T.C.
İSTANBUL UNIVERSITY-CERRAHPAŞA
INSTITUTE OF GRADUATE STUDIES

M.Sc. THESIS

SYNTHESIS AND CHARACTERIZATION OF NOVEL 2,3-DI(SUBSTITUTED)NAPHTHOQUINONE COMPOUNDS

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FOREWORD

Praise be to God who enabled me to overcome many difficulties and complete my study. I am really grateful to my supervisor Prof. Dr. Zeliha Gökmen who has never spared any effort to help me finish my thesis. All respect and appreciation for her.

My husband and my parents surely deserve my love and appreciation for their support, encouragement, and trust.

December 2018 Heba ALAHMAD

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LIST OF ABBREVIATIONS

Abbreviation	Explanation
NQ	: Naphthoquinone
EtOH	: Ethanol
AcOH	: Acetic acid
KO_2	: Potassium superoxide
Na_2CO_3	: Sodium carbonate
H_2O_2	: Hydrogen peroxide
$CHCl_3$	: Chloroform
CH_2Cl_2	: Dichloromethane
SeO_2	: Selenium dioxide
$CaCl_2$	: Calcium cloride
Ar-C's	: Aromatic carbons
rt	: room temperature

ÖZET

YÜKSEK LİSANS TEZİ

Heba ALAHMAD

YENİ 2,3-Dİ (SÜBSTİTÜE) NAFTAKİNON BİLEŞİKLERİNİN SENTEZİ VE KARAKTERİZASYONU

İstanbul Üniversitesi-Cerrahpaşa

Lisansüstü Eğitim Enstitüsü

Kimya Anabilim Dalı

Danışman : Prof. Dr.Zeliha GÖKMEN

Bu çalışmada, yeni sübstitüe naftakinon bileşikleri, N-, S- nükleofilleri ile dört başlangıç maddeleri olan naftakinon bileşiklerinin reaksiyonları ile sentezlenmiştir.

2-(1-(2-siyanofenil)piperazinil)-3-kloro-1,4-naftakinon bileşiği **(2)**, 2,3-diklor-1,4-NQ bileşiği **(1)'** nin 1-(2-siyanofenil)piperazin bileşiğinin reaksiyonu ile sentezlendi. Bu bileşik yeni bir bileşiktir ve başlangıç maddesi olarak kullanılmıştır.

Yeni 2-(1-(2-siyanofenil)piperazinil)-3-(2-hidroksietiltiyo)-1,4-NQ **(3)**, 2-(1-(2-siyanofenil)piperazinil)-3-(4-hidroksibütiltiyo)-1,4-NQ **(4)**, 2-(1-(2-siyanofenil)piperazinil)-3-(2-hidroksi-1-propiltiyo)-1,4-NQ **(5)** ve 2-(1-(2-siyanofenil)piperazinil)-3-(6-hidroksiheksiltiyo)-1,4-NQ **(6)** bileşikleri **(2)** bileşiğinin EtOH/Na_2CO_3' da bazı S-nükleofiller (2-merkaptoetanol, 4-merkapto-1-bütanol, 1-merkapto-2-propanol, 6-merkaptoheksanol) ile reaksiyonundan sentezlendi.

2,3-Diklor-1,4-NQ **(1)** ile 6-amino-1-heksanol'un reaksiyonundan bilinen 2-(6-aminoheksil-1-ol)-3-kloro-1,4-NQ bileşiği **(7)** sentezlenmiştir. Yeni 2-(6-aminoheksil-1-ol)-3-(2-hidroksietiltiyo)-1,4-NQ **(8)**, 2-(6-aminoheksil-1-ol)-3-(4-hidroksibutiltyio)-1,4-NQ**(9)**, 2-(6-aminoheksil-1-ol)-3-(6-hidroheksiltiyo)-1,4-NQ **(10)**, 2-(6-aminoheksil-1-ol)-3-(11-hidroksiundesiltiyo)-1,4-NQ **(11)**, 2-(6-aminoheksil-1-ol)-3-(2-klorobenzenmetiltiyo)-1,4-NQ **(12)** ve 2-(6-aminoheksil-1-ol)-3-(2-feniletiltiyo)-1,4-NQ **(13)** bileşikleri **(7)** bileşiğinin sırasıyla 2-merkaptoetanol, 4-merkapto-1-bütanol, 6-merkaptoheksanol, 11-merkapto-1-undekanol, 2-klorobenzilmerkaptan ve 2-fenil-etantiyol reaksiyonundan elde edildi.

Bilinen 2-(1-piperonilpiperazin-1-ol)-3-kloro-1,4-NQ bileşiği **(14)**, 2,3-diklor-1,4-naftakinon(NQ) **(1)** bileşiğinin 1-piperonilpiperazin ile kloroformda oda sıcaklığında reaksiyondan sentezlendi. Yeni 2-(1-piperonilpiperazin-1-ol)-3-(2-hydroksietiltiyo)-1,4-NQ **(15)**,2-(1-piperonilpiperazin-1-ol)-3-(4-hidroksibütiltiyo)-1,4-NQ **(16)**, 2-(1-piperonilpip-

erazin-1-ol)-3-(6-hidroksi-heksiltiyo)-1,4-NQ **(17)**,2-(1-piperonilpipe-razin-1-ol)-3-(2-hidroksi-1-propiltiyo)-1,4-NQ **(18)** ve 2-(1-piperonilpiperazin-1-ol)-3-(11-hidroksiundesiltiyo)-1,4-NQ **(19)** bileşikleri **(14)** bileşiğinin S-nükleofiller (2-merkaptoetanol, 4-merkapto-1-bütanol, 6-merkaptoheksanol, 1-merkapto-2-propanol, 11-merkapto-1-undekanol) ile reaksiyonundan kazanıldı.

Sentezlenen yeni onaltı bileşik kromatografik yöntemlerle saflaştırılmıştır. Bileşiklerin yapısı MS, IR, ^{1}H NMR ve ^{13}C NMR vb. spektroskopik yöntemler ile incelendi.

Aralık 2018, 142 sayfa.

Anahtar kelimeler: Naftakinon türevleri, N-nükleofiller, S-nükleofiller, 2,3-Disübstitüe-1,4-naftakinon bileşikleri.

SUMMARY

M.Sc. THESIS

SYNTHESIS AND CHARACTERIZATION OF NOVEL 2,3-DI(SUBSTITUTED)NAPHTHOQUINONE COMPOUNDS

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Institute of Graduate Studies

Department of Chemistry

Supervisor : Prof. Dr.Zeliha GOKMEN

In this work, new substituted naphthoquinone compounds were synthesized by the reactions of N- , S- nucleophiles with four naphthoquinone (NQ) compounds which were used as starting materials.

2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ compound **(2)** was synthesized by the reaction of 2,3-dichloro-1,4-NQ compound **(1)** with 1-(2-cyanophenyl)piperazine. This compound is new and was used as starting material.

New compounds 2-(1-(2-cyanophenyl)piperazinyl)-3-(2-hydroxyethylthio)-1,4-NQ **(3)**, 2-(1-(2-cyanophenyl)piperazinyl)-3-(4-hydroxybutylthio)-1,4-NQ **(4)**, 2-(1-(2-cyanophenyl)piperazinyl)-3-(2-hydroxy-1-propylthio)-1,4-NQ **(5)** and 2-(1-(2-cyanophenyl)piperazinyl)-3-(6-hydroxyhexylthio)-1,4-NQ **(6)** were synthesized by the reaction of compound (**2)** with some S-nucleophiles (2-mercaptoethanol**,** 4-mercapto-1-butanol, 1-mercapto-2-propanol and 6-mercaptohexanol) in Na_2CO_3/ EtOH.

2,3-Dichloro-1,4-NQ **(1)** was reacted with 6-amino-1-hexanol, and known 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ compound **(7)** was synthesized. New compounds 2-(6-aminohexyl-1-ol)-3-(2-hydroxyethylthio)-1,4-NQ **(8)**, 2-(6-aminohexyl-1-ol)-3-(4-hydroxybutylthio)-1,4-NQ **(9)**, 2-(6-aminohexyl-1-ol)-3-(6-hydroxyhexylthio)-1,4-NQ **(10)**, 2-(6-aminohexyl-1-ol)-3-(11-hydroxyun-decylthio)-1,4-NQ **(11)**, 2-(6-aminohexyl-1-ol)-3-(2-chlorobenzene-methylthio)-1,4-NQ **(12)** and 2-(6-aminohexyl-1-ol)-3-(2-phenylethylthio)-1,4-NQ **(13)** were obtained from the reaction of compound **(7)** with 2-mercaptoethanol, 4-mercapto-1-butanol, 6-mercaptohexanol, 11-mercapto-1-undecanol, 2-chlorobenzylmercaptane and 2-phenyl-ethanethiol, respectively.

The known 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ compound **(14)** was synthesized from the reaction of compound **(1)** with 1-piperonylpiperazine in chloroform at room temperature. New compounds 2-(1-piperonylpiperazin-1-yl)-3-(2-hydroxyethylthio)-1,4-NQ **(15)**, 2-(1-piperonylpiperazin-1-yl)-3-(4-hydroxybutylthio)-1,4-NQ **(16)**, 2-(1-piperonylpiperazin-1-yl)-3-(6-hydroxyhexylthio)-1,4-NQ **(17)**, 2-(1-piperonylpiperazin-1-yl)-3-(2-hydroxy-1-propylthio)-1,4-NQ **(18)** and 2-(1-piperonylpiperazin-1-yl)-3-(11-hydroxyundecylthio)-1,4-NQ **(19)** were obtained from the reaction of compound **(14)** with S-nucleo-philes (2-mercaptoethanol, 4-mercapto-1-butanol, 6-mercaptohexanol, 1-mercapto-2-propanol and 11-mercapto-1-undecanol).

The new sixteen compounds which were synthesized were purified by chromatographic methods. The structure of the compounds was determined by spectroscopic methods such as MS, IR, ^{1}H NMR and ^{13}C NMR.

