were elucidated, examined and confirmed by spectral data IR, UV-VIS, ^{1}H-NMR and GC-MS.

Coupling of the *p*-quinones with the required aryl amines furnished the required compounds.

Recommendation:

1- Biological and pharmacological activities, antibacterial and antifungal, of the synthesized amino-*p*-quinones should be tested and evaluated.
2- The effect of the reaction medium and pH must be investigated.
3- Study of the effect of reactant molar ratio in the percentage of yield product.
4- Chromatographic techniques, HPLC-M S, can be used in structural elucidation of prepared compounds.
5- C^{13}-NMR is recommended in order to complete the spectral analysis of the prepared compounds.

Chapter Four

4. References

- Ambrogi, V.; Artini, D.; Carneri, I.; Castellino, S.; Dradi, E.; Logemann, W.; Meinardi, G.; Di Somma, M. and Tosolini, G. (1970). Studies on the antibacterial and antifungal properties of 1,4-naphthoquinones; Br. J. pharmacy., 40: 870-880.

- Andrew, R. L. (1996). Molecular modeling principles and applications; Person Education Limited., Second Edition: 1-5.

- Ball, E. G.; Anfinsen, C. B. and Cooper, O. (1947). The inhibitory action of naphthoquinones on respiratory processes; J. Biol. Chem., 168(1): 257-70.

- Barbara, H. S. (2004). Infrared Spectroscopy: Fundamentals and Applications; John Wiley and Sons, Incorparated, John, 1st Edition: 3-242.

- Berger, S. and Rieker, A. (1974). In the Chemistry of the Quinonoid Compounds; Second Edition. S. Patai, John Wiley and Sons, London. New York: 163-229.

- Beynon, J. H. and Williams, A. E. (1960). Electron impact and molecular dissociation.; Appl. Spec., 14: 156-161.

- Bowie, J. H.; Hoffmann, P. Y. and White, P. Y. (1970). Electron impact studies- XLII: Peri-effects in the mass spectra of alkoxyquinones; Tetrahedron, 26(4): 1163-1168.

- Bowie, J. H.; Cameron, D. W. and Williams, D. H. (1965). Mass spectra of substituted naphthoquinones; J. Ame. Chem. Soc., 87: 5094-5099.

- Bowie, J. H. and White, P. Y. (1969). Proximity effects in the mass spectra of aromatic carbonyl compounds containing adjacent methoxy-substituents; J. Chem. Soc., (B): 89-93.

- David, A. E. and Wong, Y. R. (1977). Synthesis of antibacterial *p*-quinonles from Marine Sponges. Synthetic application of masked quinines; J. Org. Chem., 42 (2): 350-351.

- Fernandez, M. and Caballero, J. (2007). QSAR models for predicting the activity of non-peptide luteinizing hormone-releasing hormone (LHRH) antagonists derived from erythromycin A using quantum chemical properties; J. Mol. Mod.; 13(4): 465–476.

- Fieser, L. F. and Turner, R. B. (1947). The addition of sulfhydryl derivatives to 2-methyl-1,4-naphthoquinone; J. Am. Chem. Soc., 69: 2335-2338.

- Finar, I. L. (1963). Organic chemistry: The fundamental principles; Longmans, 4th edition (volume 1), pp: 163 and (668-738).

- Francis, A. C. and Richard, J. S. (2007). Advanced Organic Chemistry Part A: structure and mechanisms; Acid-free Paper. Springer Science + Business Media., 5th Edition, pp: 1003–1056.

- Furniss, B. S.; Hannaford A. J.; Smith, P. W. G. and Tatchll, A. R. (2004). Practical organic chemistry; Longmans., 5th edition, chapter 3 and 6, pp, 390, 890:1068 and (745-727).

- Gant, T. W.; Doherty, M.; Odowole, D.; Sales, K. D. and Cohen, G. M. (1986). Semiquinone anion radicals formed by the reaction with glutathione or amino acids; FEBS Letters., 201(2): 296-299.

- Gershon, H. and Shnks, L. (1975). Fungitoxicity of 1,4-naphthoquinones to candida albicans and trichophyton mentagrophytes; Can. J. Microbial., 21: 1317-1321.

- Harmon, R. E.; Phipps, L. M.; Howell, J. A. and Gupa, S. K. (1969). A spectral study of tautomerism in 4-arylamino-1,2-naphthoquinones; Tetrahedron., 25(24), 5807-5813.

- Heiss, J.; Zeller, K.P. and Rieker, A. (1969). Mass spectrometry of derivatives and heterocyclic compounds.; J. Mass Spec., 2(12): 1325-1334.

- Hudson, A. T.; Randall, A. W.; Fry, M.; Ginger, C. D.; Hill, B.; Latter, V. S.; Mc Hardy, N. and Williams, R. B. (1985). Novel antimalarial hydroxynaphthoquinones with potent broad spectrum antiprotozol activity; J. Parasitology., 90: 45-55.

- Johnson, C. R.; Kirchoff, R. A.; Reischer, R. J. and Katekar, G. F. (1973). Cyclization reactions of quinones; J. Am. Chem. Soc., 95: 4287-4291.

- Mark, T. D. C. (2009). Quantitative structure–activity relationships (QSARs)–applications and methodology; Chall. Adv. Comp. Ch. Phy., 8: 3-11.

- Matthias, D.; Kurt, V. and Danail, B. (2012). Statistical Modeling of Molecular Descriptors in QSAR/QSPR, Wiley-Blackwell, 2: 1-26.

- Mirrison, M.; Steele, W. and Danner, D. J. (1969). The reaction of benzoquinone with amines and proteins; Arch. Bioch. Bioph., 134: 515-523.

- Morrison, R. T and Boyd, R. N. (1973). Organic chemistry; Longmans. Fourth edition: 878-880.

- Nakai, N. and Hase, J. (1968). The reaction of 2-methyl-1,4-naphthoquinone with sulfhydryl compounds; J. Chem. Pharm. Bull, 16 (12), 2334-2338.

- Navakovic, I.; Zoran, V.; Tatjana, B.; Natasa, B.; Nenad, M. and Dusan, S. (2003). Chemical modification of β-lactoglobulin by quinones; J. Serb. Chem. Soc., 68(4-5): 243-248.

- Nickerson, W. J.; Falcone, G. and Strauss, G. (1963). Studies on quinone-thioethers: Mechanism of formation and properties of thiodione; J. Biochem., 2(3): 537-543.

- OECD; (2007). Guidance Document on the Validation of (Quantitative) Structure–Activity Relationships Models, Organisation for Economic Co-operation and Development.

- Ogata. R. T.; Singh, I.; Moore, R. E.; Change, C. W. J. and Scheuer, P. J. (1968). Electronic spectra of substituted naphthoquinones, Tetrahdron., 24: 6053-6073.

- Osman, S. A. A.; Abdalla, A. A. and Alaib, M. O. (1983). Synthesis of sulfanilamide-naphthoquinones as potential antituberculous agent; J. Pharm. Sci., 72 (1): 68-71.

- Pal, P.; Saha, A.; Mukherjee, A. K. and Mukherjee, D, C. (2004). Study of charge transfer complexes of menadione (vitamin K_3) with a series of anilines; J. Spectrochimica acta. part A., 60: 167-171.

- Paulino, M.; Iribarne, F.; Dubin, M.; Aguilera, S. M.; Tapia, O. and Stoppari, A. M. O. (2005). The chemotherapy of chagas disease; mini reviews in Medical Chem., 5 (5): 499-519.

- Porter, T. H.; Tasi, C. S.; Kishi, H. and Folkers, K. (1978). Synthesis of new 2-alkylmercapto-1,4-naphthoquinones as antimetabolites of co-enzyme Q and as antitumor agent, Acta Pharm. Soc, 15: 97-104.

- Roushdi, I. M.; Mikhail, A. A. and Chaaban, I. (1977). Synthesis of substituted benzoquinones and naphthoquinones with potential antituberculous activity; Pharmazia., 32: 269-270.

- Roushdi, I. M.; Mikhail, A. A. and Chaaban, I. (1976). Synthesis of some quinones of potential therapeutic interest; Acta Pharm. Jugoslav., 26: 287-284.

- Silverstein, R. and Bassler, G. C. (1964). Spectrometric identification of organic compounds; 2nd edn, John Wiley and Sons. New York: 90-103.

- Song, K. and Jeon, S. (2003). Modulation of hydrogen bonding through redox chemistry of quinones and urea-functionalized porphyrin; J. Bull. Korean .Chem. Soc., 24 (2): 153-154.

- Spyroudis. (2000). Hydroxyquinones: Synthesis and reactivity, Molecules., 5: 1291-1330.

- Szulejko, J. E. and Bursey, M. M. (1985). Organic mass spectrometry; Org. Mass Spectrom., 20: 374-376.

- Takahashi, K. (1993). Conjugation-extended ring assemblies with central heterocycles. New multistage redox system; J. Pure and Appl. Chem., 65(1): 127-134.

- Take, Y.; Sawada, M.; Kunai, H.; Inouye, Y. and Nakamura, S. (1985). Role of the naphthoquinone moiety in the biological activities of sakyomicin A, J, Antibiotics., 39(4): 557-563.

- Tedder, J. M. and Nechvatal, A. (1975). Quinones and related compounds in: Basic organic chemistry, (part 2), John Wiley and Sons, London chapter19, pp: 237-254.

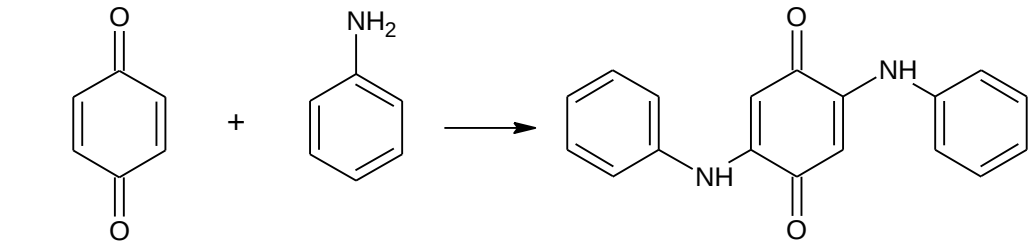
- Thomson, R. H. (1971). Naturally Occurring Quinones; second edition,Academic Press London and New York, chapter 2, pp: 39-92.

- Tremblay, M. S. and Sames, D. (2005). A new fluorogenic transformation : development of of an optical probe for co-enzyme Q, Organic letters., 7 (12): 2417-2420.

- Worth, A. P.; Bassan, A.; De Bruijn, J.; Gallegos Saliner, A.; Netzeva, T.; Patlewicz, G.; Pavan, M.; Tsakovska, I.; and Eisenreich, S. (2007). SAR and QSAR in Environmental Research., 18: 111–125.

- Zeller, K. P. and Roland, M. (1988). Mass spectra of quinones; (Ed. S. Patai), John Wiley and Sons, London. New York, pp: 87-109.

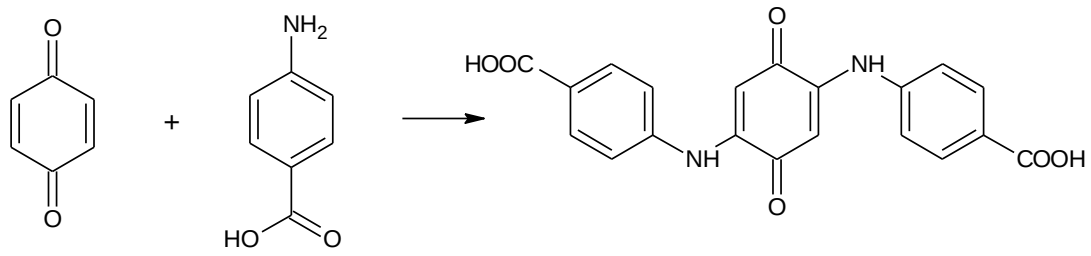
4.1. Examples of ACD/Lab calculated values of some amino-*p*-quinones derivatives:



1,4-benzoquinone aniline

Log P: 2.47+/- 0.75

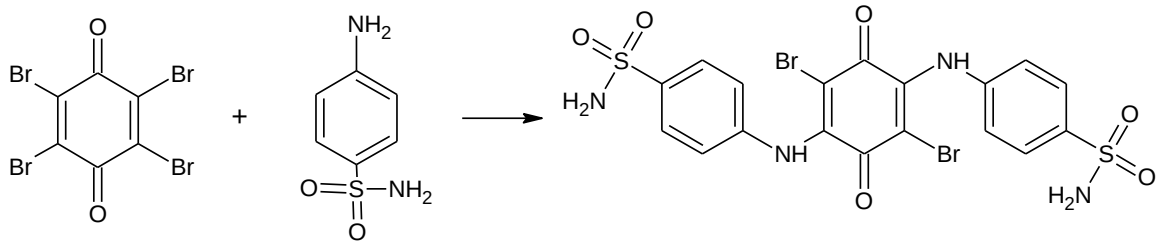
Molecular Formula: $C_{18}H_{14}N_2O_2$
Formula Weight: 290.31596
Composition: C(74.47%) H(4.86%) N(9.65%) O(11.02%)
Molar Refractivity: 85.58 ± 0.3 cm^3
Molar Volume: 211.9 ± 3.0 cm^3
Parachor: 622.9 ± 6.0 cm^3
Index of Refraction: 1.741 ± 0.02
Surface Tension: 74.7 ± 3.0 dyne/cm
Density: 1.370 ± 0.06 g/cm^3
Dielectric Constant: Not available
Polarizability: 33.92 ± 0.5 $10^{-24}cm^3$
RDBE: 13
Monoisotopic Mass: 290.105528 Da
Nominal Mass: 290 Da
Average Mass: 290.316 Da
M+: 290.104979 Da
M-: 290.106076 Da
[M+H]+: 291.112804 Da
[M+H]-: 291.113901 Da
[M-H]+: 289.097154 Da
[M-H]-: 289.098251 Da



1,4-benzoquinone 4-aminobenzoic acid

Log P: 2.68+/- 0.75

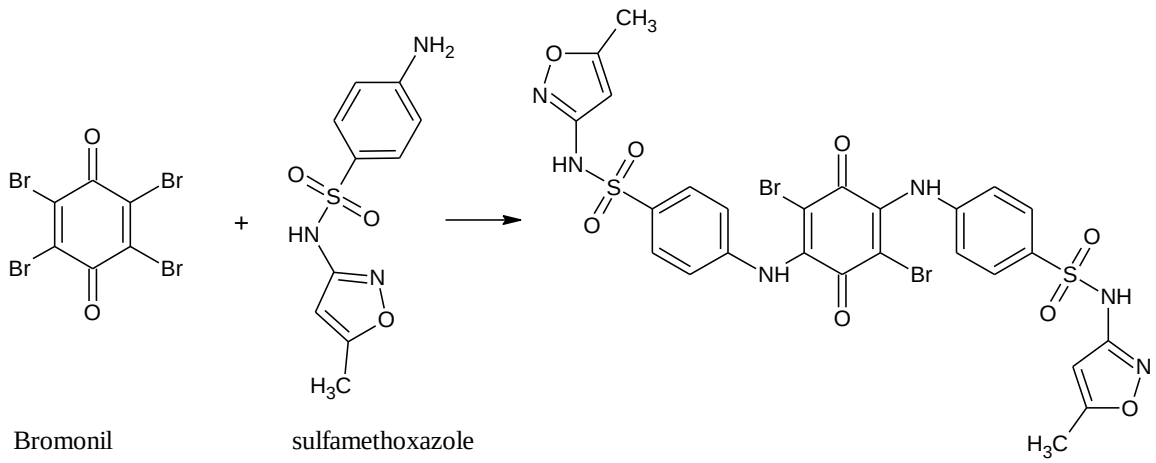
Molecular Formula: $C_{20}H_{14}N_2O_6$
Formula Weight: 378.33496
Composition: C(63.49%) H(3.73%) N(7.40%) O(25.37%)
Molar Refractivity: 99.44 ± 0.3 cm^3
Molar Volume: 236.9 ± 3.0 cm^3
Parachor: 743.9 ± 6.0 cm^3
Index of Refraction: 1.780 ± 0.02
Surface Tension: 97.1 ± 3.0 dyne/cm
Density: 1.596 ± 0.06 g/cm^3
Dielectric Constant: Not available
Polarizability: 39.42 ± 0.5 $10^{-24}cm^3$
RDBE: 15
Monoisotopic Mass: 378.085186 Da
Nominal Mass: 378 Da
Average Mass: 378.335 Da
M+: 378.084638 Da
M-: 378.085735 Da
[M+H]+: 379.092463 Da
[M+H]-: 379.09356 Da
[M-H]+: 377.076813 Da
[M-H]-: 377.07791 Da



Bromonil sulphanilamide

Log P: 0.80+/- 0.75

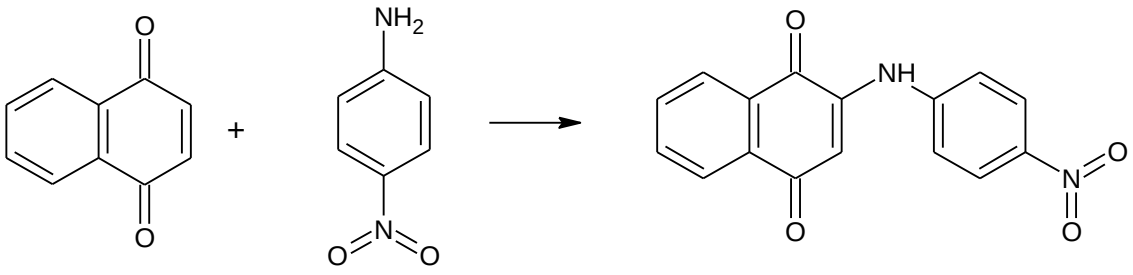
Molecular Formula: $C_{18}H_{14}Br_2N_4O_6S_2$
Formula Weight: 606.26496
Composition: C(35.66%) H(2.33%) Br(26.36%) N(9.24%) O(15.83%) S(10.58%)
Molar Refractivity: 123.97 ± 0.4 cm^3
Molar Volume: 294.5 ± 3.0 cm^3
Parachor: 936.4 ± 6.0 cm^3
Index of Refraction: 1.783 ± 0.02
Surface Tension: 102.2 ± 3.0 dyne/cm
Density: 2.058 ± 0.06 g/cm^3
Dielectric Constant: Not available
Polarizability: 49.14 ± 0.5 $10^{-24}cm^3$
RDBE: 17
Monoisotopic Mass: 603.872134 Da
Nominal Mass: 604 Da
Average Mass: 606.265 Da
M+: 603.871586 Da
M-: 603.872683 Da
[M+H]+: 604.879411 Da
[M+H]-: 604.880508 Da
[M-H]+: 602.863761 Da
[M-H]-: 602.864858 Da