December 2018, 142 pages.

Keywords: Naphthoquinone Derivatives, N-nucleophiles, S-nucleophiles, 2,3-Disubstituted-1,4-naphthoquinone compounds.

1. INTRODUCTION

Quinones have many applications in chemistry, biology and medicine [1]. Quinones, particularly derivatives of naphthoquinones, are found frequently in animals and have been repeatedly isolated from higher and lower species of plants. In addition to quinones having biological function as electron carriers in cell metabolism, this class have other compounds that have been found active against fungi and bacteria [2].

There are many studies showing that quinone compounds exhibit properties such as antiviral [3], antibacterial [4], anticancer [5], anti-artherosclerotic [6] and anti-inflammatory effects[7]. Additionally, hetero 1,4-naphthoquinones showed strong biological affinity for malarial, leishmanial and molluscidal diseases and this is due to their redox properties [8, 9, 10]. Many drugs are known to have the structure of quinones such as saintopin, daunorubicin, anthracyclines and mitomycin which are used for the treatment of cancer [11,12,13].

Really, 1,4-naphthoquinone has a biological importance that make chemists interested in synthesizing new derivatives of this kind of compounds [14]. However, the importance of quinones is not limited for their biological activity. These compounds are also used as magnetic materials, photo-conductors and dyes [15].

Naphthoquinones can react with aliphatic and aromatic nucleophiles such as amines and thiols. As a result, (N- and S-) substituted naphthoquinones can be synthesized. Actually, 1,4-naphthoquinones which are substituted with N- and S- nucleophiles are reported to have an observable increase in their biological activity profile [16].

In this study, 2,3-dichloro-1,4-naphthoquinone and other three naphthoquinone compounds, prepared in laboratory, were used as starting materials. New compounds were synthesized by carrying out reactions of naphthoquinones with one derivative of piperazine and different thiols at room temperature.

In the first part of this study; general information, nomenclature, physical and chemical properties, synthesis methods, reactions and uses of quinones and naphthoquinones, thiols and piperazines are given.

Secondly, all the reactions of naphthoquinones with N- and S- nucleophiles were investigated and new compounds were synthesized. The new compounds synthesized in this work are

thought to contribute to the literature of organic chemistry and we hope that they will provide support for a new work and exhibit a biological activity.

1.1. GENERAL SECTIONS

In this part of the thesis, general information has been given about quinones and naphthoquinones, thiols and piperazines which were used as starting materials.

1.1.1. Quinones

1.1.1.1. General Inoformation about Quinones

Quinone is a common name for a group of cyclic organic compounds. They are colored dioxo derivatives of dihydroaromatic systems. In these compounds, oxygen atoms are bonded as carbonyl groups and are located either ortho or para to each other. Thus, benzene forms the nucleus for two quinones, o- and p- quinone (o- and p-benzoquinone) which are shown in Figure 1.1. Metaquinone does not exist [17].

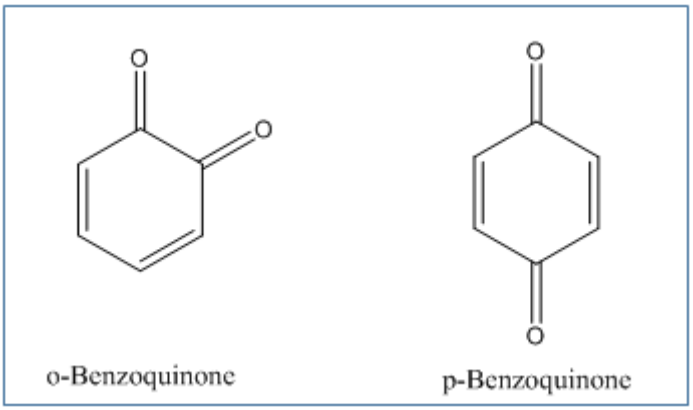
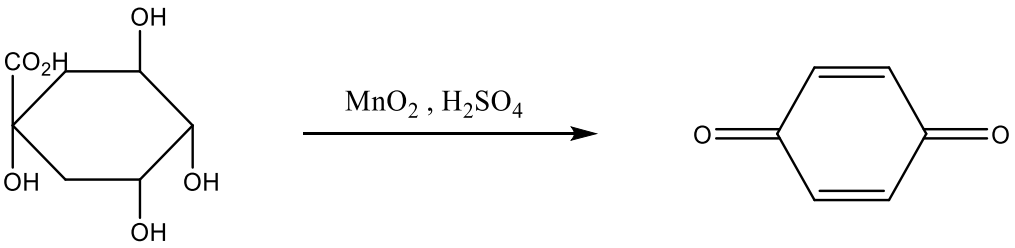


Figure 1.1: Structure of o- and p-benzoquinone

o-Benzoquinone has little practical value and it is less commonly than p-benzoquinone which is most commonly.

The simplest member of quinones was obtained in 1838. During the transformation of quinic acid to quinone dehydration, decarboxylation and oxidation occur [18, 19].



Quinic acid Quinone

(1.1)

Quinones are mainly classified into three categories: benzoquinone, naphthoquinone and anthraquinone [20].

1.1.1.2. Nomenclature of Quinones

Quinones are usually referred to by a prefix (benzo-, naphtho- and anthra-) and the quinone suffix. (Benzoquinone, naphthoquinone) [21].

Three quinones are formed corresponding to naphthalene, they are: 1,2- , 1,4- and 2,6-naphthoquinones shown in Figure 1.2. Anthracene shoud be able to form eight quinones, of which three are known, 1,2- , 1,4- and 9,10-anthraquinone shown in Figure 1.3 [22].

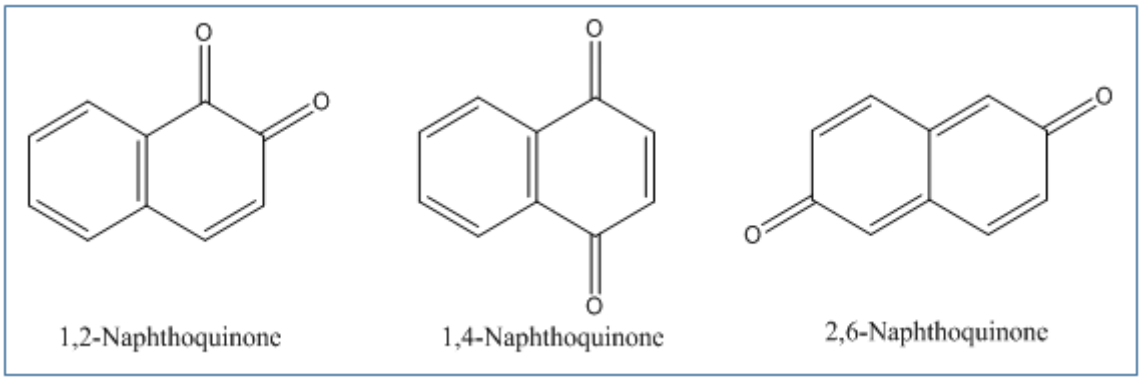


Figure 1.2: Structures of 1,2- ; 1,4- ; 2,6-naphthoquinones

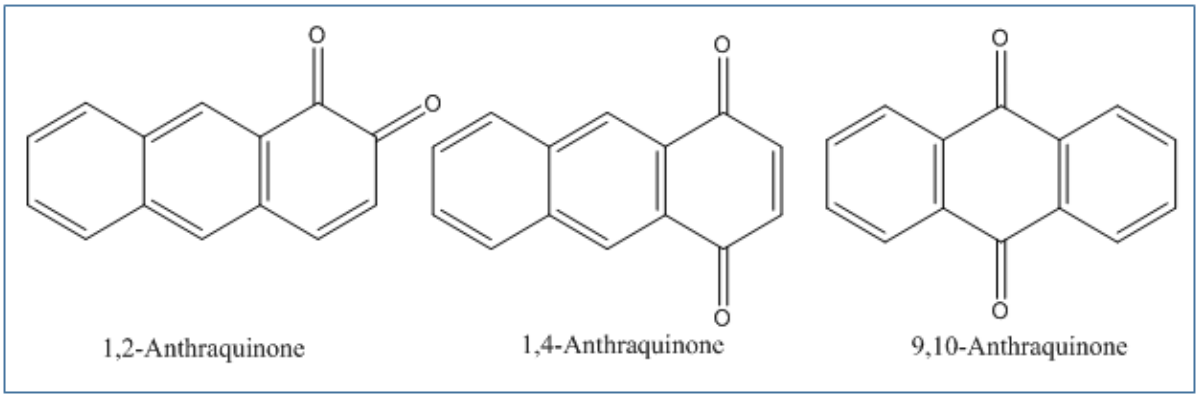


Figure 1.3: Structures of 1,2- ; 1,4- ; 9,10-anthraquinones

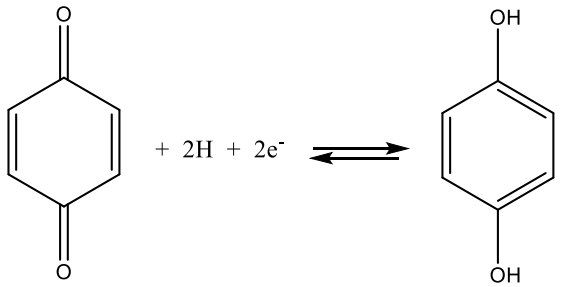
1.1.1.3. Physical and Chemical Properties of Quinones

One of the features of quinones is color and a general distinction between ortho and para quinones is that most of para quinones are yellow and the majority of ortho quinones are red or orange.

p-Benzoquinone has a bright yellow crystalline structure with a melting point of 115-116 ºC and it sublimes easily, it can be distilled with water vapors, and has a strange odor that causes sneezing, it is soluble in water, alcohol, ether and other organic solvents.

Naphthoquinones are generally yellow and has an odor like that of p-benzoquinone. It has a melting point of 125-128 ºC [23].

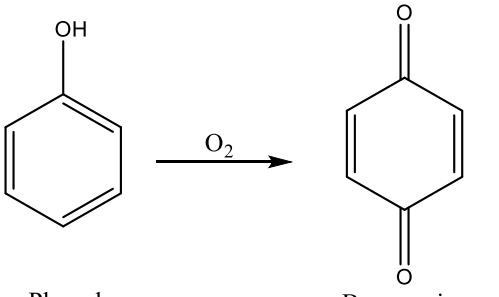
Quinones can be converted to dihydroxy phenols, i.e., hydroquinones, by reduction. Quinone and hydroquinone combine directly in equimolar proportions to give quinhydrone, which is a black crystalline solid and gives intense colored solutions. In aqueous solution it behaves as an equimolar mixture of quinone and hydroquinone [24]. Commertially, p-benzoquinone is reduced to hydroquinone by a suspension of iron powder in water [25].



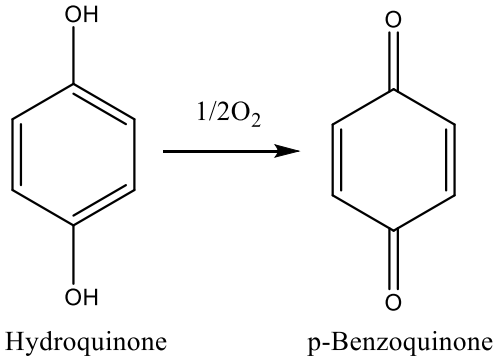
(1.2)

1.1.1.4. Synthesis of Quinones

Usually, quinones are synthesized by oxidation, since it is the only completely general method. Phenols and hydroquinones can be oxidized to quinones.

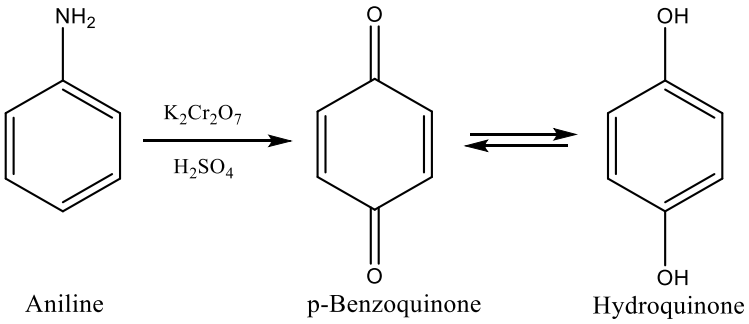


(1.3)



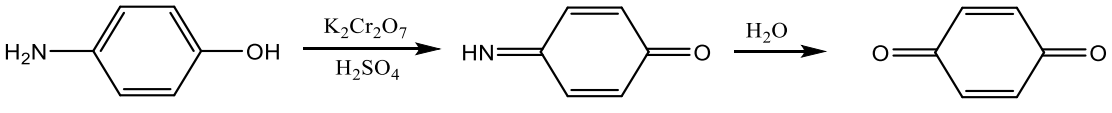
(1.4)

p-Benzoquinone can also be prepared by the oxidation of aniline as shown in the following equation:



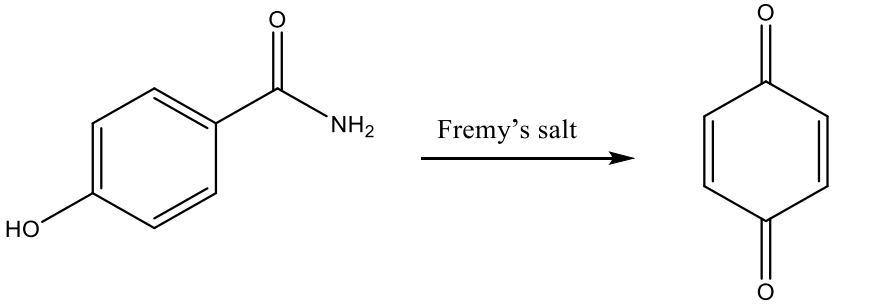
(1.5)

Quinones also can be obtained by oxidation from o- or p-aminophenols as shown in the following equation:



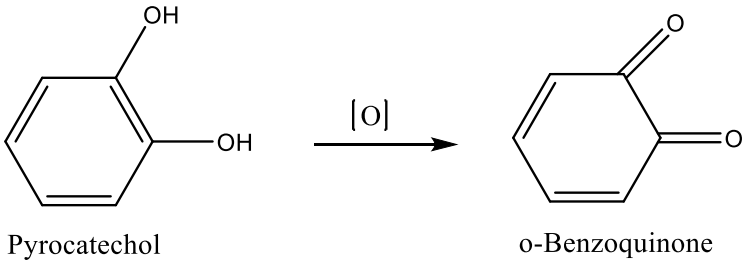
p-Aminophenol p-Benzoquinone (1.6)

Furthermore, quinones can be prepared by oxidative degradation of benzamide derivatives using Fremy's salt, $K_2NO(SO_3)_2$, and this transformation is limited with very few substrate.



4-hydroxybenzamide 1,4-Benzoquinone (1.7)

o-Benzoquinone can be achieved from the oxidation of pyrocatechol as below [26].



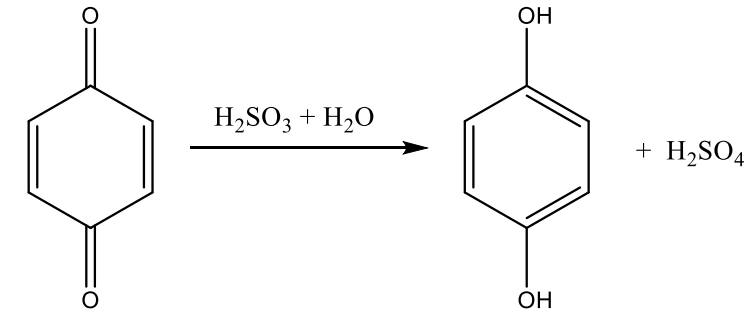
Pyrocatechol o-Benzoquinone (1.8)

1.1.1.5. Reactions of Quinones

In fact, quinones participate in a large number of reactions [27].

Reduction reaction;

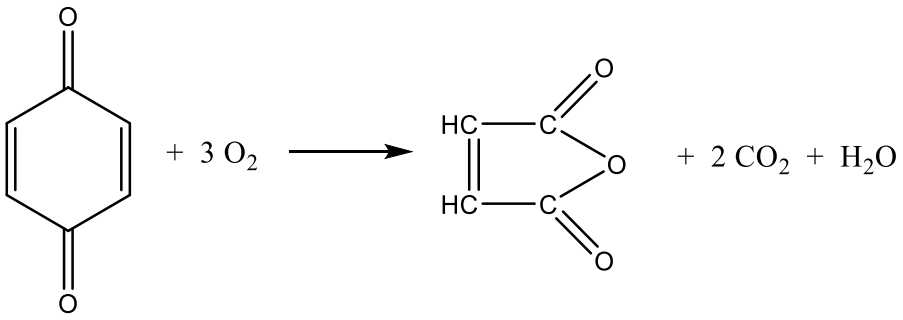
Hydroquinones are obtained by reduction of the quinones. The most suitable reducing agent is SO_2 [28].



p-Benzoquinone Hydroquinone (1.9)

Oxidation reaction;

Oxidation of quinone leads to degradation of ring structure and formation of maleic anhydride [29].

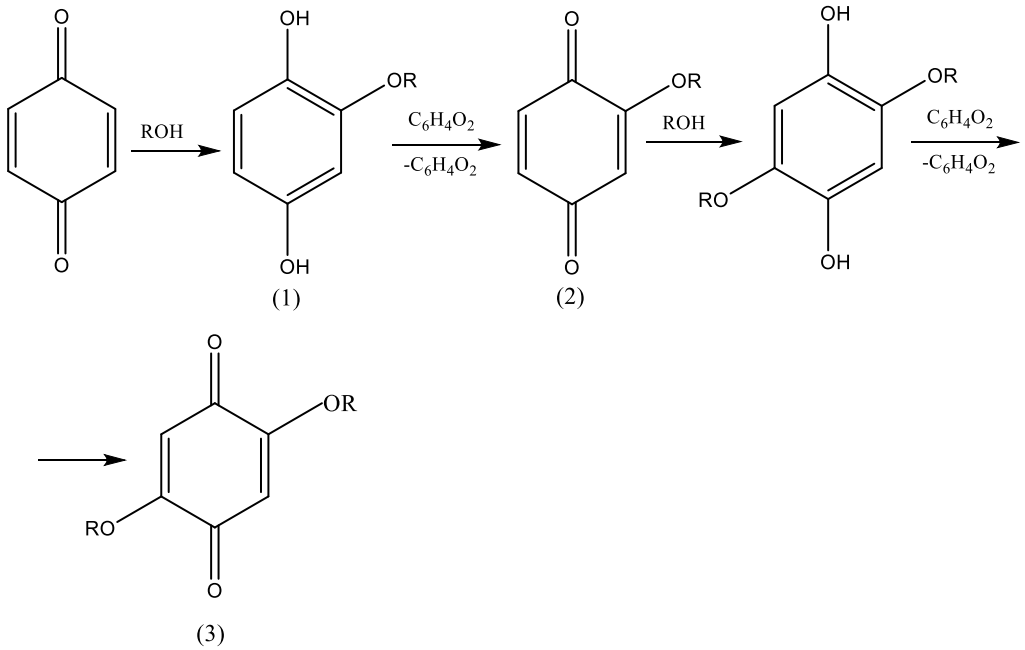


maleic anhydride (1.10)

Nucleophilic addition reactions;

Reactions with alcohols;