Bromonil sulfamethoxazole

Log P: 3.97+/- 0.75

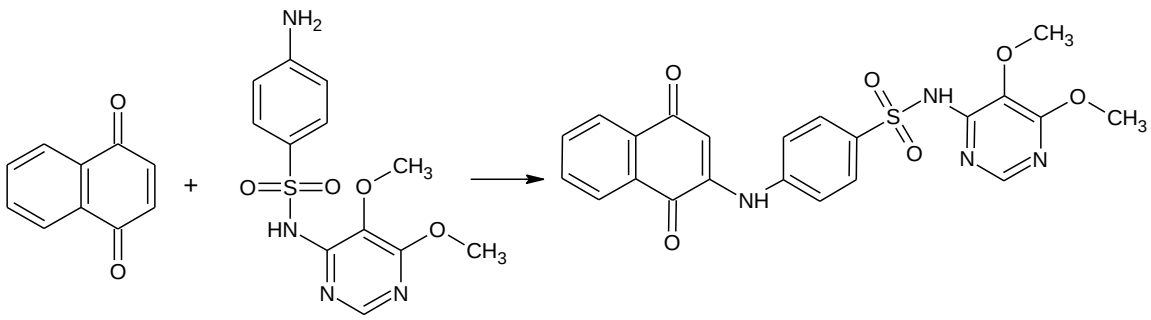
Molecular Formula: $C_{26}H_{20}Br_2N_6O_8S_2$
Formula Weight: 768.4104
Composition: C(40.64%) H(2.62%) Br(20.80%) N(10.94%) O(16.66%) S(8.35%)
Molar Refractivity: 163.26 ± 0.4 cm^3
Molar Volume: 399.4 ± 3.0 cm^3
Parachor: 1259.3 ± 6.0 cm^3
Index of Refraction: 1.753 ± 0.02
Surface Tension: 98.8 ± 3.0 dyne/cm
Density: 1.923 ± 0.06 g/cm^3
Dielectric Constant: Not available
Polarizability: 64.72 ± 0.5 $10^{-24}cm^3$
RDBE: 23
Monoisotopic Mass: 765.915062 Da
Nominal Mass: 766 Da
Average Mass: 768.4104 Da
M+: 765.914513 Da
M-: 765.91561 Da
[M+H]+: 766.922338 Da
[M+H]-: 766.923435 Da
[M-H]+: 764.906688 Da
[M-H]-: 764.907785 Da



p-naphthoquinone sulphadoxine

log P: 3.35+/- 0.75

Molecular Formula: $C_{16}H_{10}N_2O_4$
Formula Weight: 294.2616
Composition: C(65.31%) H(3.43%) N(9.52%) O(21.75%)
Molar Refractivity: 78.67 ± 0.3 cm^3
Molar Volume: 197.3 ± 3.0 cm^3
Parachor: 585.9 ± 6.0 cm^3
Index of Refraction: 1.728 ± 0.02
Surface Tension: 77.7 ± 3.0 dyne/cm
Density: 1.491 ± 0.06 g/cm^3
Dielectric Constant: Not available
Polarizability: 31.18 ± 0.5 $10^{-24}cm^3$
RDBE: 14
Monoisotopic Mass: 294.064057 Da
Nominal Mass: 294 Da
Average Mass: 294.2616 Da
M+: 294.063508 Da
M-: 294.064605 Da
[M+H]+: 295.071333 Da
[M+H]-: 295.07243 Da
[M-H]+: 293.055683 Da
[M-H]-: 293.05678 Da

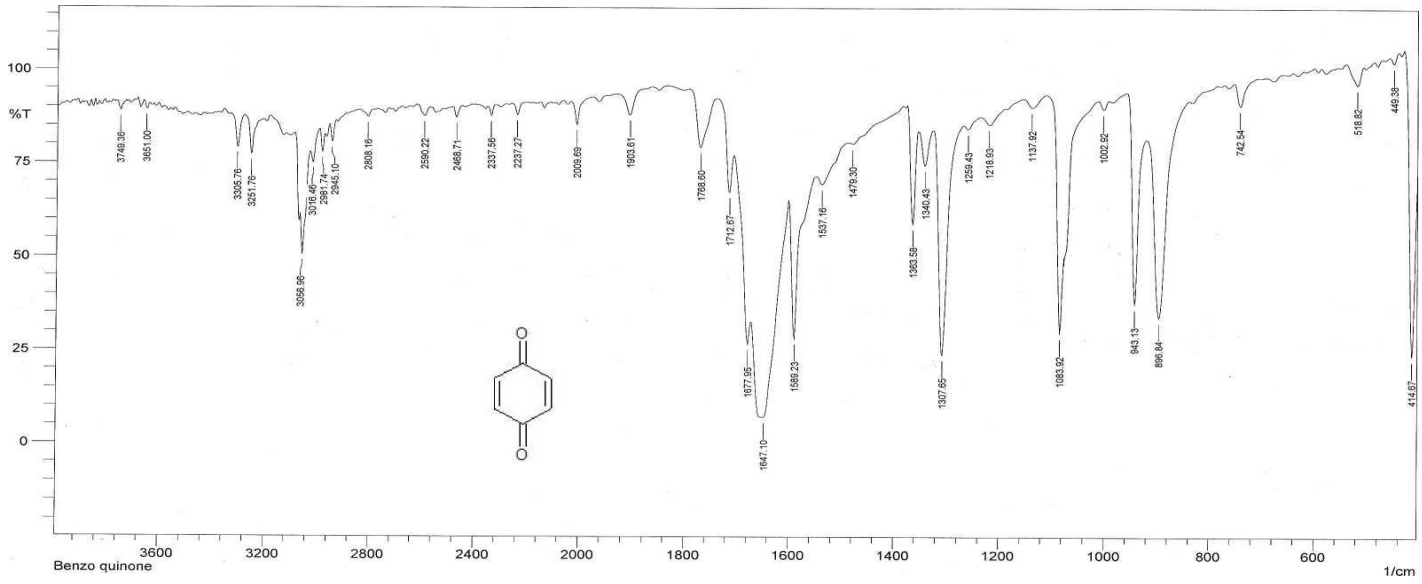


p-naphthoquinone sulphadoxine

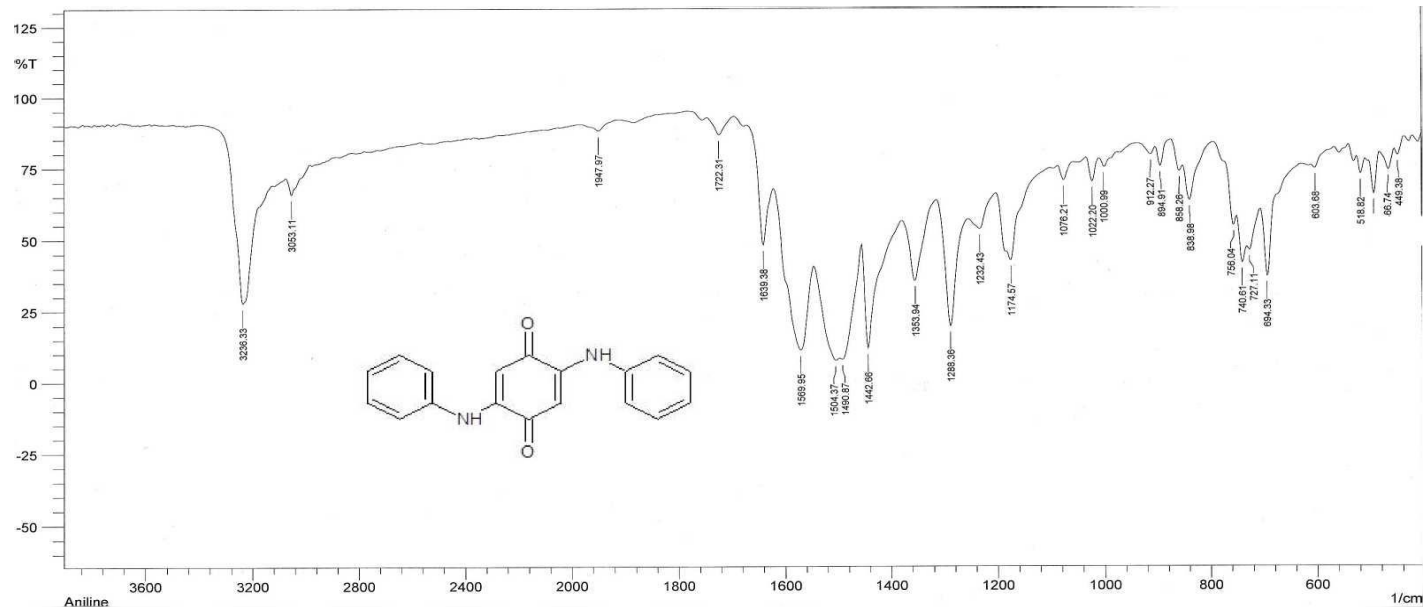
log P: 2.74+/- 0.75

Molecular Formula: $C_{22}H_{18}N_4O_6S$
Formula Weight: 466.46652
Composition: C(56.65%) H(3.89%) N(12.01%) O(20.58%) S(6.87%)
Molar Refractivity: 117.00 ± 0.4 cm^3
Molar Volume: 309.0 ± 3.0 cm^3
Parachor: 917.2 ± 6.0 cm^3
Index of Refraction: 1.681 ± 0.02
Surface Tension: 77.5 ± 3.0 dyne/cm
Density: 1.509 ± 0.06 g/cm^3
Dielectric Constant: Not available
Polarizability: 46.38 ± 0.5 $10^{-24}cm^3$
RDBE: 18
Monoisotopic Mass: 466.094704 Da
Nominal Mass: 466 Da
Average Mass: 466.4665 Da
M+: 466.094156 Da
M-: 466.095253 Da
[M+H]+: 467.101981 Da
[M+H]-: 467.103078 Da
[M-H]+: 465.086331 Da
[M-H]-: 465.087428 Da

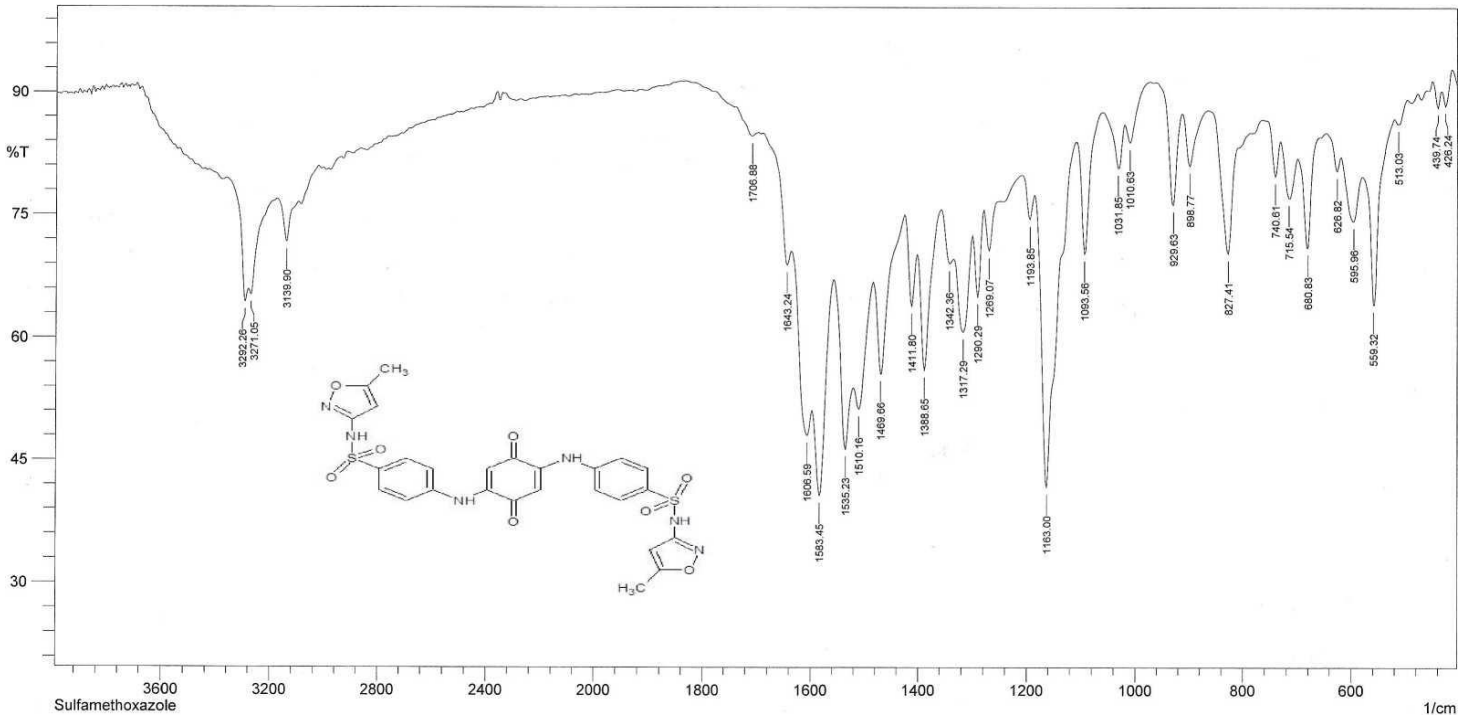
4.2. IR spectral data:



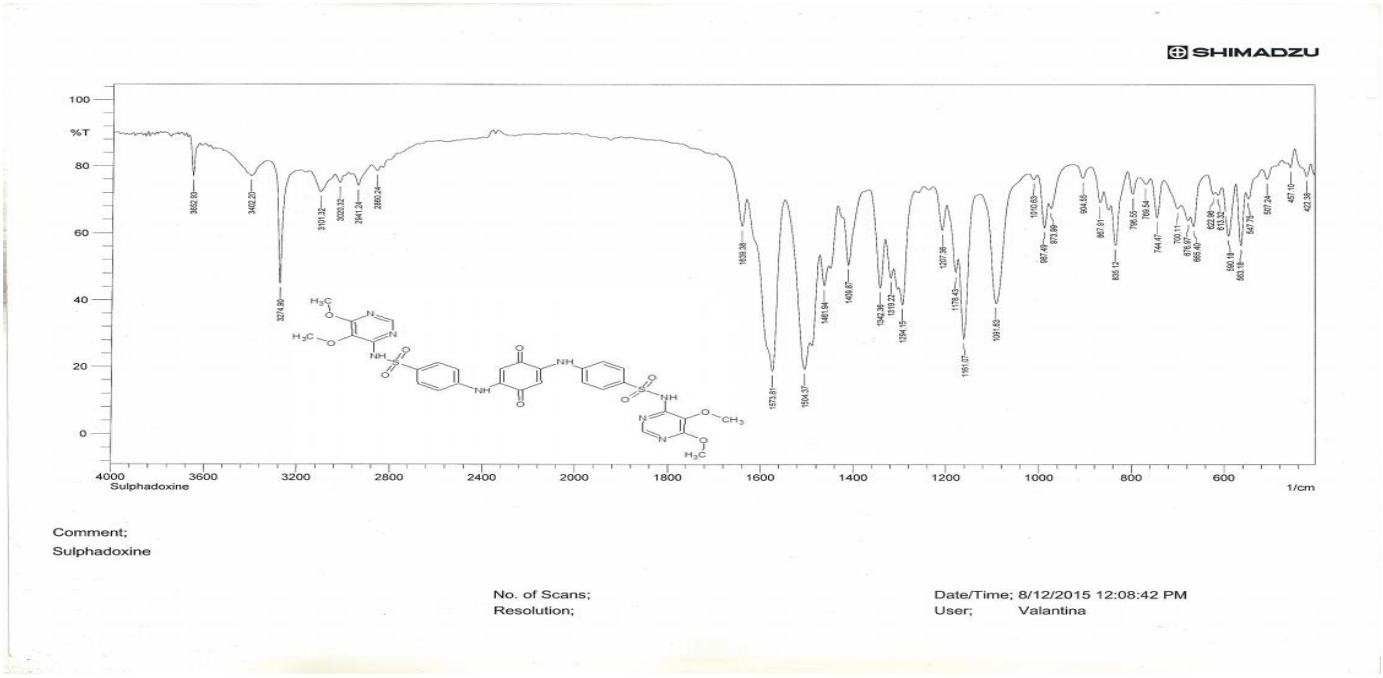
Appendix (1) IR spectrum of compound (I)



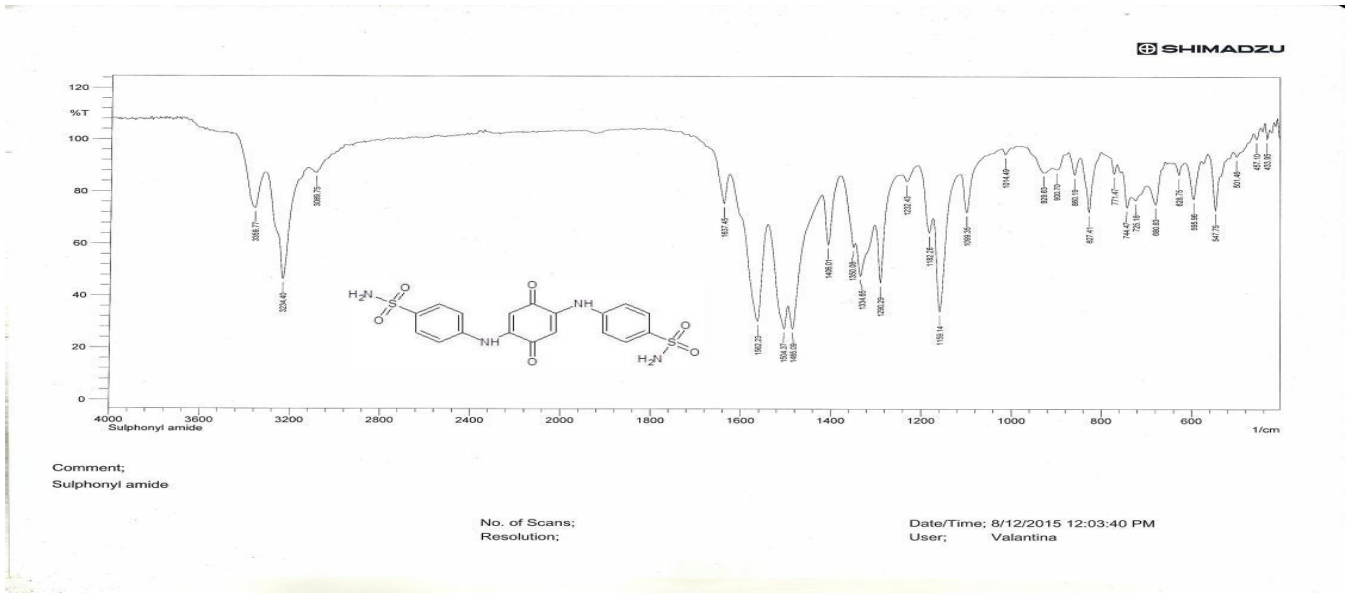
Appendix (2) IR spectrum of compound (Ia)



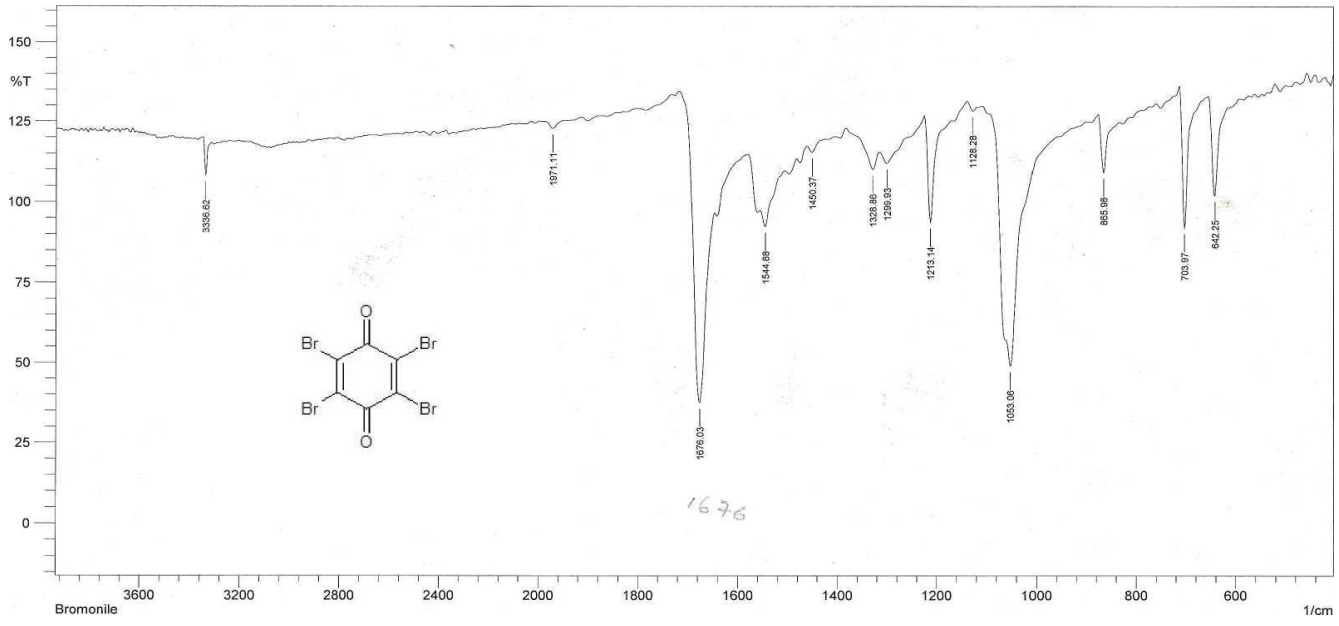
Appendix (3) IR spectrum of compound (Ib)