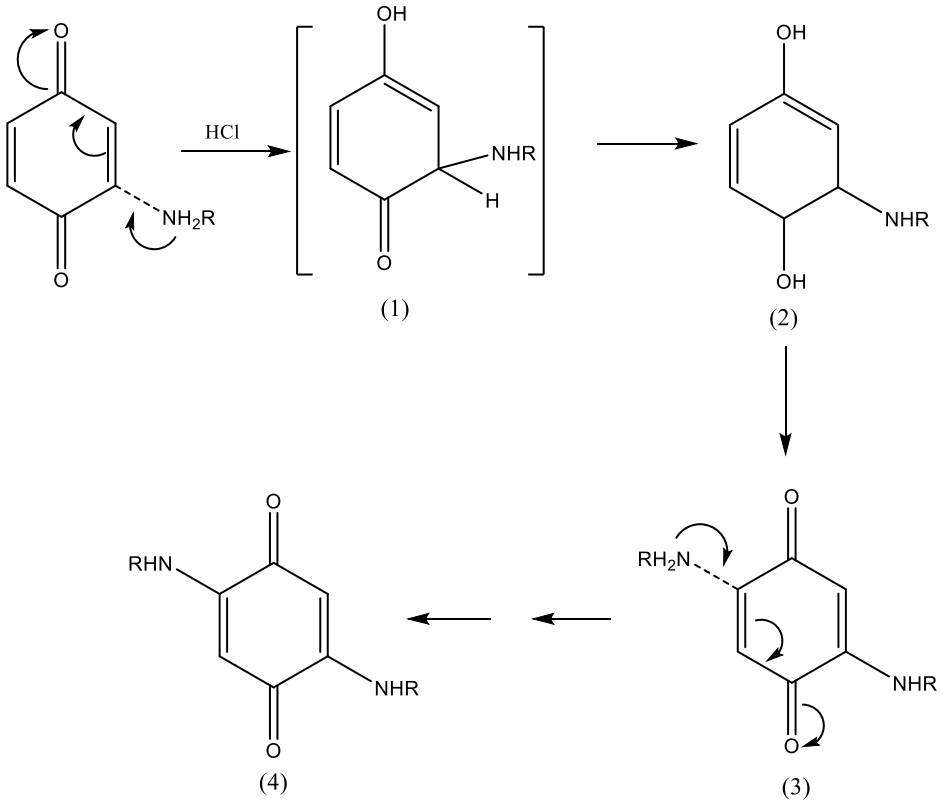
Quinones react with alcohols in Magnesium/ Cadmium/ Zinc or Calcium catalyst. In the first stage, the alkoxyhydroquinone (1) is formed; which is then oxidised to alkoxyquinone (2) by the starting quinone. After the addition of a second molecule of alcohol to the latter; 2,5-dialkoxy-l,4-benzoquinone (3) is formed as a final product. [30, 31, 32].



(1.11)

Reactions with R-NH_2;

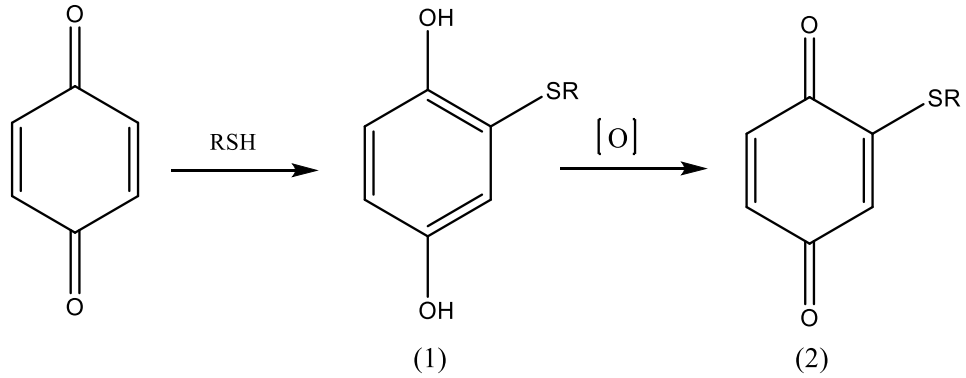
In the reaction of R-NH_2 with 1,4-benzoquinones, 2,5-diamino-1,4-benzoquinone is formed as the final product. The intermediate (1) isomerises to aminohydroquinone (2) followed by oxidation to the monoaminoquinone (3). The diaminoquinone (4) is then formed by the addition of a second molecule of amine.



(1.12)

Reactions with thiols;

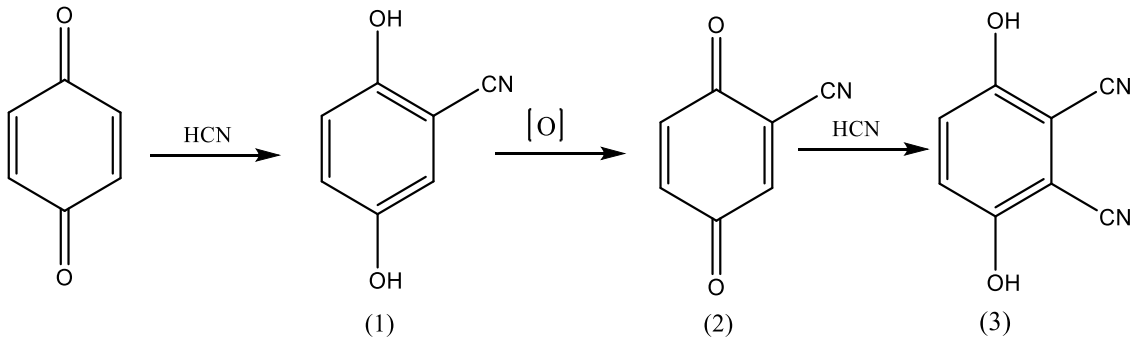
1,4-Quinone react with thiols and thiophenols to give 1,4-adduct (1), which is then oxidised by the starting quinone or by air to give arylthio- or alkylthioquinone (2).



(1.13)

Reactions with CN-acidic compounds;

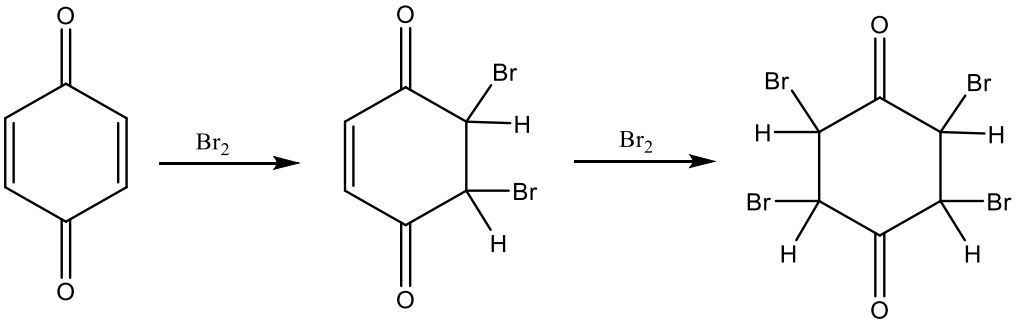
1,4-Benzoquinone react with hydrogen cyanide to give cyanohydroquinone (1). After oxidation, cyanoquinone (2) is formed. After a second molecule of hydrogen cyanide is added, dicyanohydroquinone (3) is formed. Here the second cyano group is added at the 3-position of the quinone unlike the other reactions which involve addition of nucleophiles at the 5-position in the mono-substituted 1,4-quinones. There is no clear explanation for this anomaly in the literature [27].



(1.14)

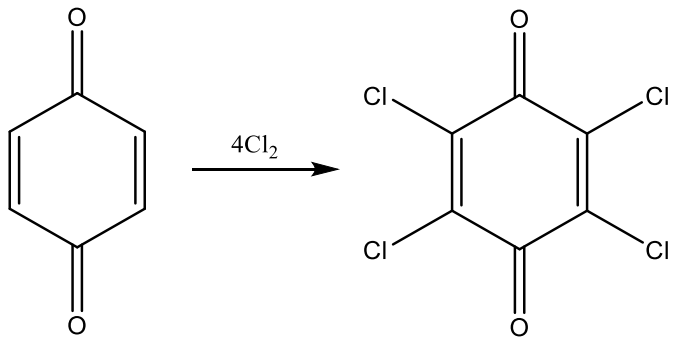
Reactions with halogens;

Addition of bromine to the double bonds of p-benzoquinone leads to the formation of 2,3,5,6-tetrabromo-1,4-benzoquinone.



(1.15)

In the above reaction bromine undergoes addition reaction with quinone, while with cholorine it will give substitution product as shown in the following equation: [33]

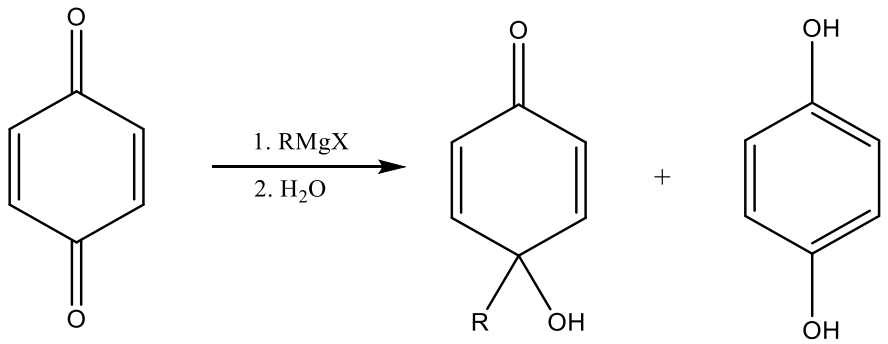


p-Chloranil

(1.16)

Reactions with Grignard reagents;

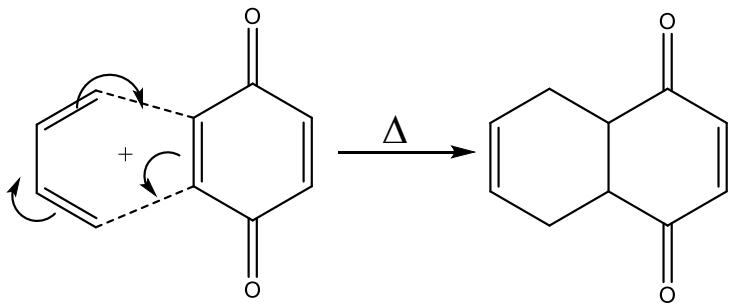
Quinones react with Grignard reagents leading to the formation of hydroquinone [34].