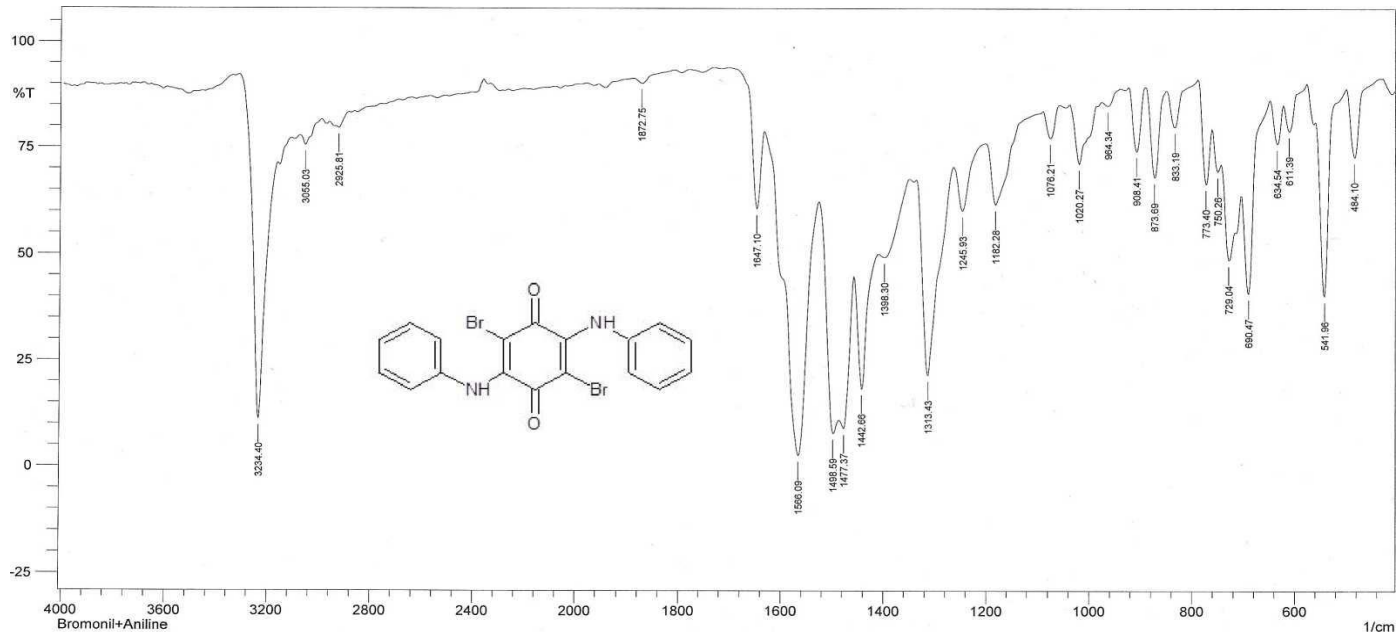
Appendix (4) IR spectrum of compound (Ic)



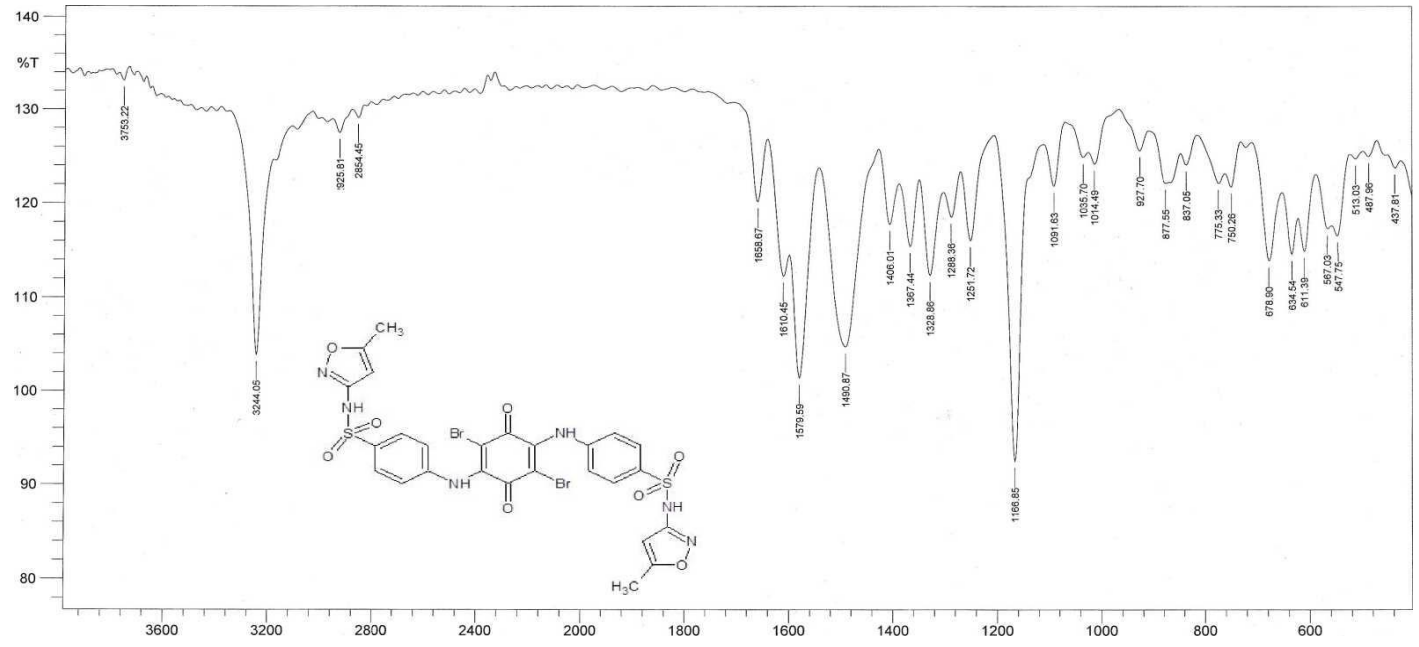
Appendix (5) IR spectrum of compound (Id)



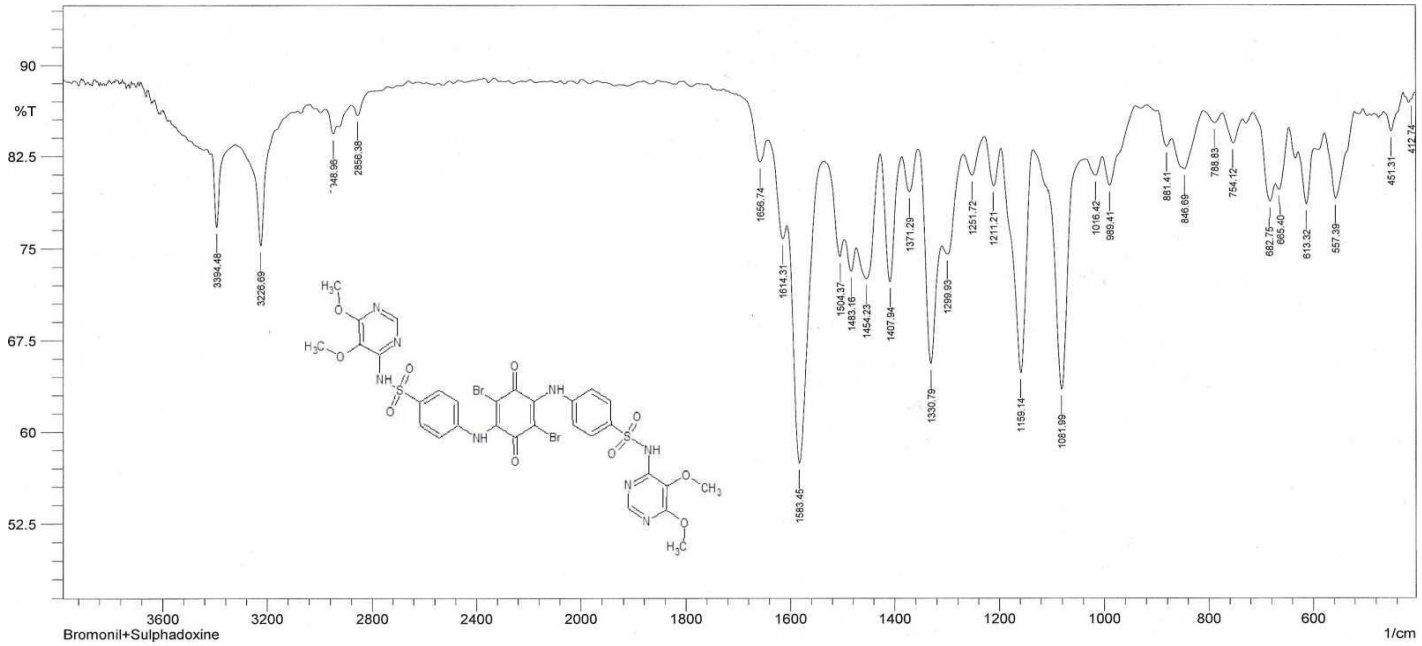
Appendix (6) IR spectrum of compound (II)



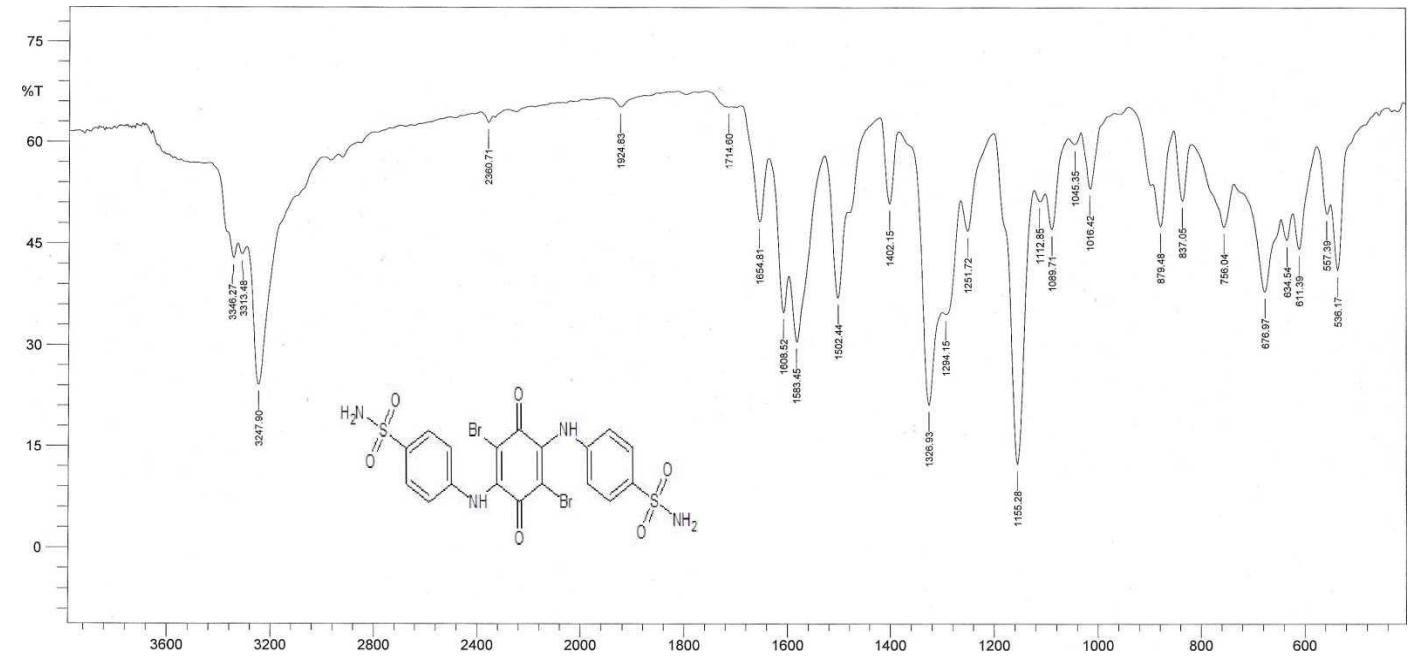
Appendix (7) IR spectrum of compound (IIa)



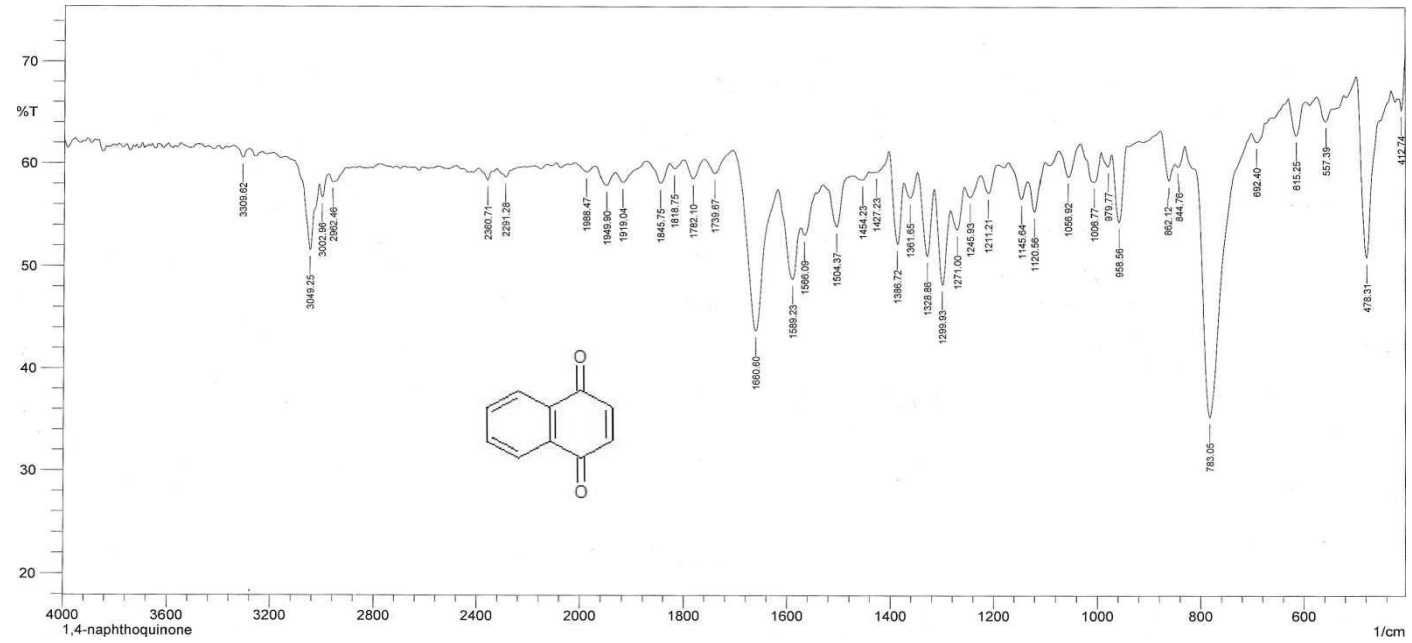
Appendix (8) IR spectrum of compound (IIb)



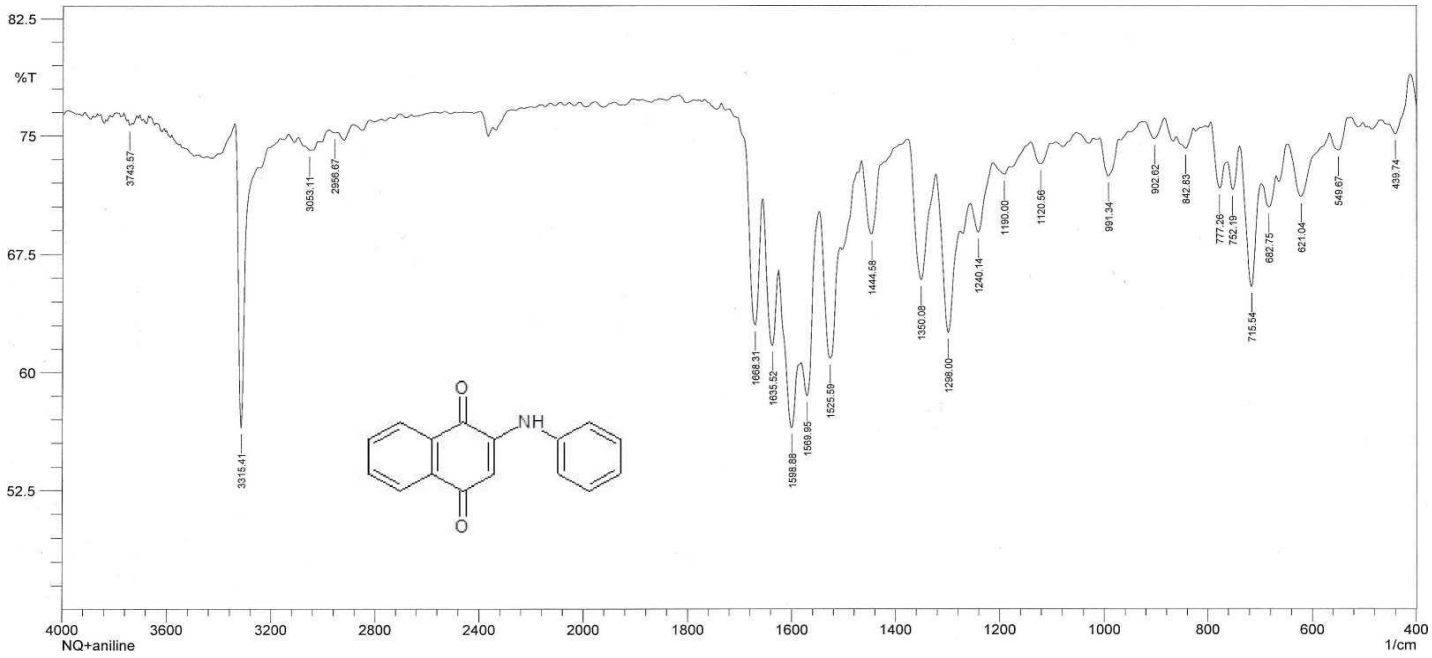
Appendix (9) IR spectrum of compound (IIc)



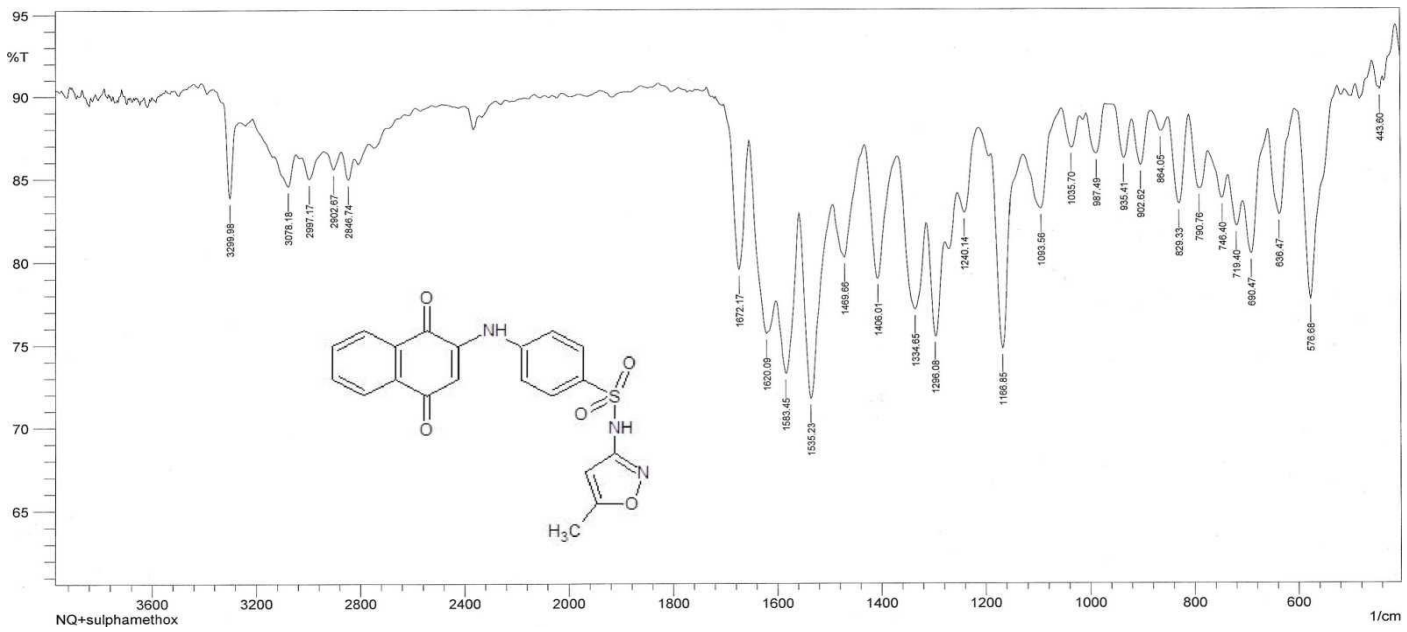
Appendix (10) IR spectrum of compound (IId)



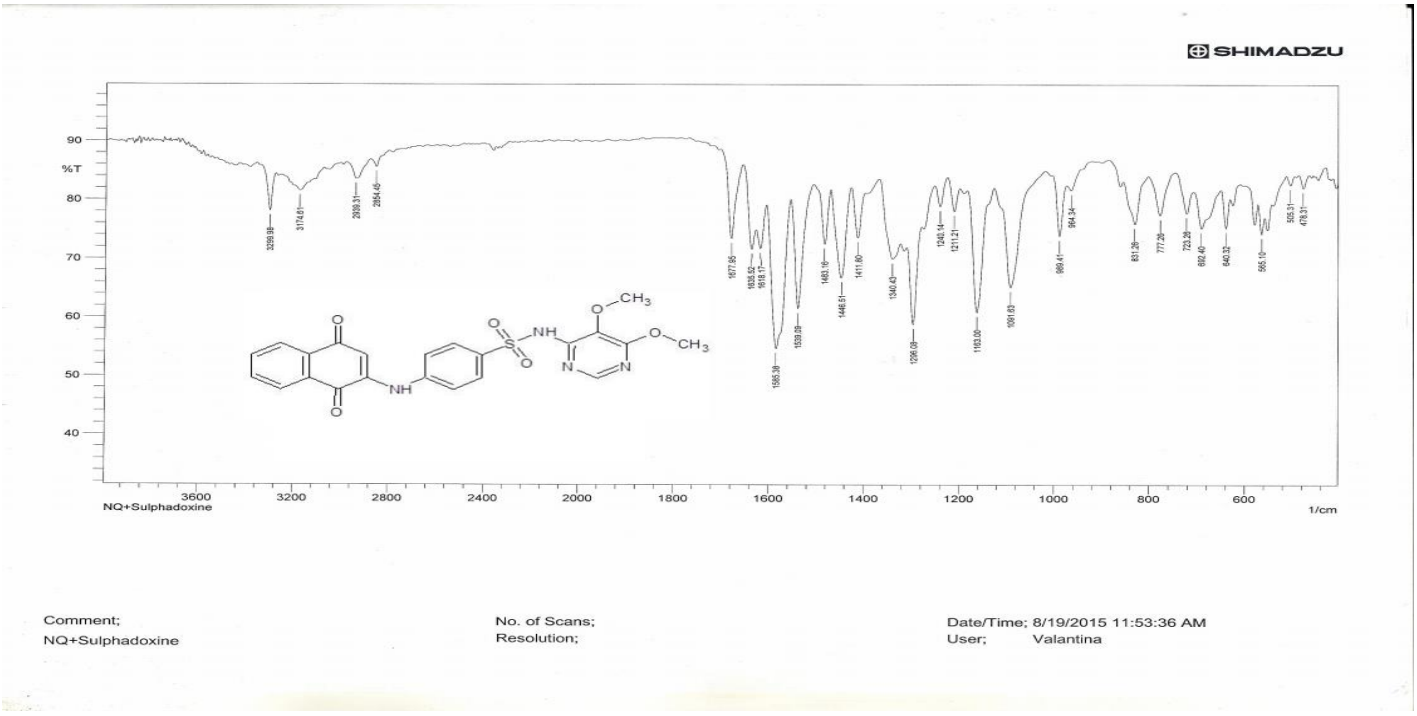
Appendix (11) IR spectrum of compound (III)



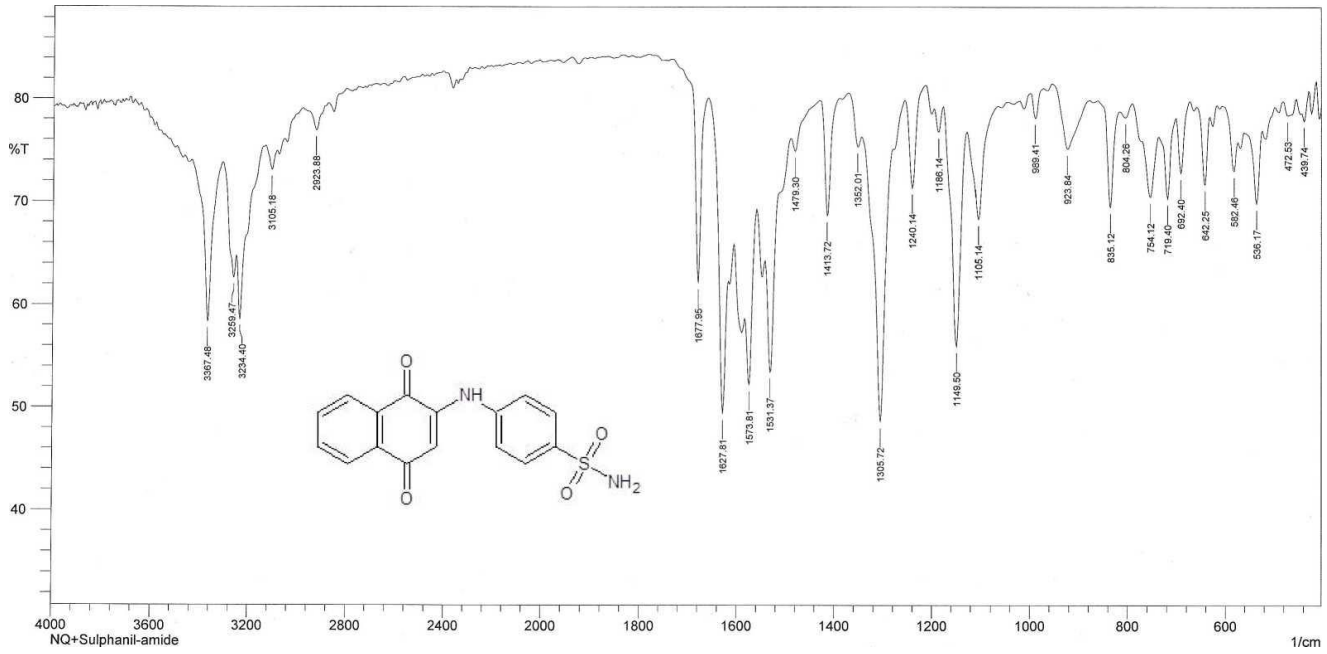
Appendix (12) IR spectrum of compound (IIIa)



Appendix (13) IR spectrum of compound (IIIb)

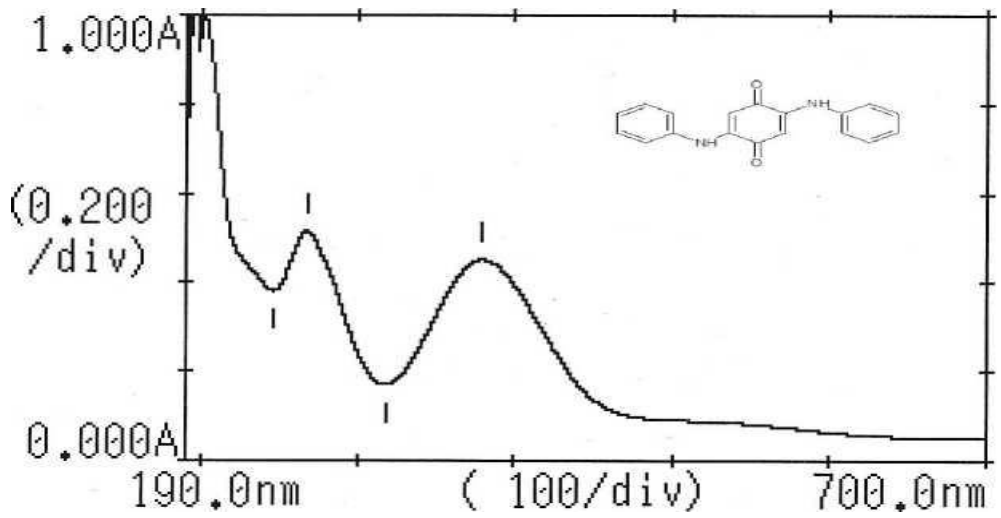


Appendix (14) IR spectrum of compound (IIIc)

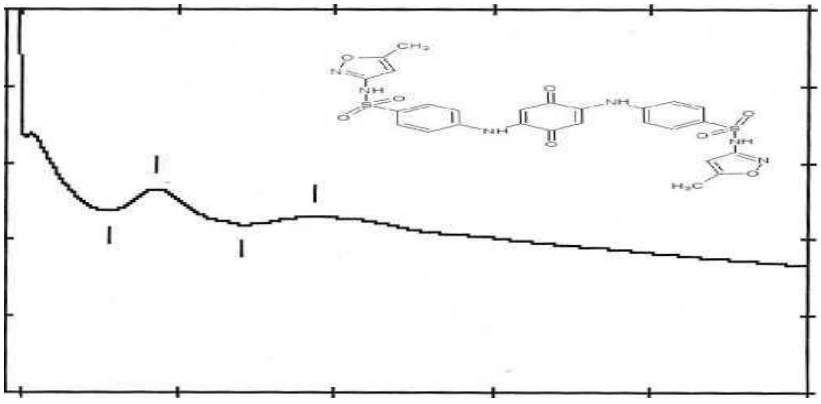


Appendix (15) IR spectrum of compound (IIId)

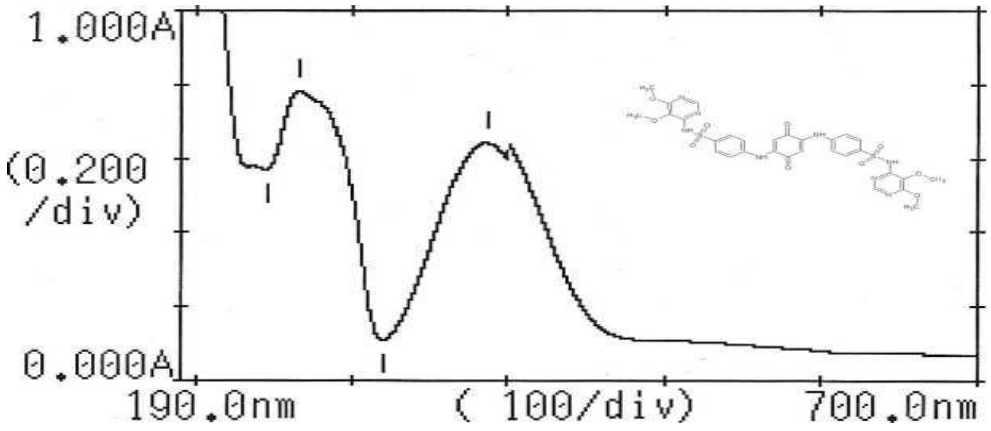
4.3. UV spectral data:



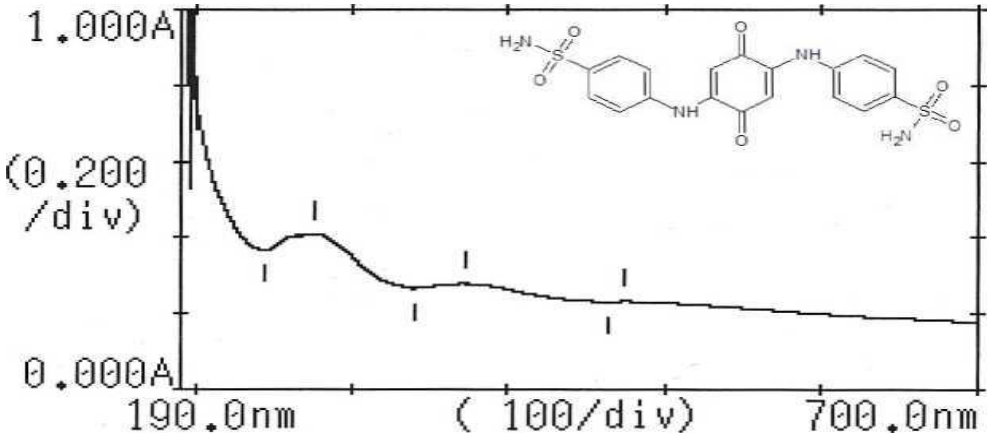
Appendix (16) UV spectrum of compound (Ia)



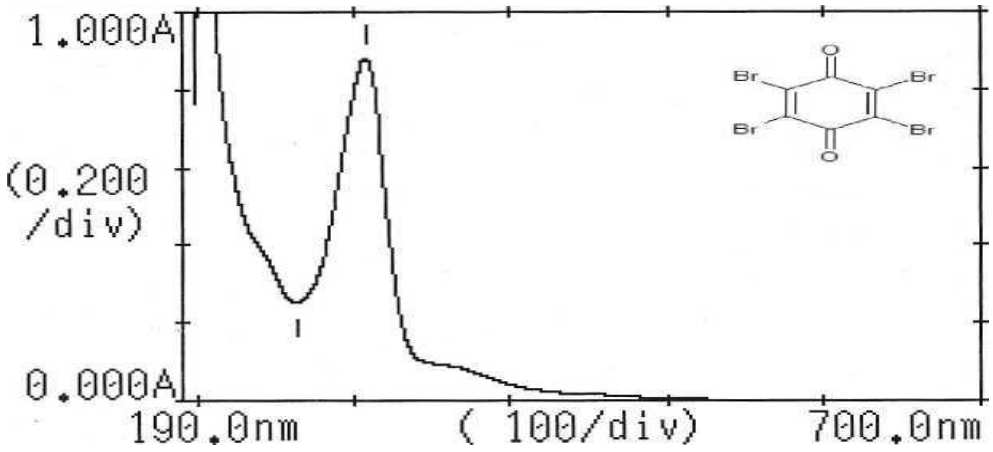
Appendix (17) UV spectrum of compound (Ib)



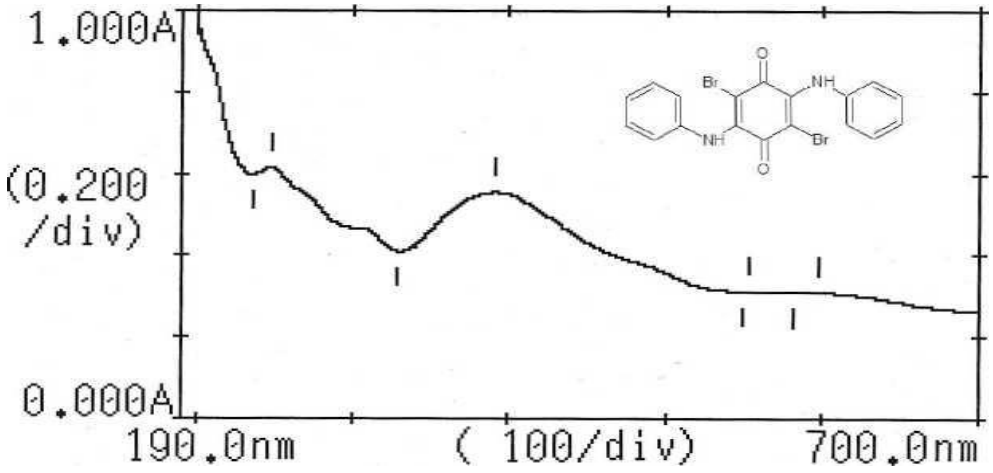
Appendix (18) UV spectrum of compound (Ic)



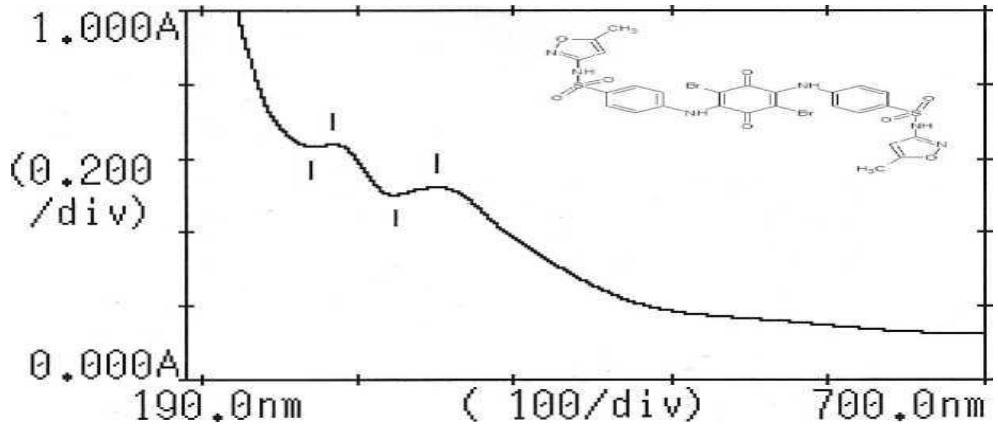
Appendix (19) UV spectrum of compound (Id)



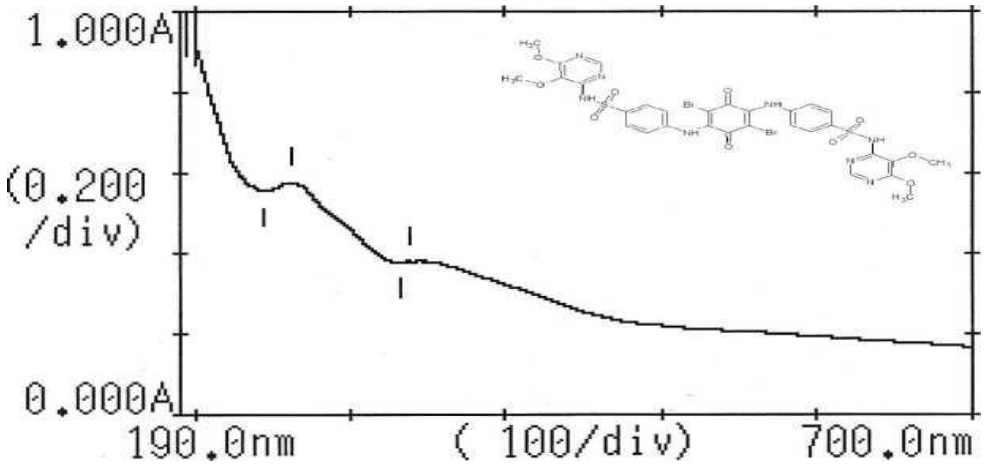
Appendix (20) UV spectrum of compound (II)