(1.17)

Dilels Alder reactions;

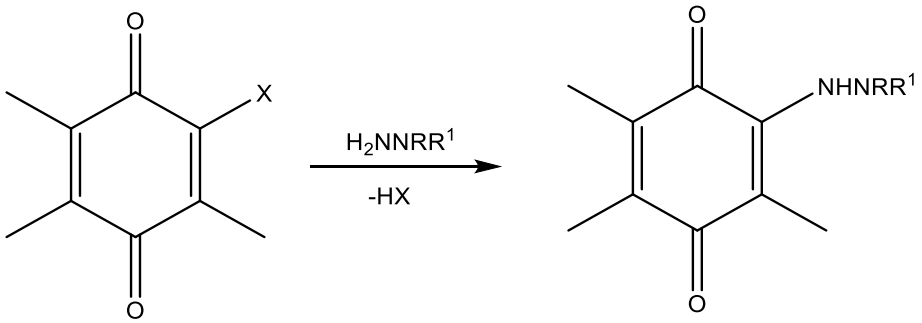
The reaction of quinones with dienes results in a ring formation (Diels-Alder) [35].



(1.18)

Nucleophilic substitution reactions;

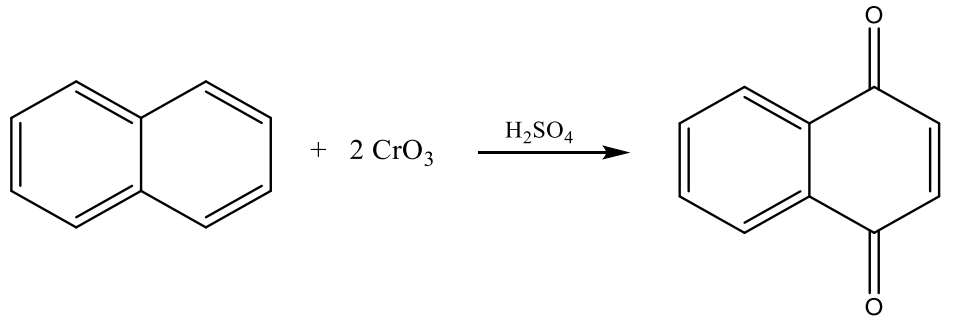
Substituted quinones can undergo nucleophilic substitution reactions when reacted with different nucleophiles such as amines, thiols and alcohols. As an example, the following equation is the reaction with hydrazines to give hydrazinoquinones [27].



(1.19)

1.1.1.6. Synthesis of Naphthoquinones

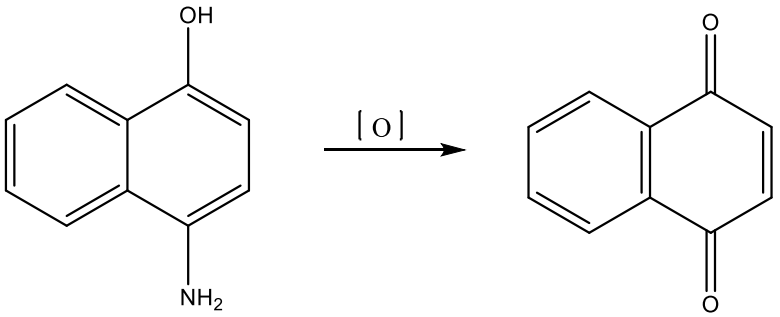
Synthesis of naphtaquinone is usually carried out by an oxidation reaction. 1,4-Naphthoquinone can be synthesized by oxidation of naphthalene as shown below [36].



1,4-Naphthoquinone

(1.20)

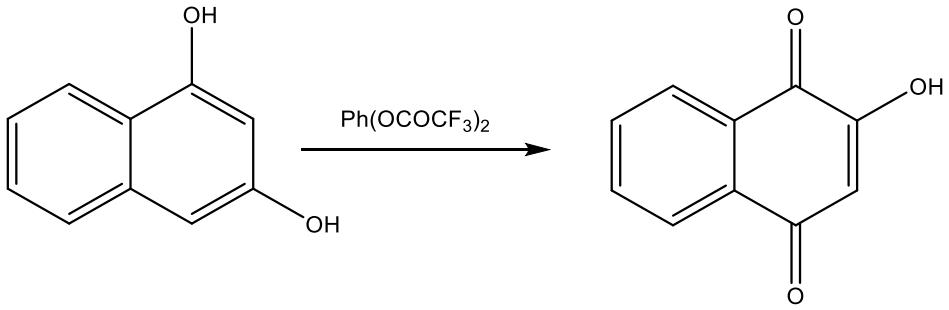
Oxidation of 4-amino-1-naphthol leads to the formation of naphthoquinone. The reaction occurs with an oxidizing agent such as CrO_3-AcOH and H_2O_2 [37].



4-Amino-1-naphthol 1,4-Naphthoquinone

(1.21)

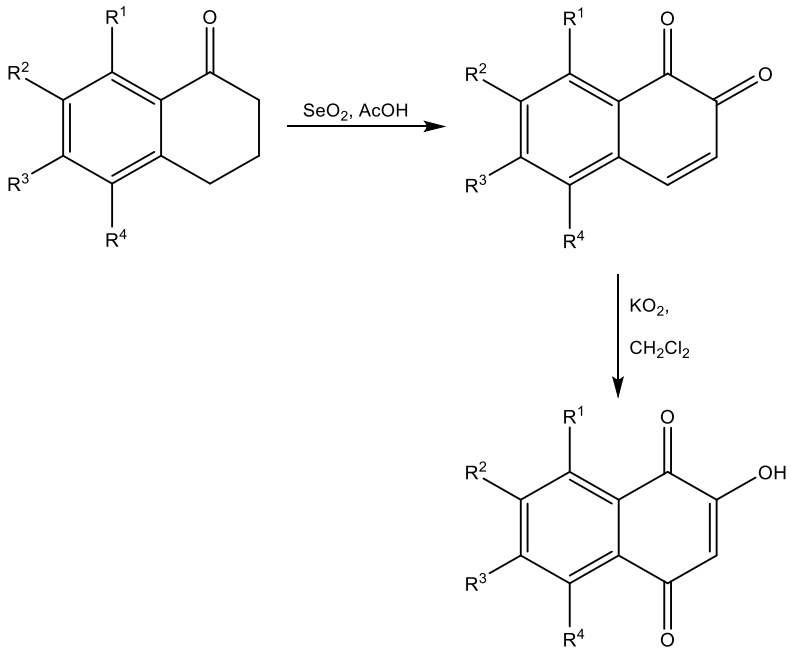
Oxidation of 1,3-dihydroxynaphthalene leads to the formation of naphtaquinone derivative.



1,3-Dihydroxynaphthalene 2-Hydroxy-1,4-Naphthoquinone

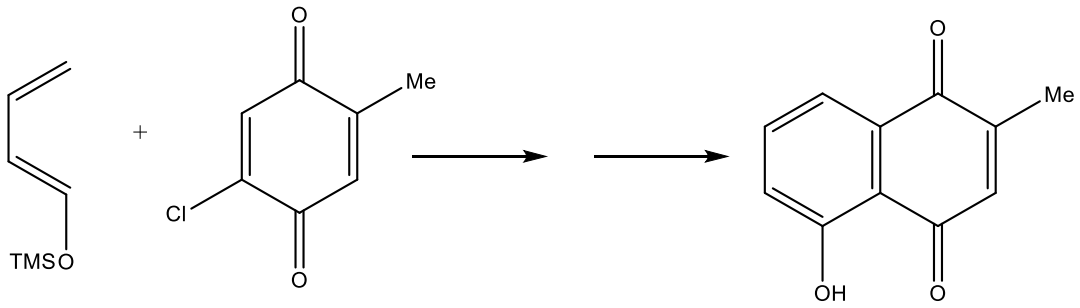
(1.22)

1,2-Naphthoquinones can be obtained in good yields, by oxidation of 1-tetralones with SeO_2 in AcOH, further oxidation with KO_2 in CH_2Cl_2 produces 2-hydroxy-1,4-naphthoquinones in excellent yields [38].



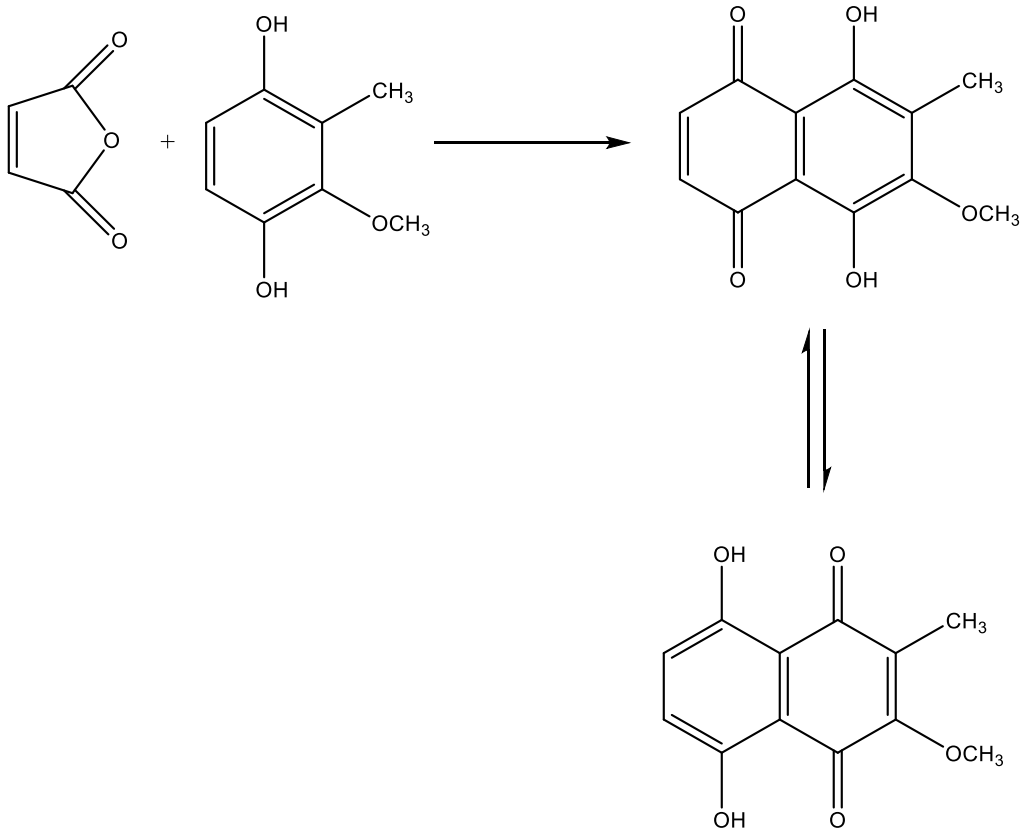
(1.23)

Another method for the synthesis of naphthoquinone is by Diels Alder reaction. Conjugated diene can react with quinones which contains olefinic bond between two carbonyl groups resulting in the formation of naphthoquinone.



(1.24)

Another method known for naphthoquinone synthesis is electrophilic reactions. In this method, H_2SO_4, $ZnCl_2$ and $AlCl_3$ can be used as catalysts. The quinone derivatives that are formed by this method get reduced to hydroquinone, due to this it is also effective for preparing poly-cyclic hydrocarbons [26].



5,8-Dihydroxy-2-methoxy-3-methyl-1,4-naphthoquinone

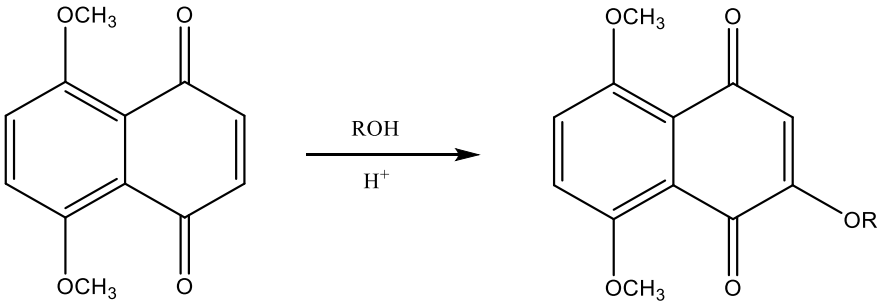
(1.25)

1.1.1.7. Reactions of Naphthoquinones

Naphthoquinones, due to having two rings attached side by side, are less reactive than benzoquinones, but their canbonyl functionl groups are more reactive.

Nucleophilic addition reactions;

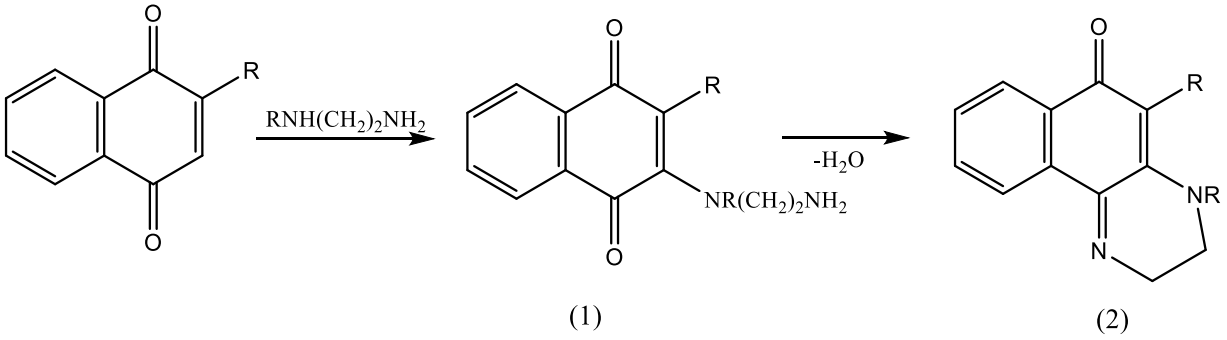
1,4-Naphtaquinone and its derivatives especially the ones which have electron donor substituent at 5 and 8 positions reacts with alcohols to give 2-alkoxy derivatives. In this reaction, the catalysts are sulfuric acid and iron sulfate.



(1.26)

Aliphatic amines react with 1,4-naphthoquinones leading to the formation of 2-amino-1,4-naphthoquinones.

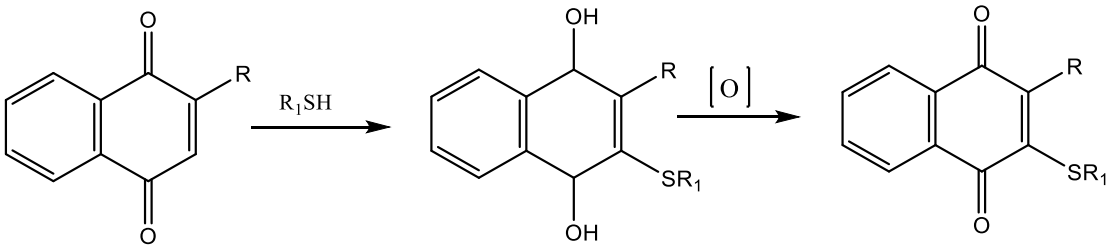
Reaction with diamines leads to the formation of an initial 1,4-adduct (1) and after losing a molecule of water a cyclic quinone imine (2) is produced.



(1) (2)

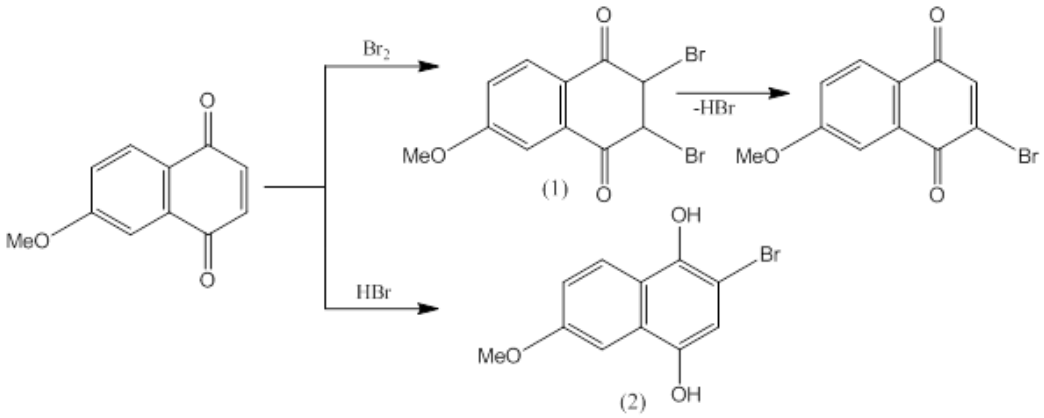
(1.27)

In the reaction of thiols with naphthoquinones, nucleophilic addition and oxidation take place resulting in the formation of alkyl thio- or arylthio-1,4-naphthoquinones.



(1.28)

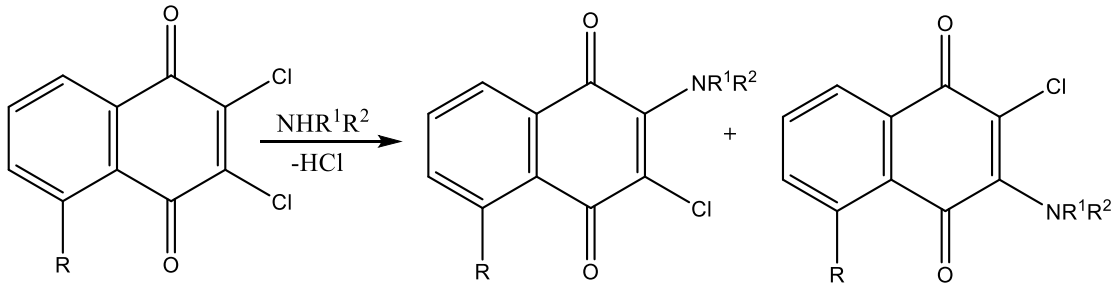
The reaction of bromine with 6-methoxy-1,4-naphthoquinone produce the adduct (1), while the reaction of the starting quinone with hydrogen bromide produce the nucleophilic addition product (2).



(1.29)

Nucleophilic substitution reactions;

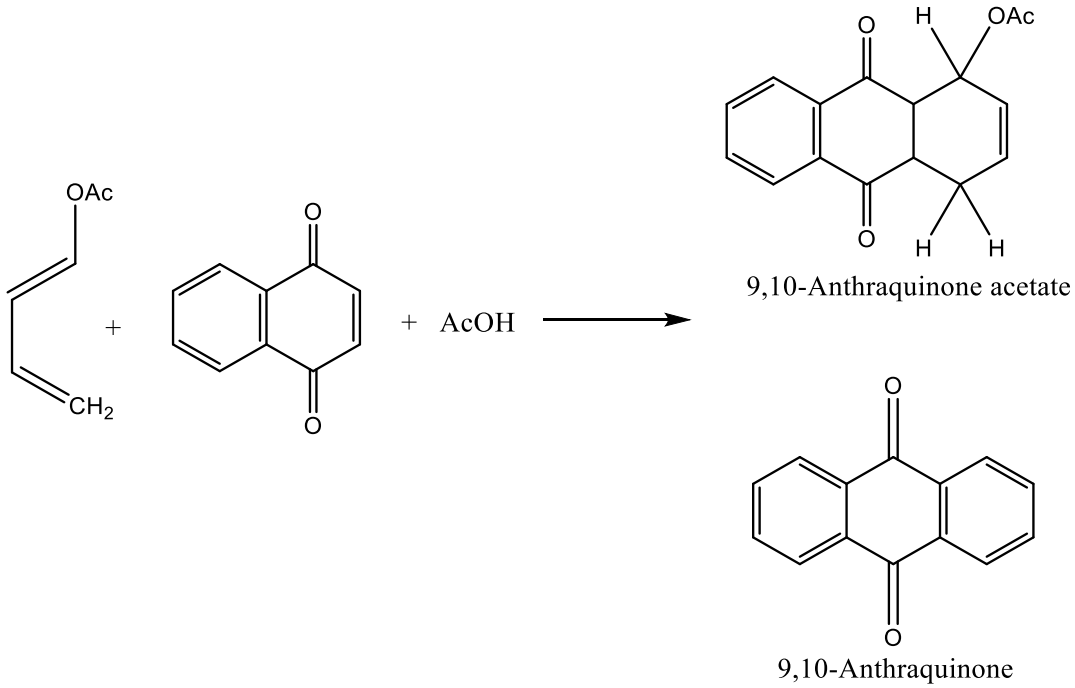
Halogen-substituted naphthoquinones can undergo nucleophilic substitution reactions when reacted with different nucleophiles such as amines, thiols and alcohols. As an example, the following equation is a reaction with amine resulted in the formation of mono amino derivatives [27].