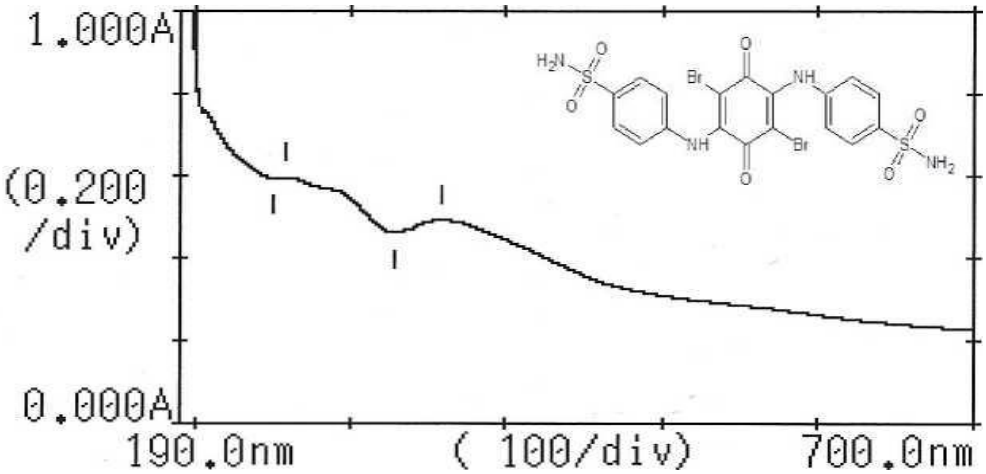
Appendix (21) UV spectrum of compound (IIa)



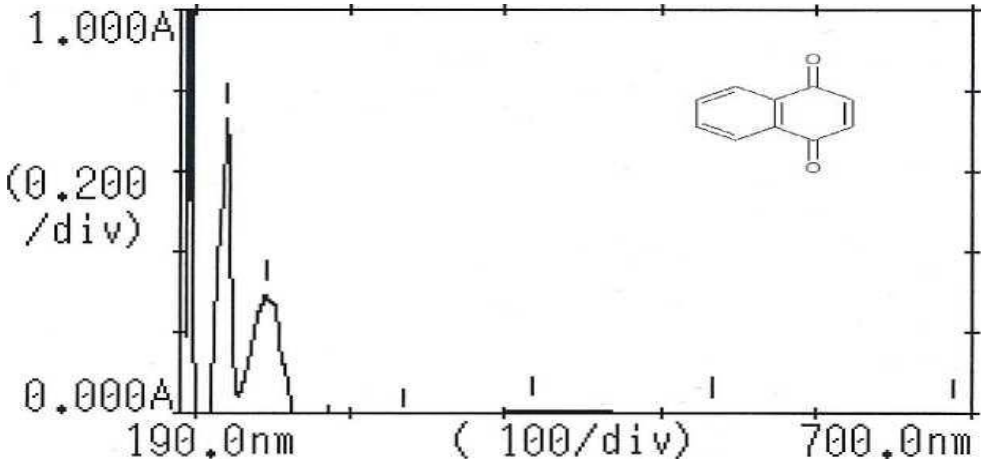
Appendix (22) UV spectrum of compound (IIb)



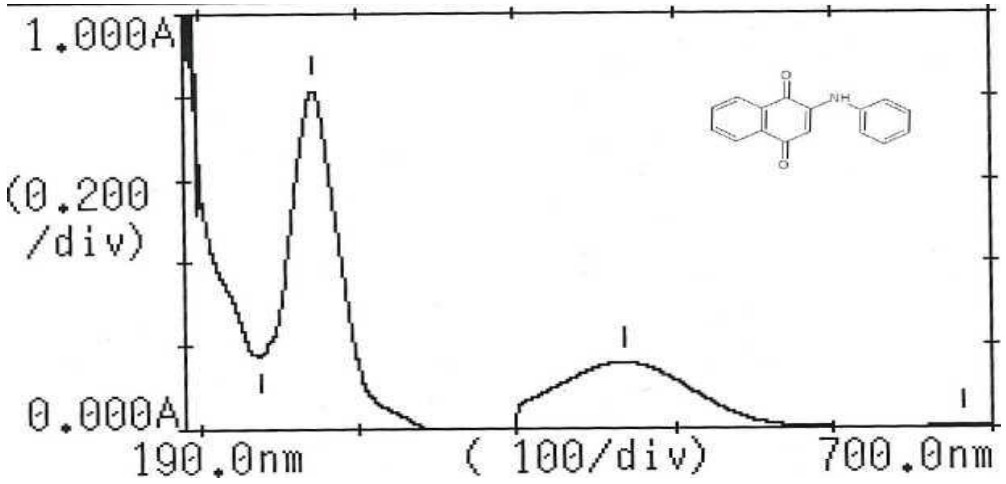
Appendix (23) UV spectrum of compound (IIc)



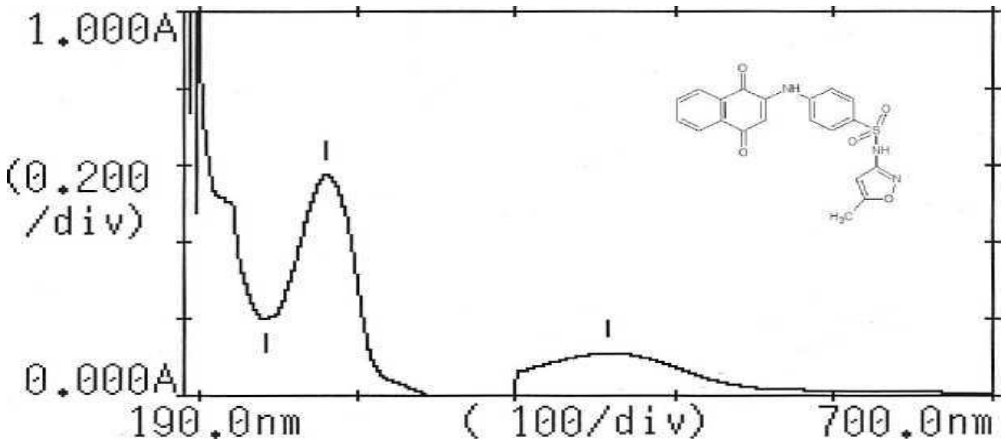
Appendix (24) UV spectrum of compound (IId)



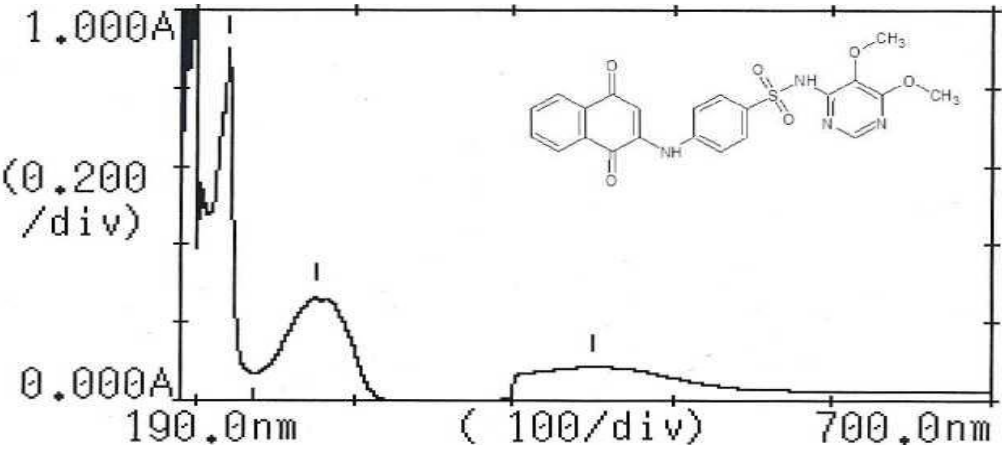
Appendix (25) UV spectrum of compound (III)



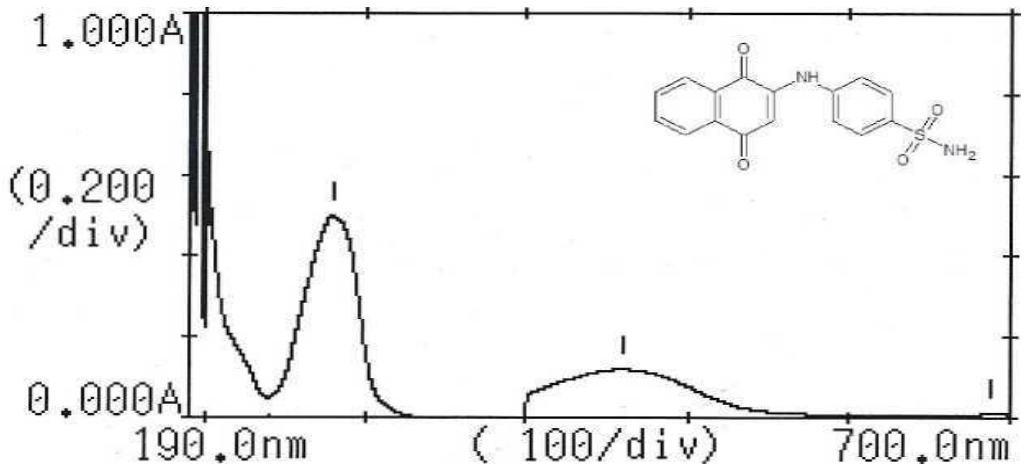
Appendix (26) UV spectrum of compound (IIIa)



Appendix (27) UV spectrum of compound (IIIb)

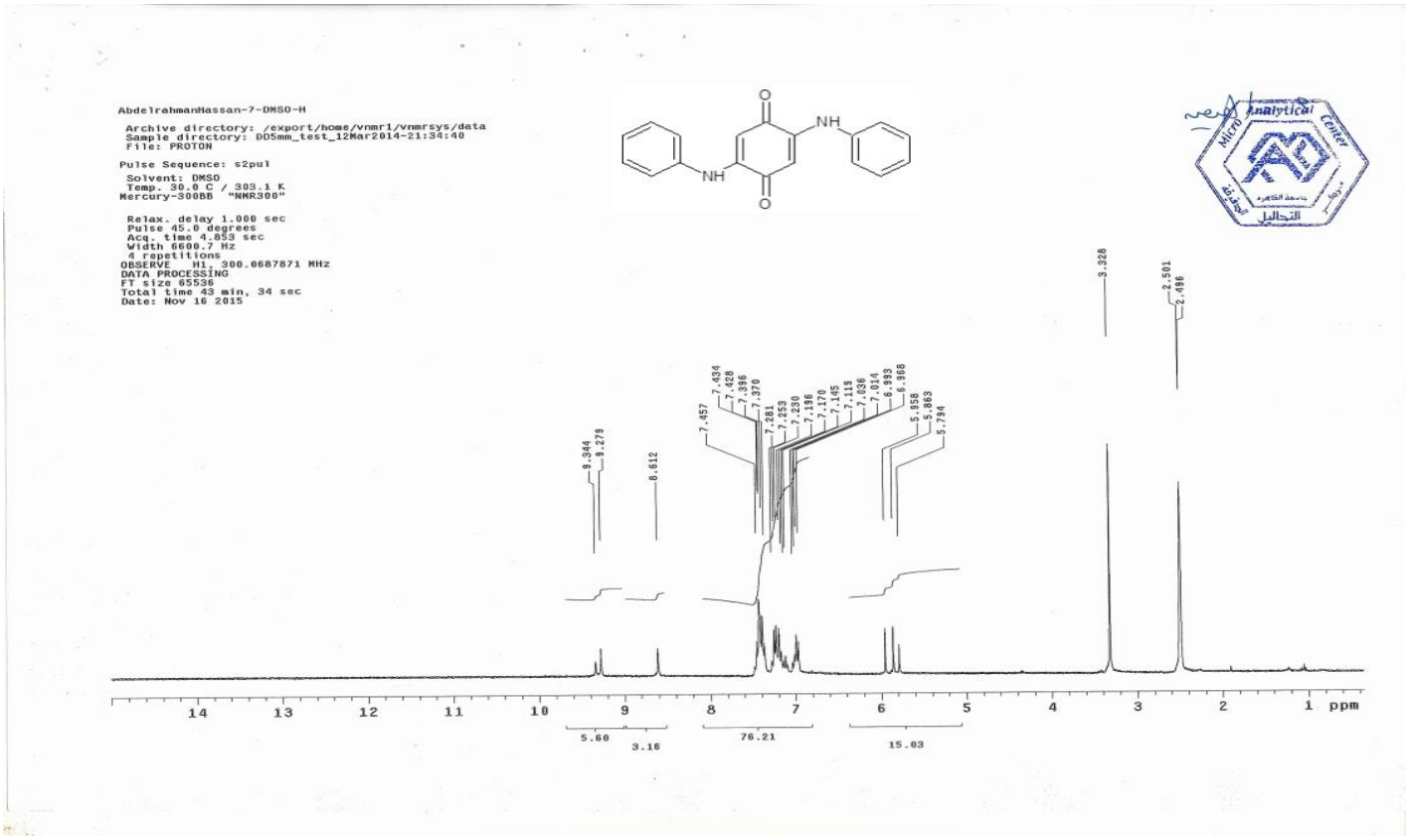


Appendix (28) UV spectrum of compound (IIIc)

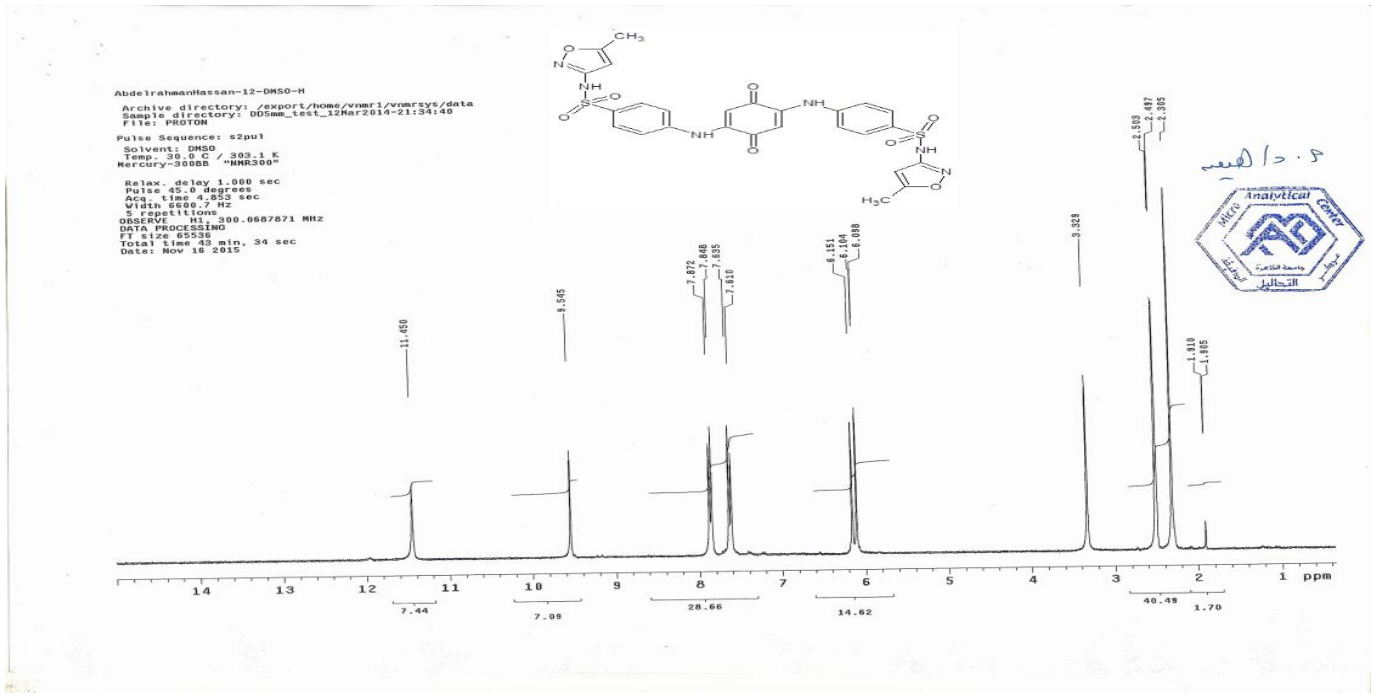


Appendix (29) UV spectrum of compound (IIId)

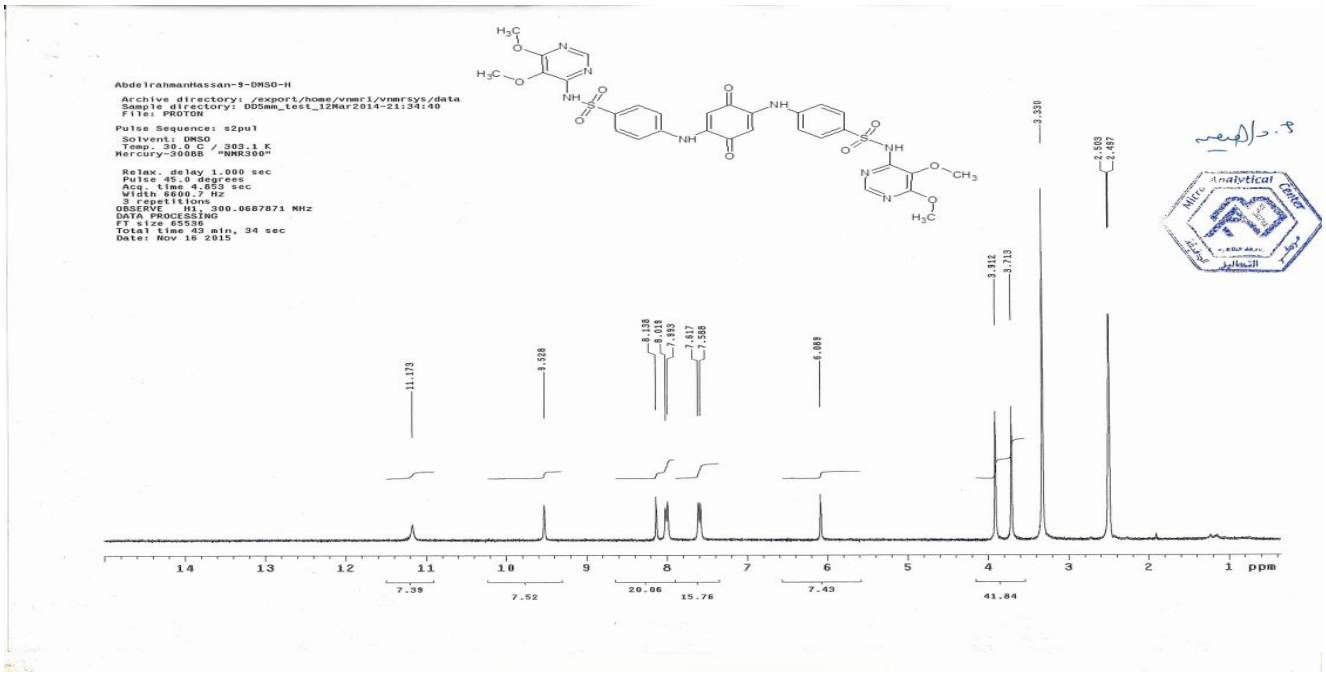
4.4. NMR spectral data:



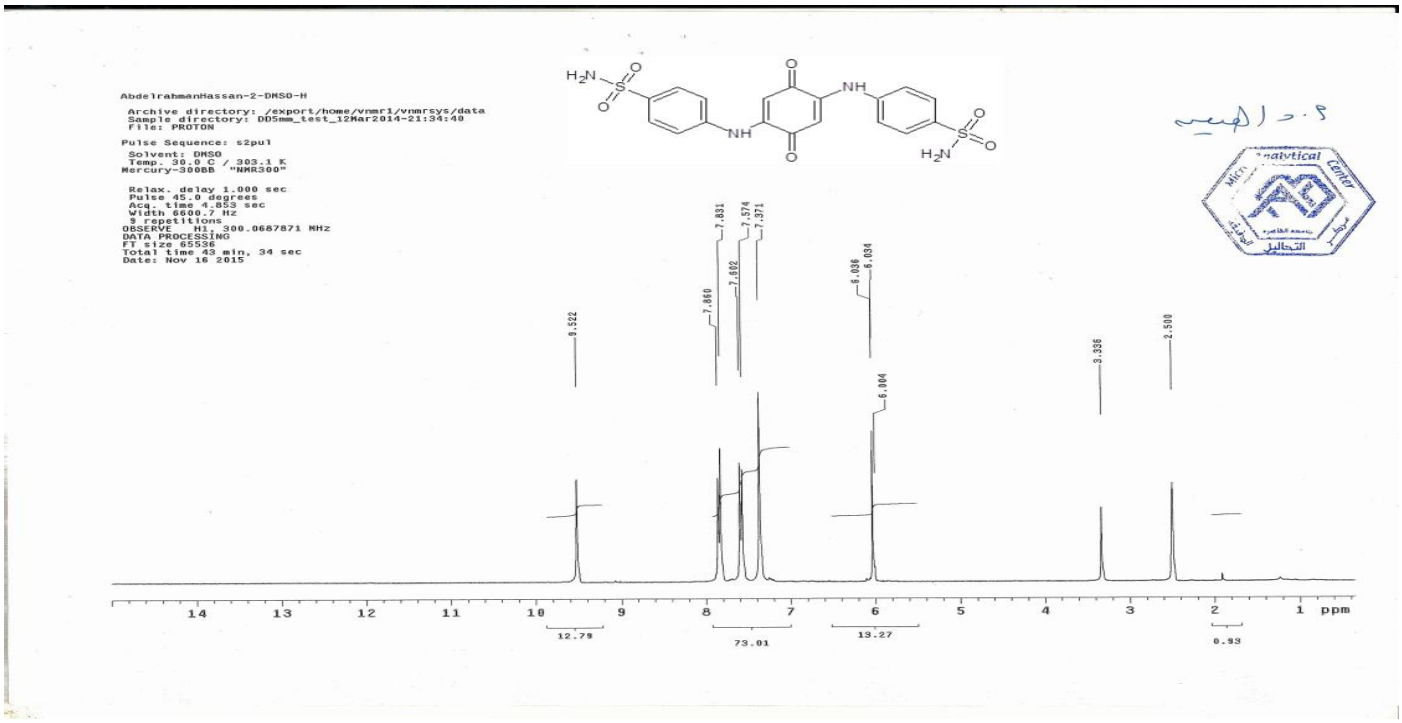
Appendix (30) NMR spectrum of compound (Ia)



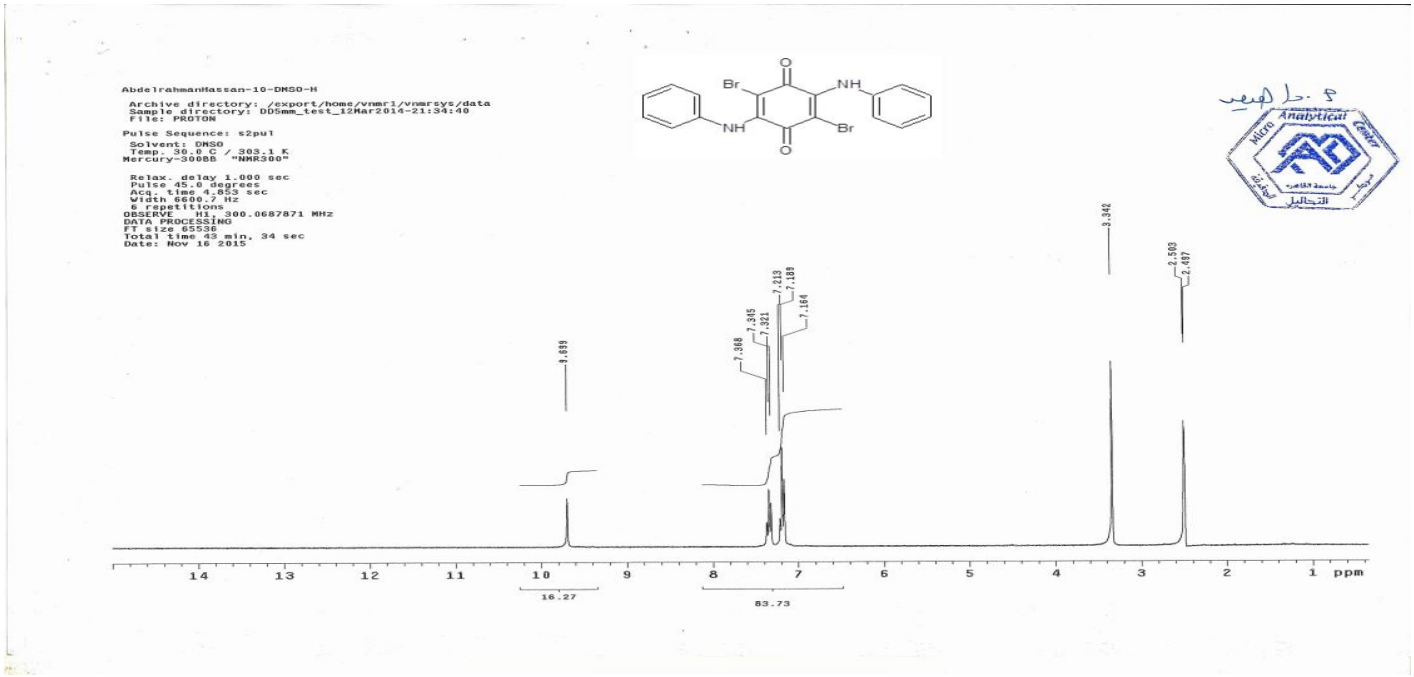
Appendix (31) NMR spectrum of compound (Ib)



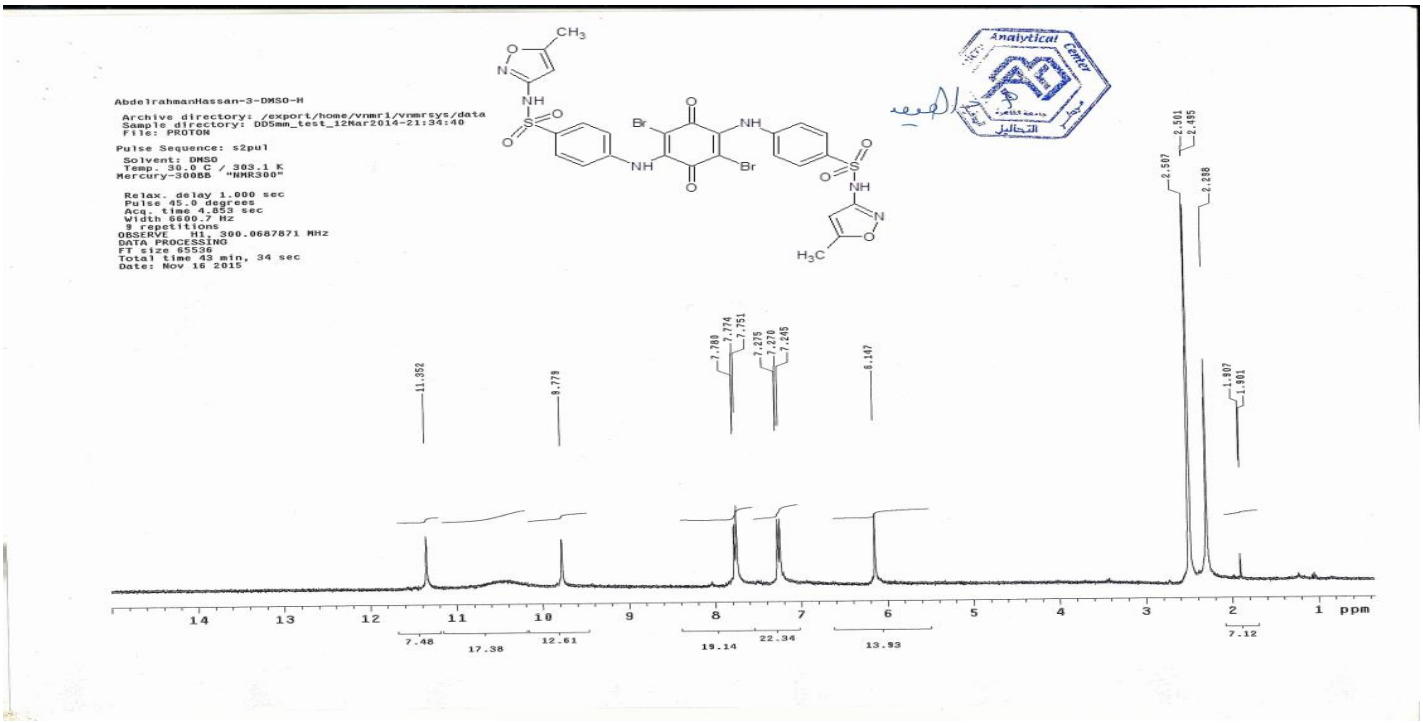
Appendix (32) NMR spectrum of compound (Ic)



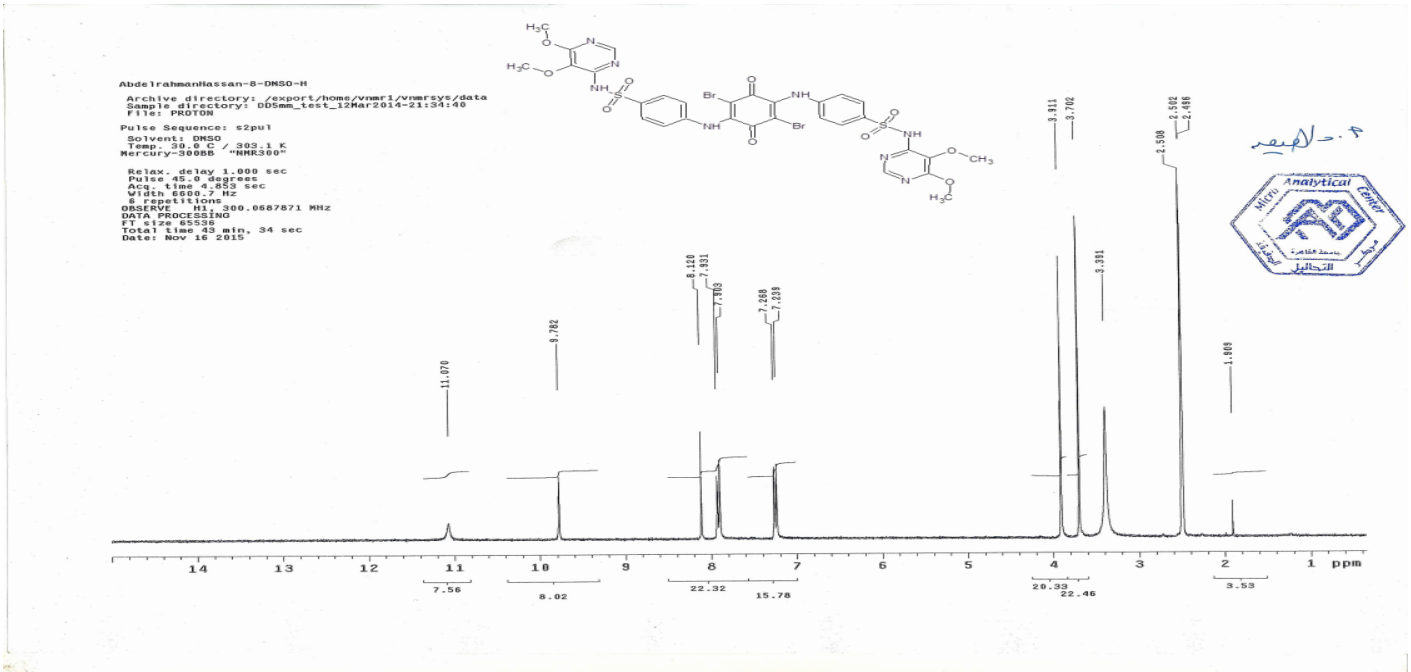
Appendix (33) NMR spectrum of compound (Id)



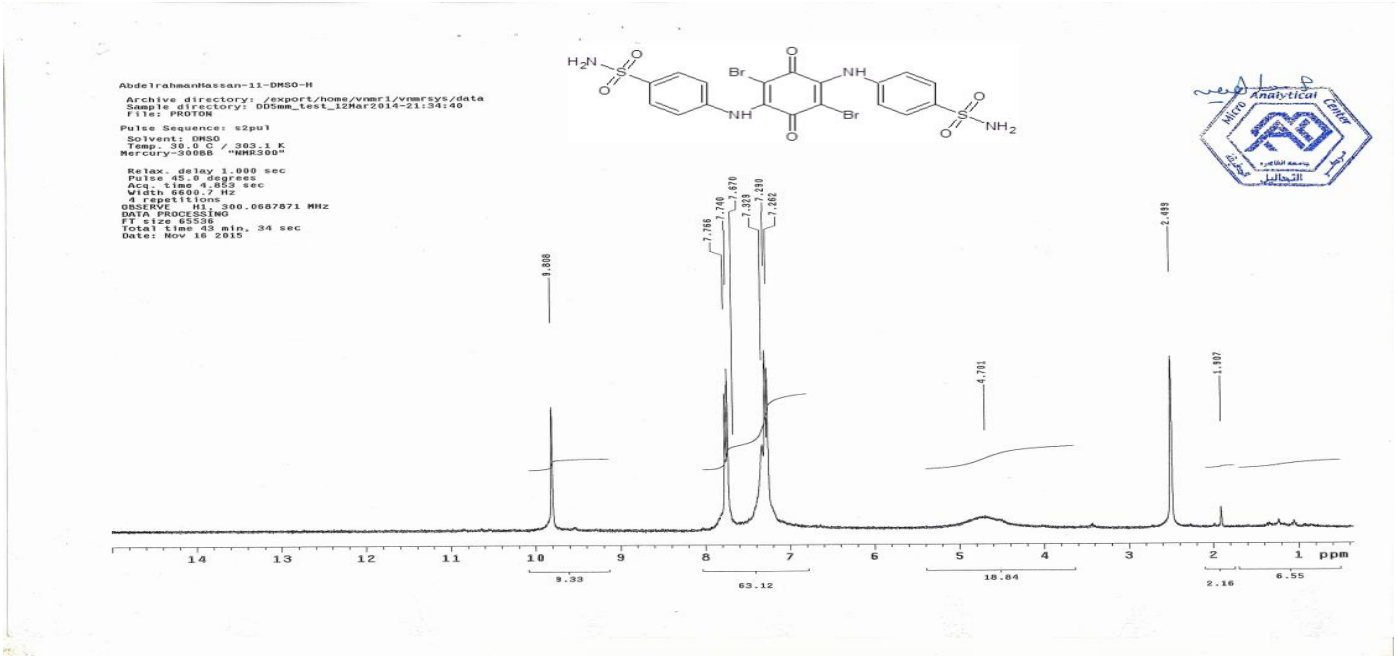
Appendix (34) NMR spectrum of compound (IIa)



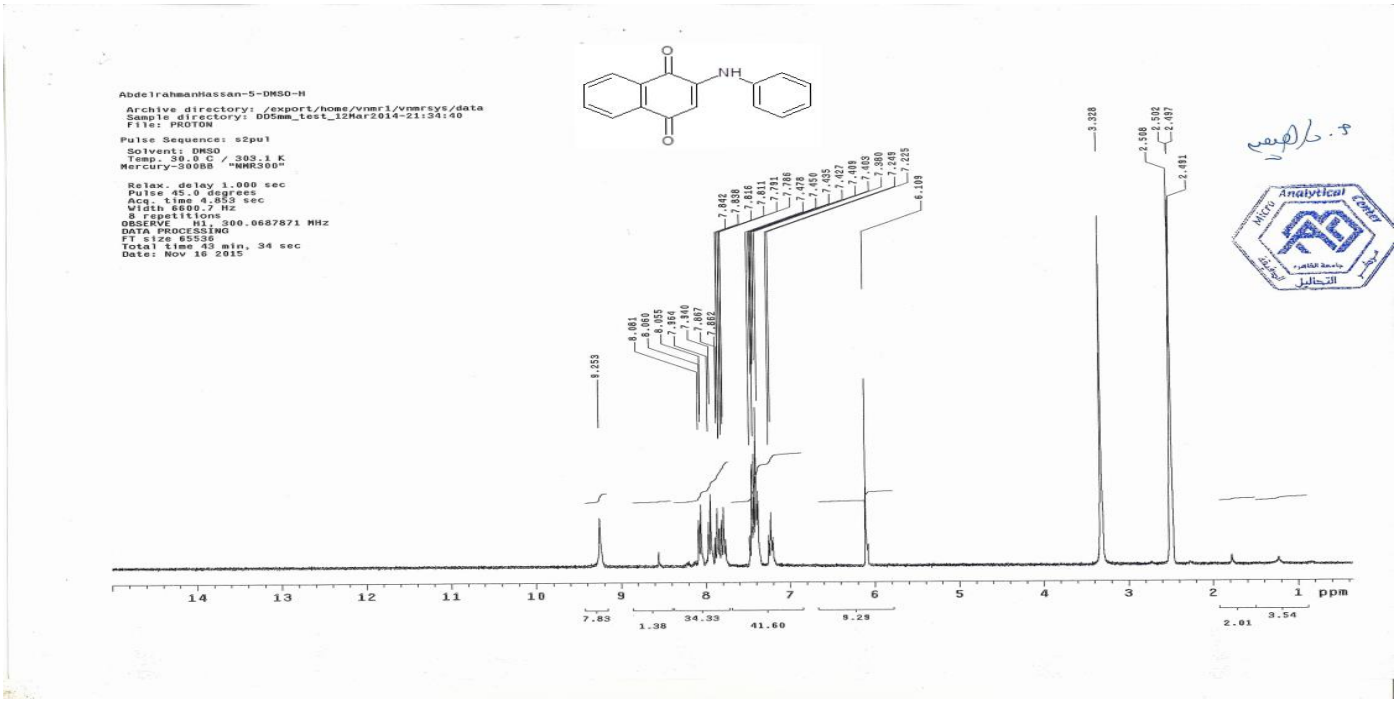
Appendix (35) NMR spectrum of compound (IIb)