(1.30)

Diels Alder Reactions;

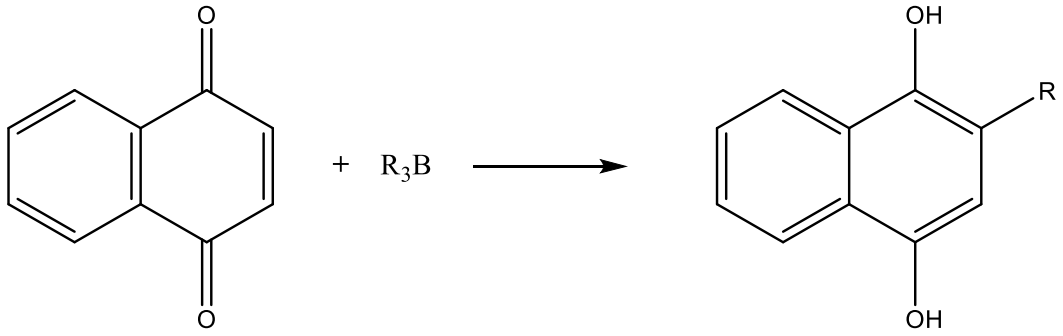
1,4-Naphthoquinone react with 1,3-butadiene acetate to produce 9,10-anthraquinone and 9,10-anthraquinone acetate [39].



(1.31)

Reactions with alkyl borate;

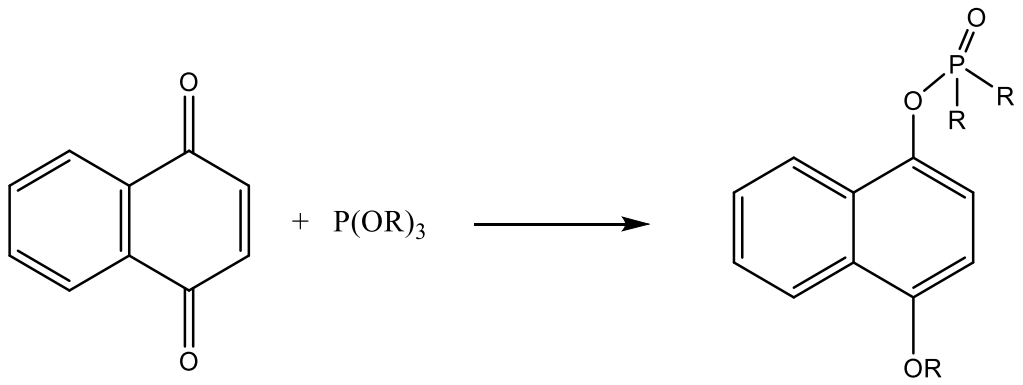
Naphthoquinones react with alkyl borate in a reduction reaction. [40].



(1.32)

Reactions with trialkyl phosphite;

Naphthoquinones undergo addition reactions with trialkyl phosphite as shown in the following equation:



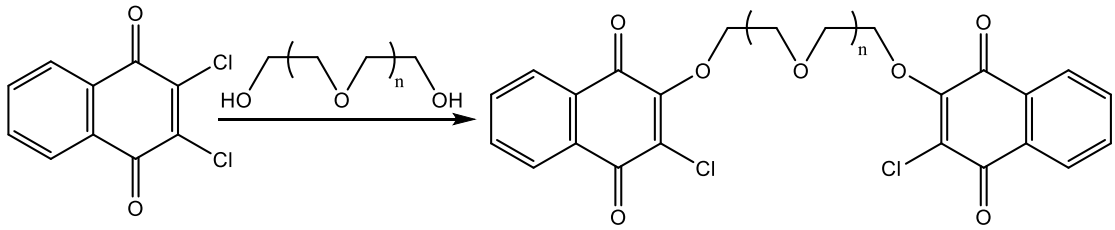
(1.33)

1.1.1.8. Uses of Quinones and Naphthoquinones

Examining reaction mechanisms of compounds having the structure of naphthoquinone (NQ) compounds is quite interesting. They are effective in human immune system. [41]

Some of naphthoquinones show also antimalarial, antiviral and antitumor activities.

2,3-Dichloro-1,4-NQ has been investigated for a long time in the last century and its practical applications have been found nowadays especially in the synthesis of crown ethers with naphthoquinone fragments [42].



(1.34)

Such substitution of all halogen atoms is only possible with active cyclic amines such as imidazoles, pyrazoles, 1,2,3- and 1,2,4-triazoles [43].

It has been known that quinones and their derivatives have significant biological effects. Vitamin K1, which is an important nutrition factor and very useful in maintaining blood coagulation properties, has 2-methyl-1,4-NQ structure. There are also other naphthoquinone compounds that have different numbers of carbon atoms in its side chain and exhibit vitamin K activity [44]. Figure 1.4 illustrates the structure of vitamin K1.

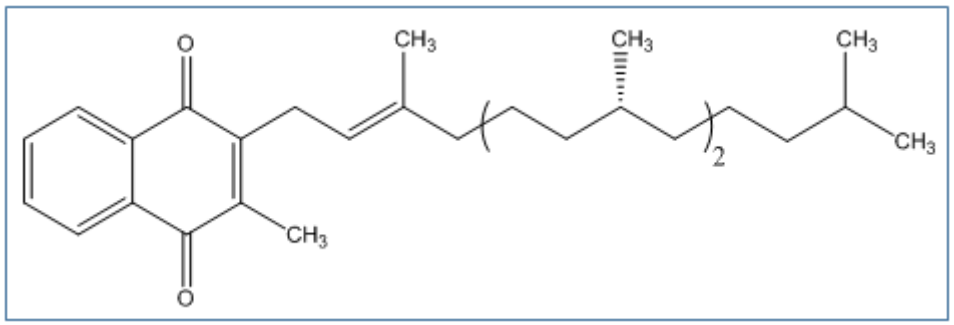


Figure 1.4: Structure of vitamin K1.

Quinone derivatives have antitumor properties (mitomycin C and doxorubicin are used as anticancer drugs with antitumor activity) [45,46,47]. Figure 1.5.

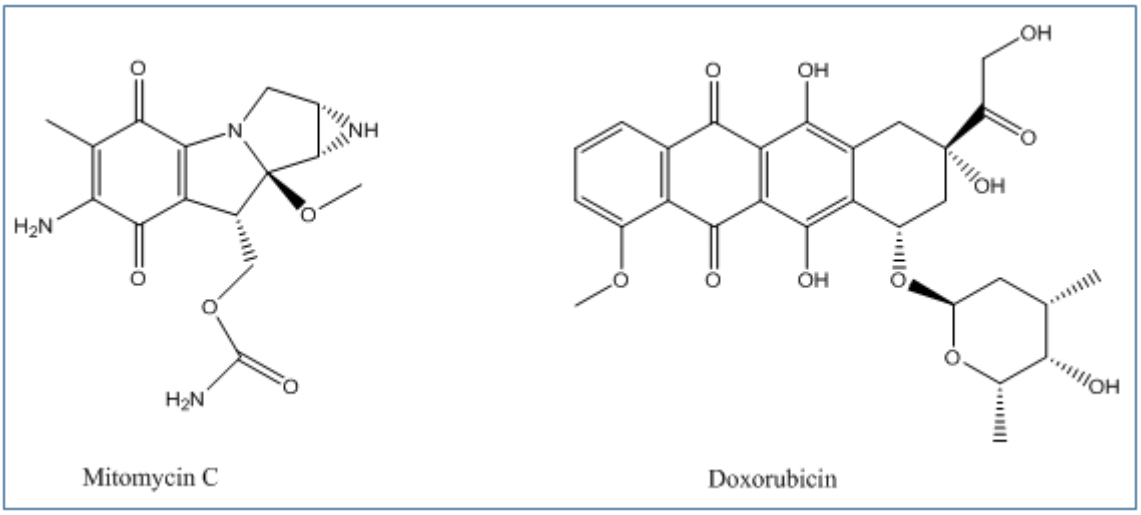


Figure 1.5: Structure of some medicinally important quinone derivatives**.**

p-Benzoquinone dioxime is used in the preparation of insecticide, bactericide and fungicide.

Plastoquinone and ubiquinone (Coenzyme Q10), that are shown in Figure 1.6, are given as an examples of biological active quinones. They catalyze some biochemical reactions in some animals, plants and microorganisms [48].