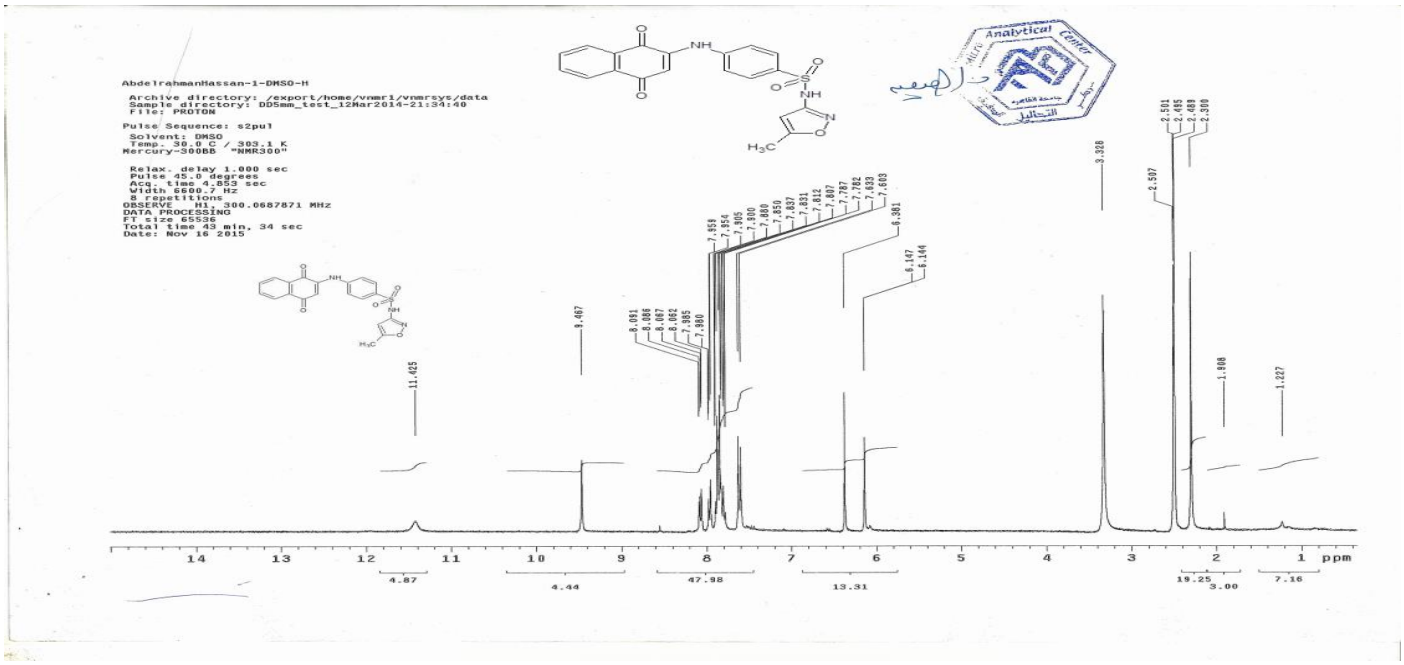
Appendix (36) NMR spectrum of compound (IIc)



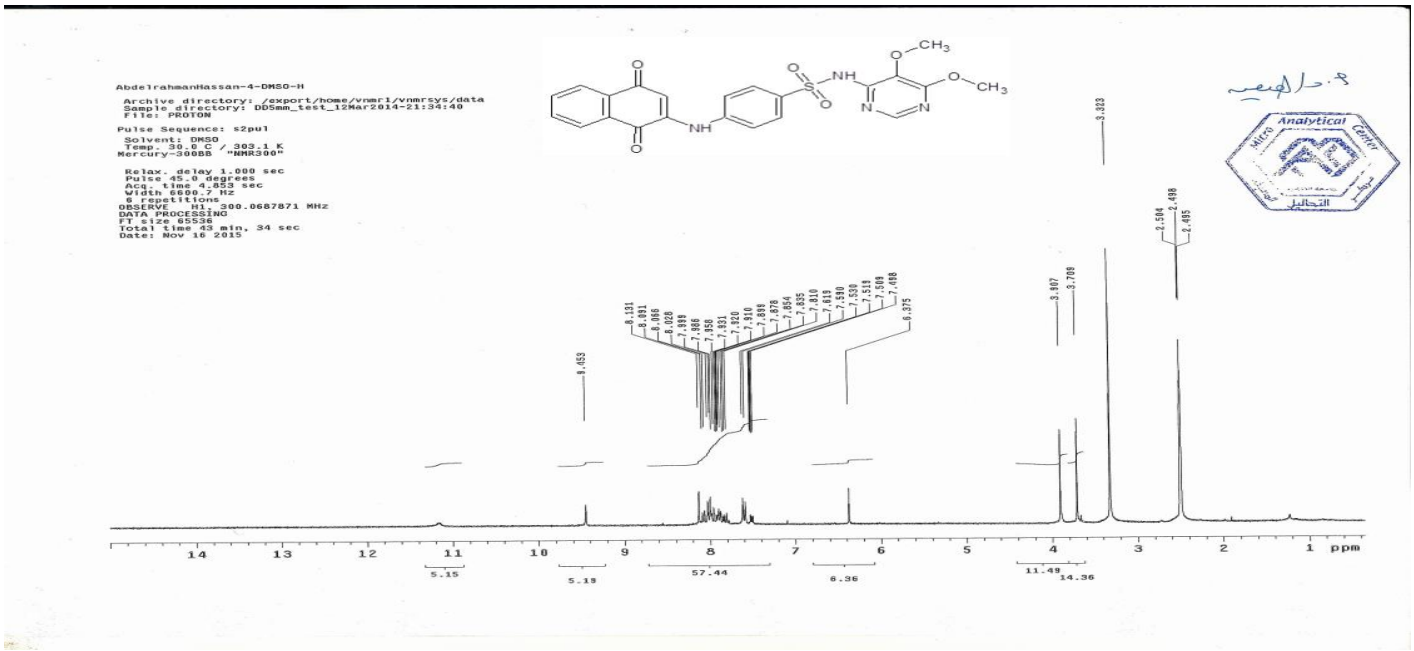
Appendix (37) NMR spectrum of compound (IId)



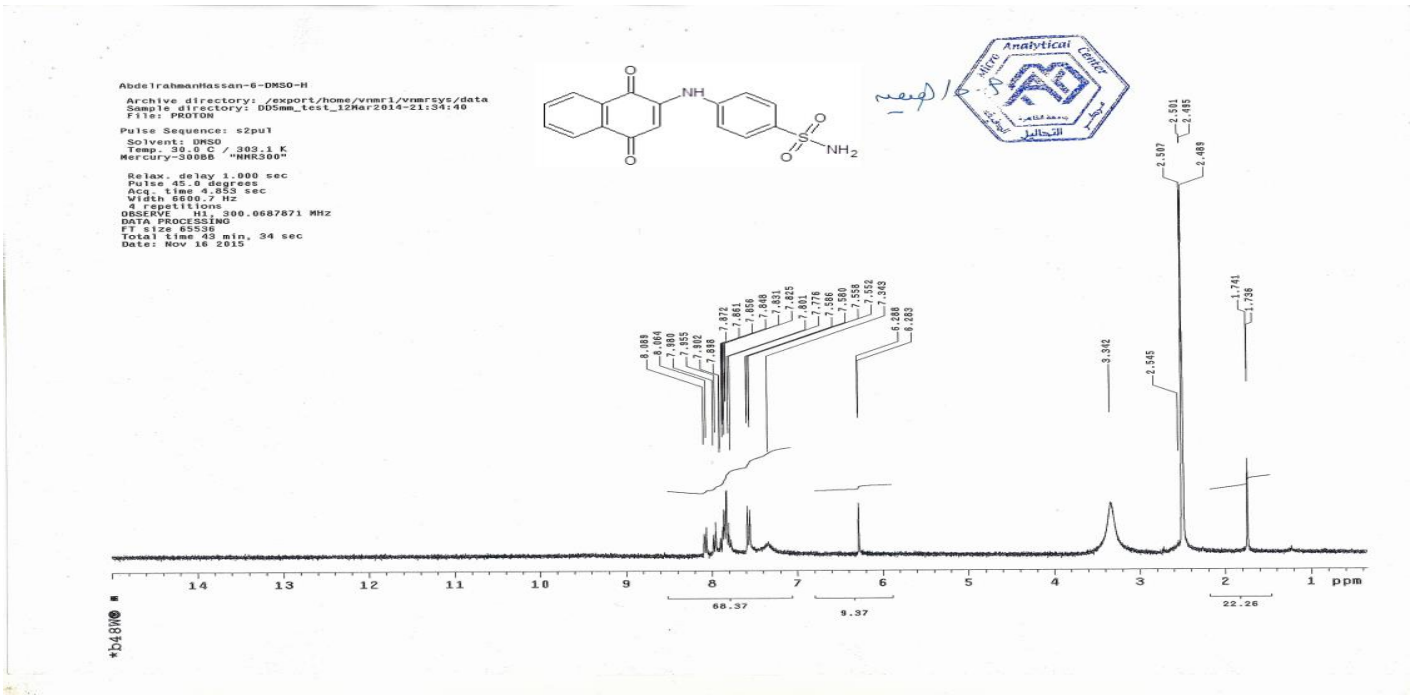
Appendix (38) NMR spectrum of compound (IIIa)



Appendix (39) NMR spectrum of compound (IIIb)

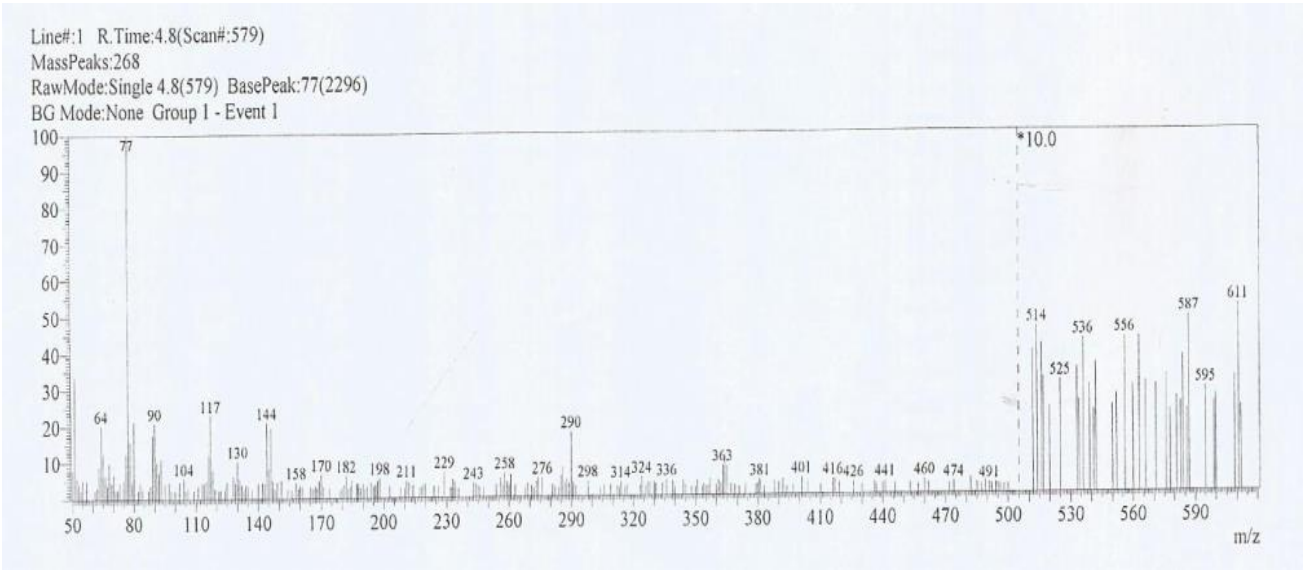


Appendix (40) NMR spectrum of compound (IIIc)

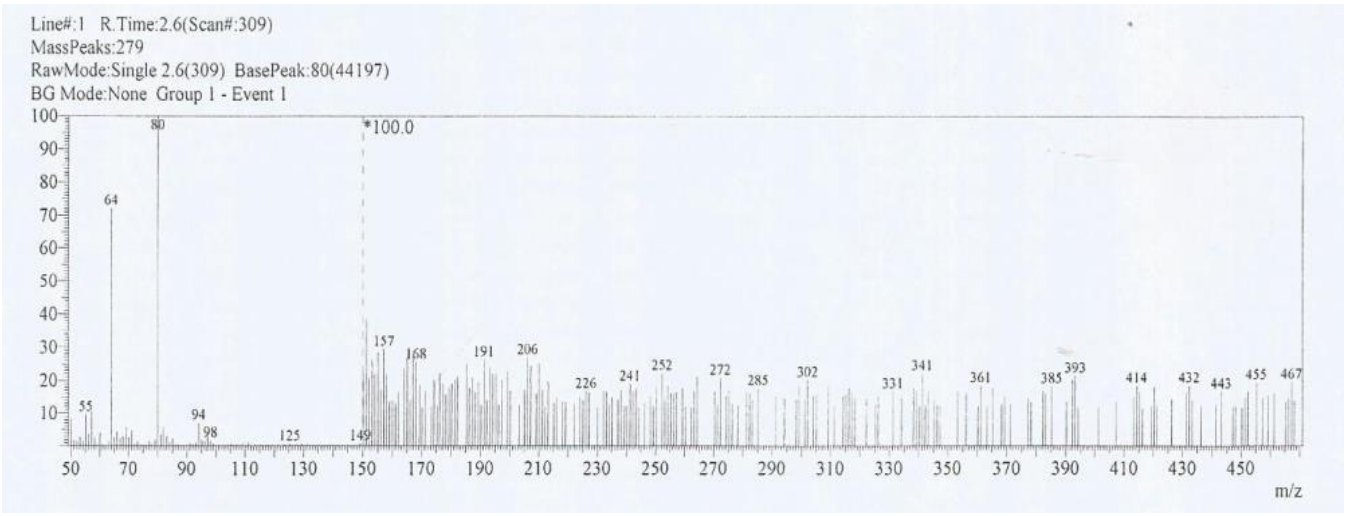


Appendix (41) NMR spectrum of compound (IIId)

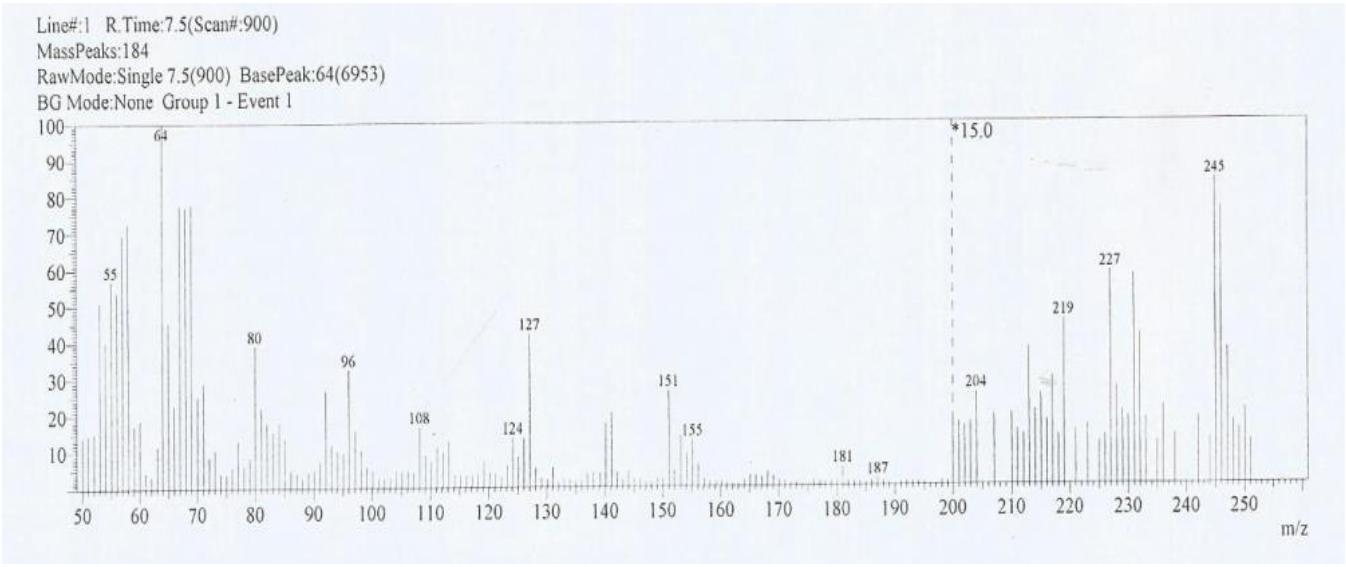
4.5. MS spectral data:



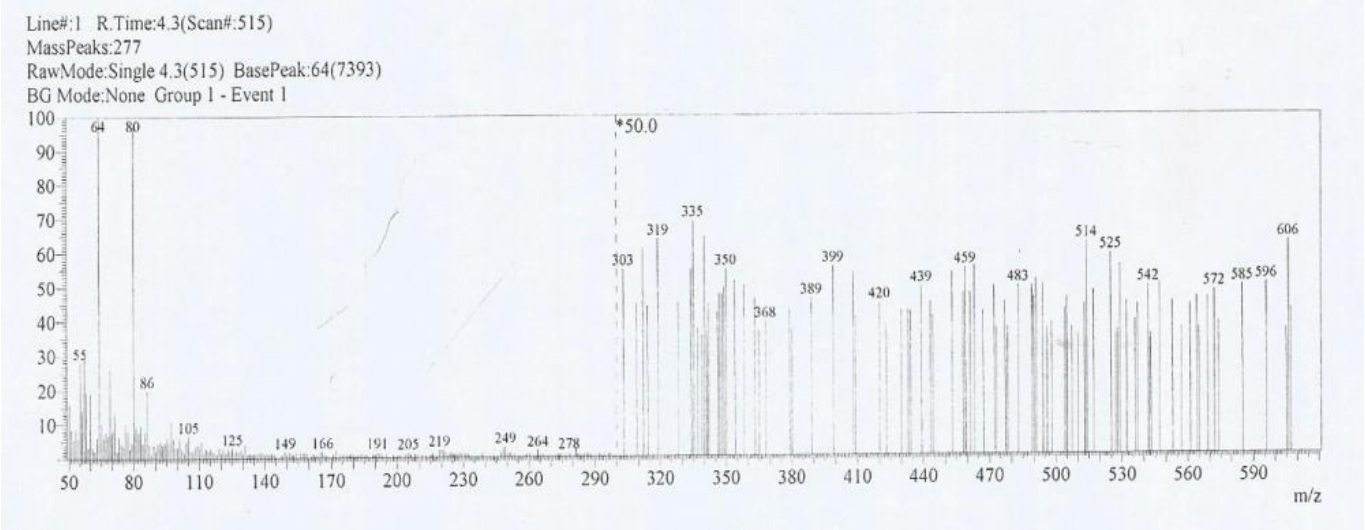
Appendix (42) MS spectrum of compound (Ia)



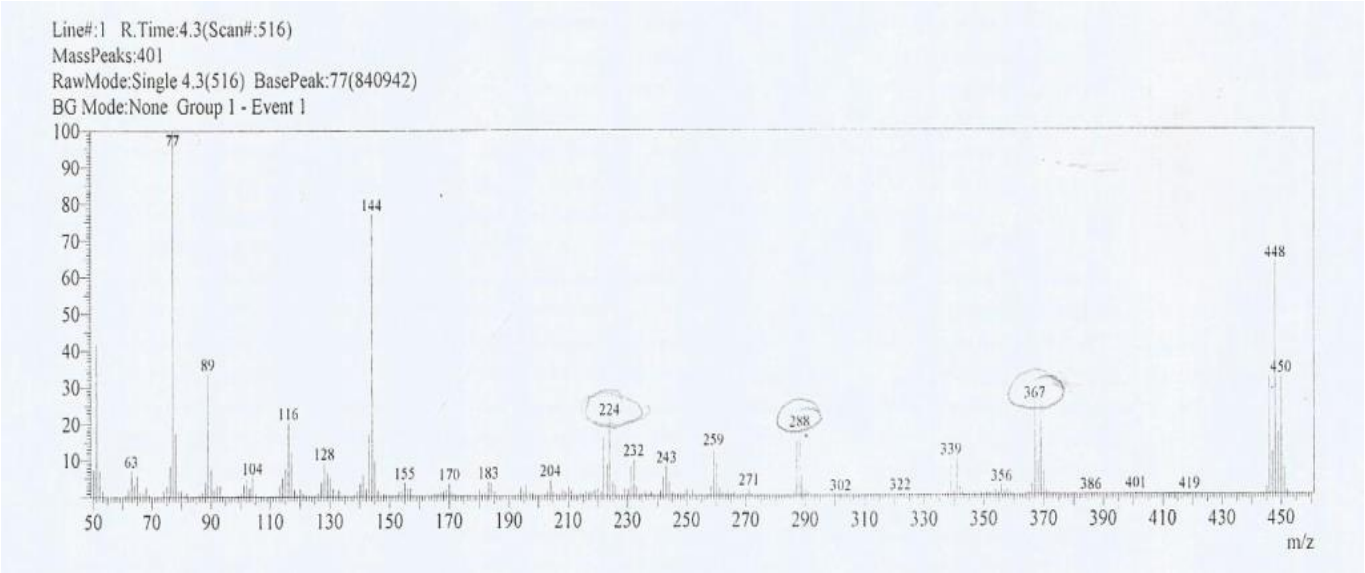
Appendix (43) MS spectrum of compound (Ib)



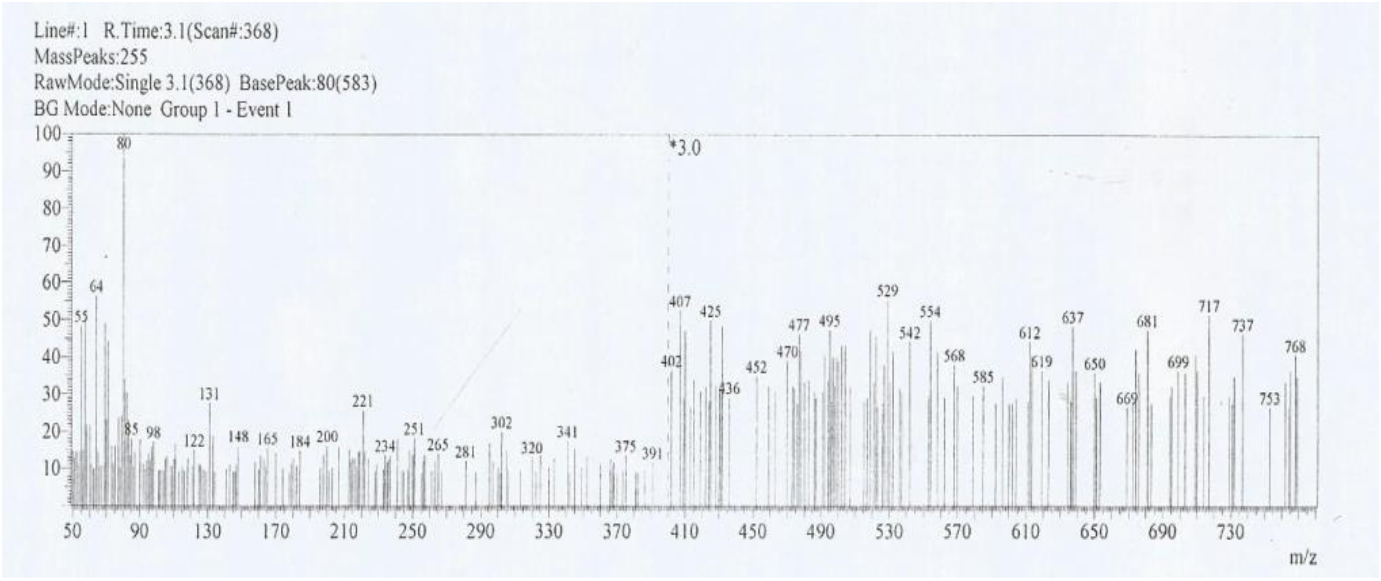
Appendix (44) MS spectrum of compound (Ic)



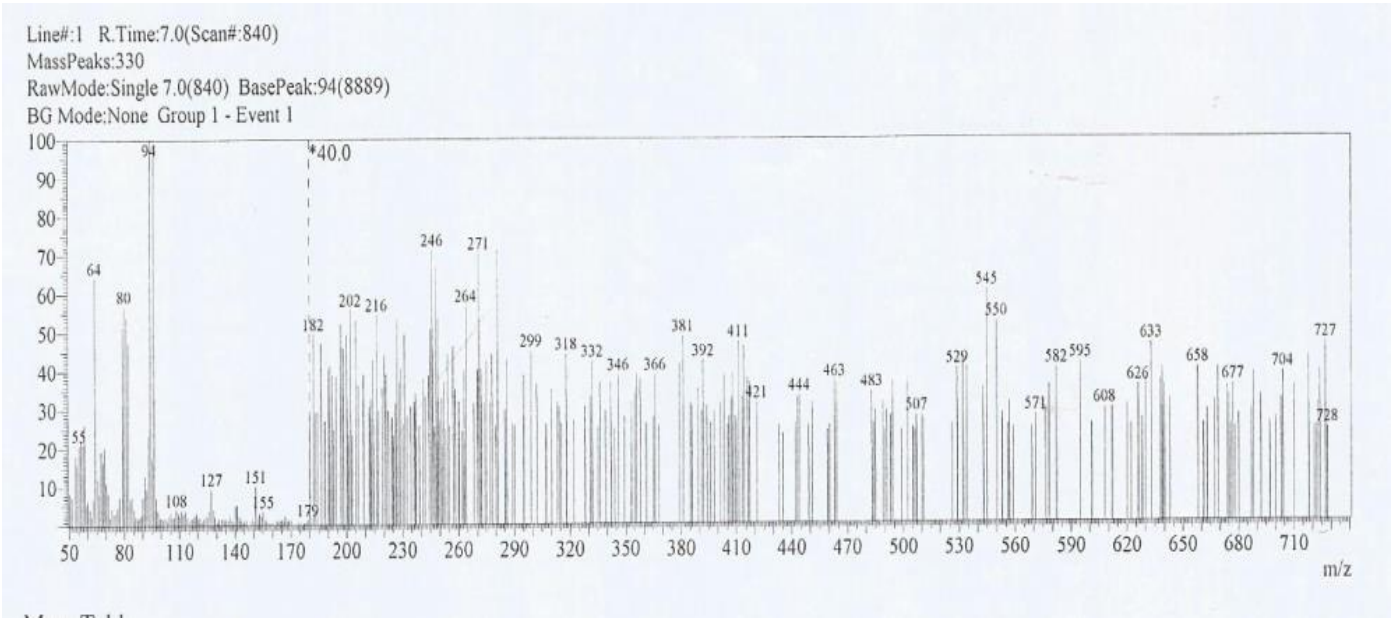
Appendix (45) MS spectrum of compound (Id)



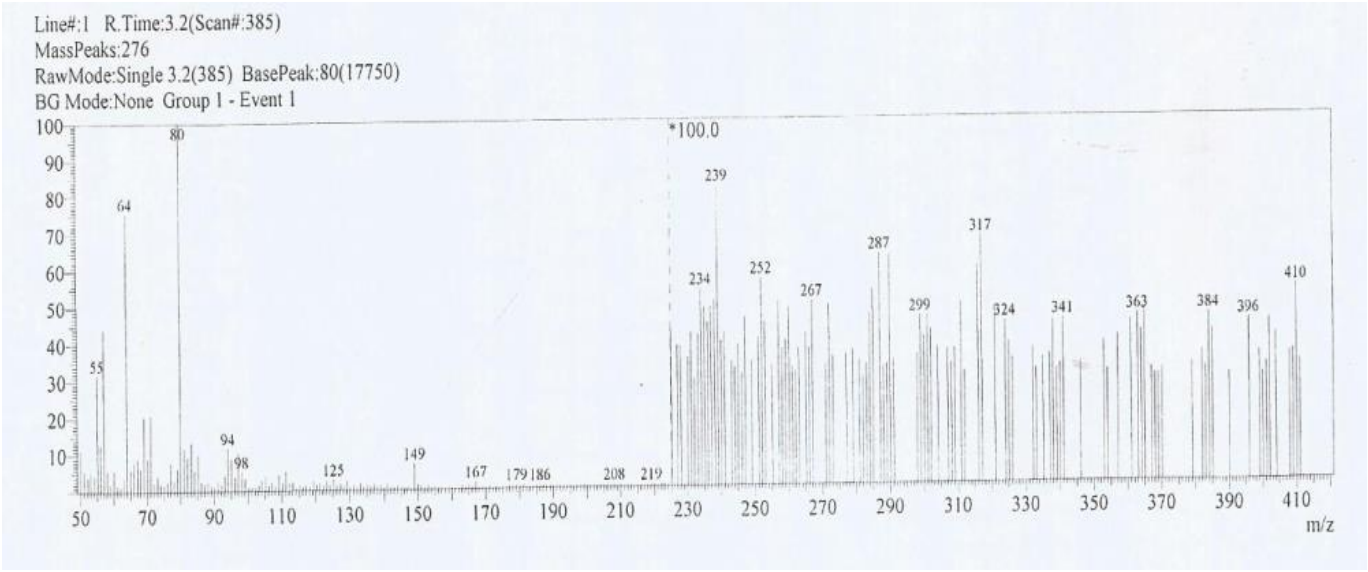
Appendix (46) MS spectrum of compound (IIa)



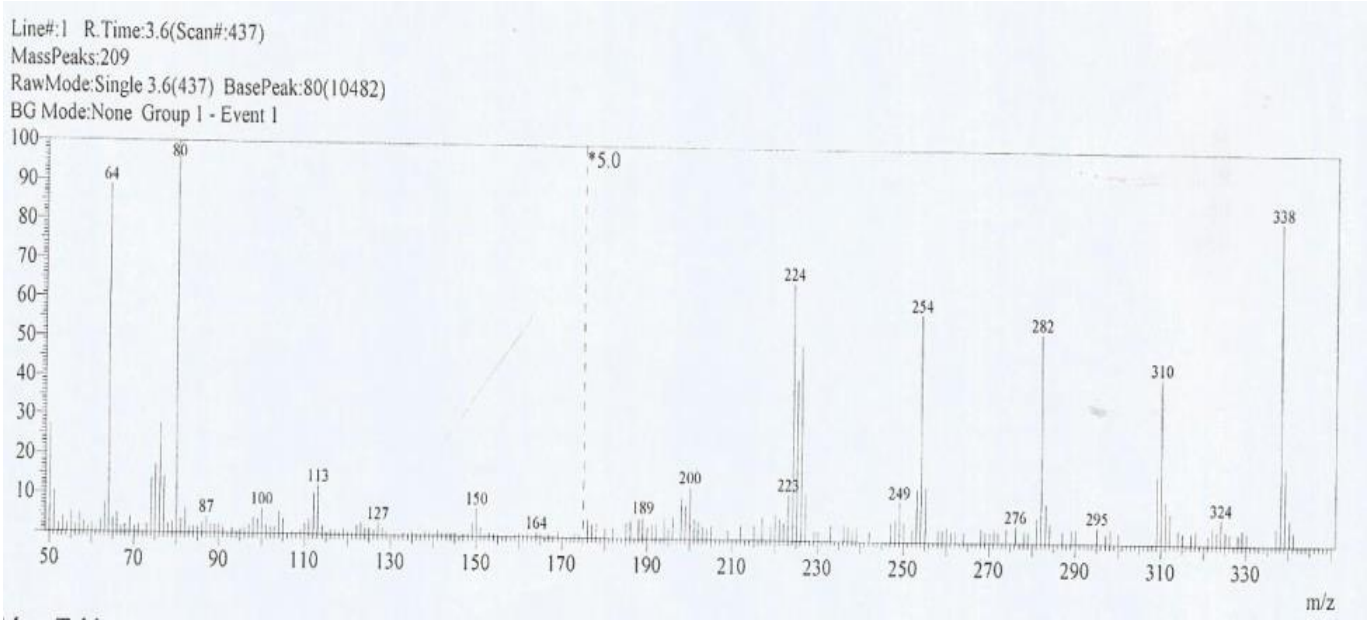
Appendix (47) MS spectrum of compound (IIb)



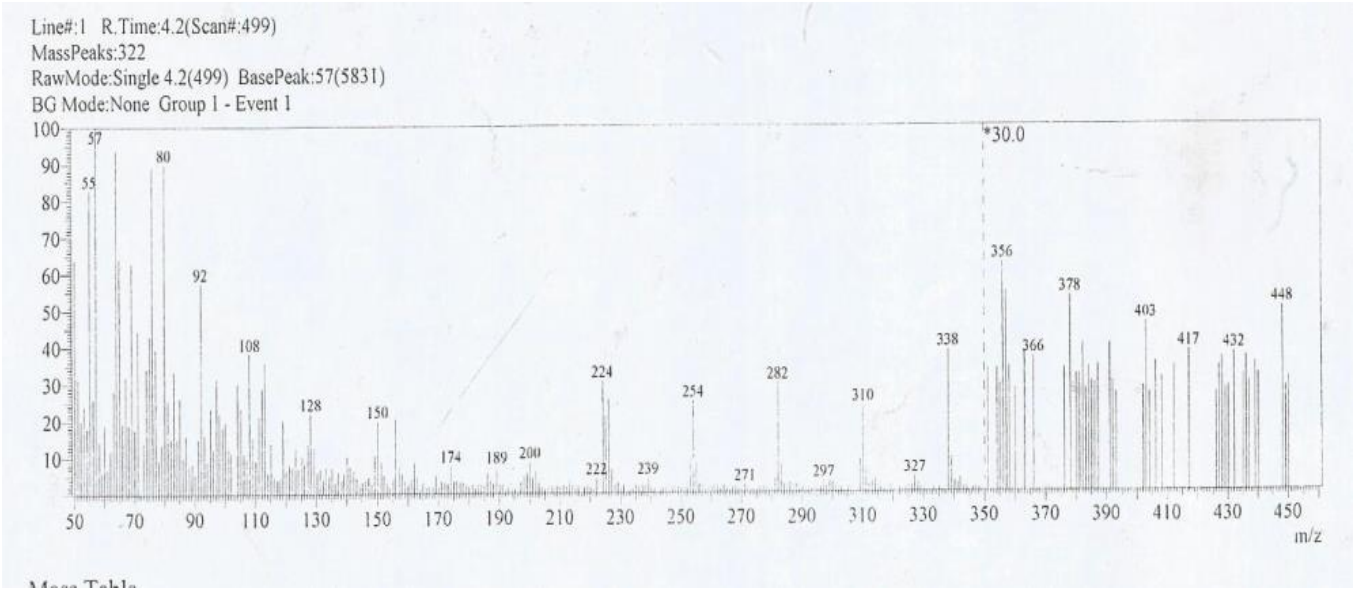
Appendix (48) MS spectrum of compound (IIc)



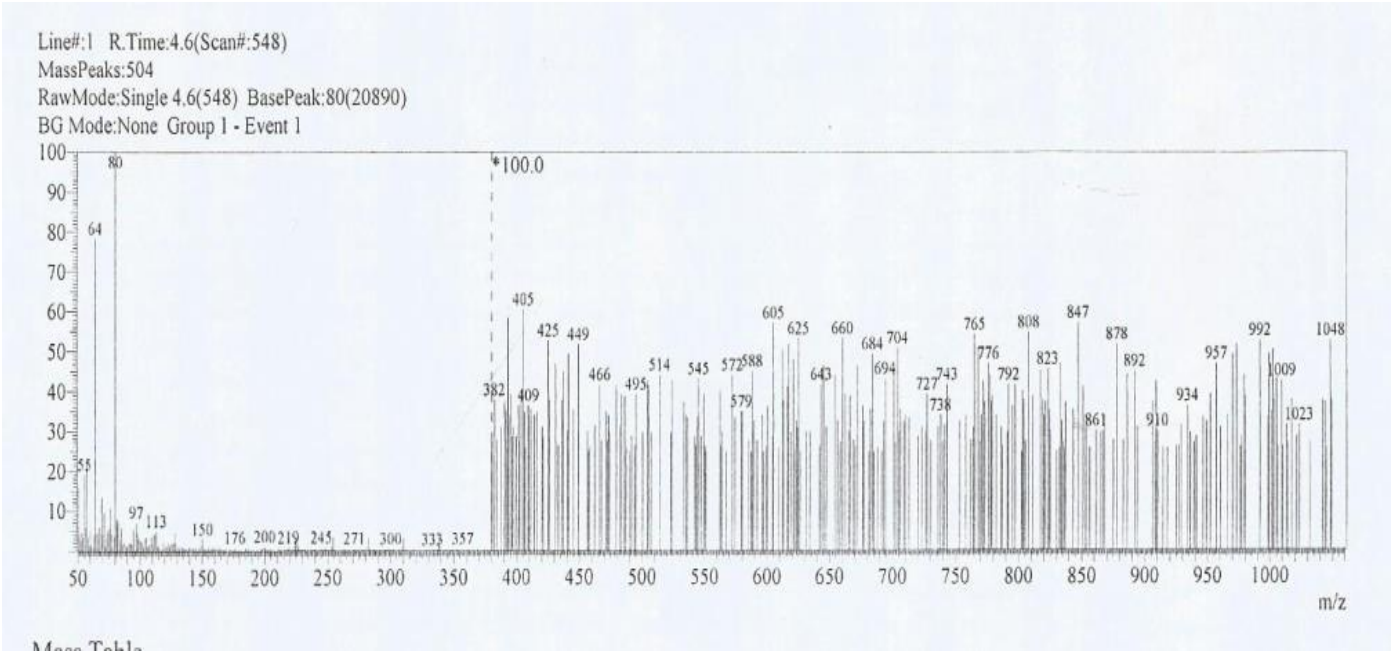
Appendix (49) MS spectrum of compound (IId)



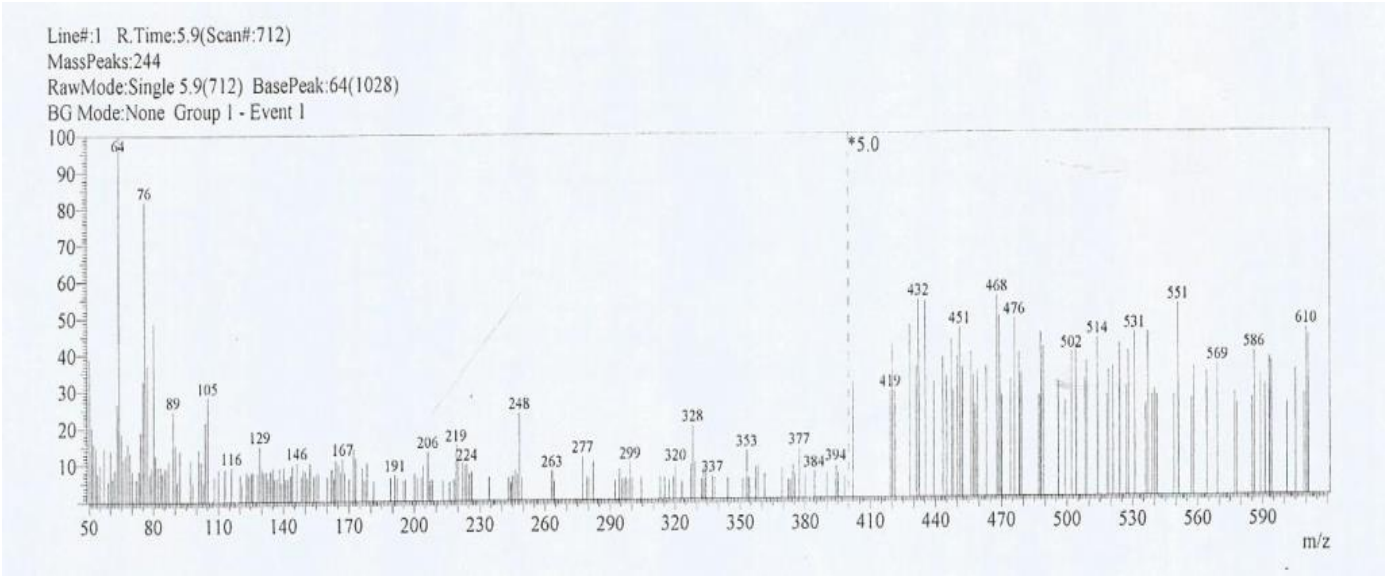
Appendix (50) MS spectrum of compound (IIIa)



Appendix (51) MS spectrum of compound (IIIb)



Appendix (52) MS spectrum of compound (IIIc)



Appendix (53) MS spectrum of compound (IIId)