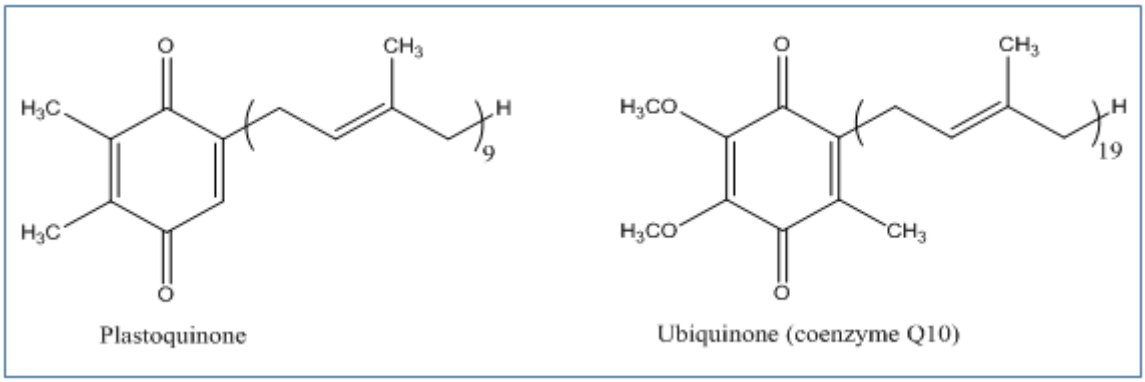


Figure 1.6: Structures of some biologically active quinones**.**

2,5-Dihydroxy-3-n-undecyl-*p*-quinone which is called Embelin, is used as a treatment for tapeworms. Figure 1.7 illustrate the structure of it.

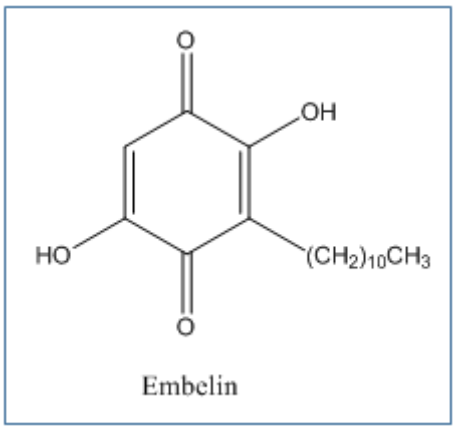


Figure 1.7: Embelin structure.

1.1.2. Thiols

1.1.2.1. General Information about Thiols

Thiols, also known as mercaptans, are similar to alcohols, but in thiols sulfur is used instead of oxygen. Many thiols have strong odors that is like the odor of rotten eggs or garlic. Thiols are used as odorants to aid in the detection of natural gas (which is odorless in its pure state), and the "smell of natural gas" originates from the odor of the thiol that is used as an odorant.

1.1.2.2. Nomenclature of Thiols

In 1834 Zeise synthesized the first thiol compound, ethanethiol [49]. He applied the name mercaptan to ethanethiol and this is because of its ability to remove mercury, as a crystalline precipitate, from solution. Mercaptan has been accepted as a descriptive name for most organic compounds that contain the –SH group. In 1930 the International Union of Chemistry Commission recommended the abandonment of the name mercaptan and adoption of thiol. In the thiol nomenclature, which is now commonly used, the name is derived from the hydrocarbon which have the longest straight chain; for example, ethyl mercaptan becomes ethanethiol. If more than one –SH group is present, then dithiol, trithiol, etc is used. Thus,

$HSCH_2CH_2CH_2SH$ is 1,3-propanedithiol, $HSCH_2CH(SH)CH_2CH_2SH$ is 1,2,4-butanetrithiol. For some compounds which have both –SH and another functional group, mercapto, which is retained in the IUPAC system in this situation, is used as a prefix. For example, $HSCH_2CH_2CH_2OH$ is 3-mercaptopropanol [23].

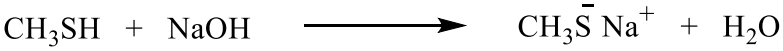
1.1.2.3. Physical and Chemical Properties of Thiols

The most characteristic feature of thiols is the unpleasant smell. With increasing the molecular weight, the odor decreases, and it has been found that 1-dodecanethiol does not have a disagreeable odor [50]. Table 1.1 contains some physical constants of some alkanethiols.

Table 1.1: Physical constants of some alkanethiols.

Compound	Formula	Boiling point, ºC	Freezing point, ºC	Refractive index, n_D^{20}	Density, d_4^{20}
methanethiol	CH_3SH	5.9	-122.97	1.4360	0,8665
ethanethiol	CH_3CH_2SH	35.0	-147.89	1.43105	0.83914
2-propanethiol	$CH_3CH(CH_3)SH$	52.6	-130.54	1.42554	0.81431
1-propanethiol	$CH_3CH_2CH_2SH$	67.8	-113.13	1.43832	0.84150
2-butanethiol	$CH_3CH_2CH(CH_3)SH$	85.0	-140.14	1.43673	0.82988
1-butanethiol	$CH_3(CH_2)_2CH_2SH$	98.4	-115.67	1.44298	0.84161
1-pentanethiol	$CH_3(CH_2)_3CH_2SH$	126.5	-75.7	1.44692	0.84209
1-hexanethiol	$CH_3(CH_2)_4CH_2SH$	152.6	-80.49	1.44968	0.84242
1-heptanethiol	$CH_3(CH_2)_5CH_2SH$	176.9	-43.23	1.45215	0.84310

Boiling points of thiols are lower than the corresponding alcohol and this is because that the hydrogen bonds in thiols are much weaker than those in alcohols. Also, thiols are more acidic than alcohols because of the weaker bondings between sulfur and hydrogen in comparison with those between oxygen and hydrogen and their proton can be removed by reaction with base.[51].

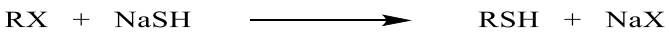


(1.35)

1.1.2.4. Synthesis of Thiols

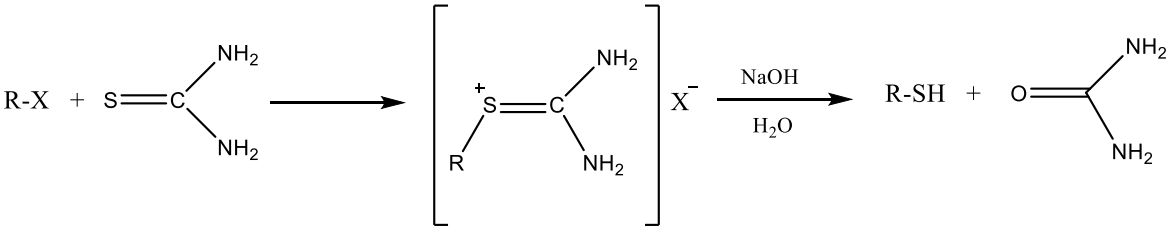
By Nucleophilic Substitution;

The reaction of organic halides with metallic hydrosulfides such as NaSH produces thiols directly as shown in the following equation [52]:



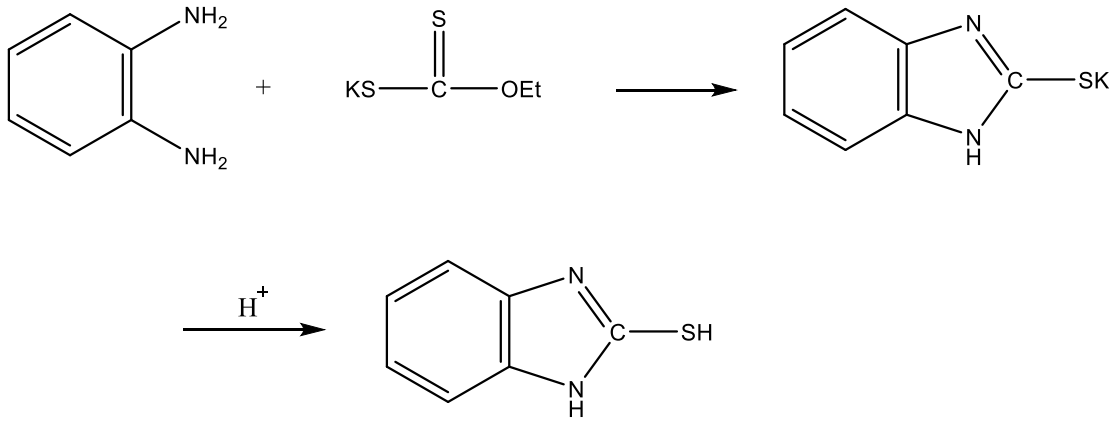
(1.36)

Thiols can be produced through the reaction of an alkylhalide with thiourea. Alkaline hydrolysis of thiouronium salt produces thiols [53].



(1.37)

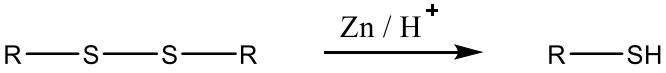
Xanthates can be used to prepare aromatic thiols as the following :



(1.38)

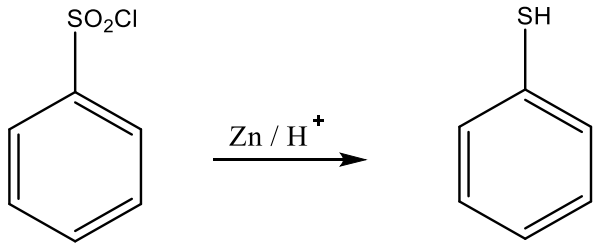
By Reduction;

Thiols can be prepared by the reduction of disulfide [54].



(1.39)

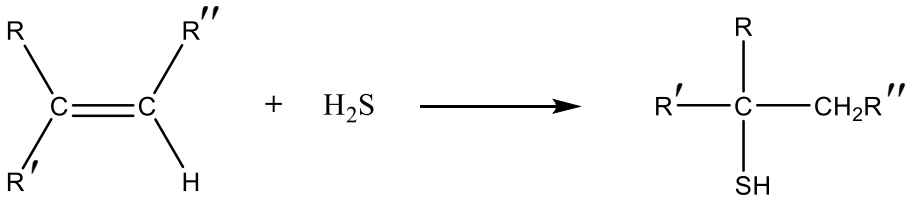
Also, reducing agents such as Zn-HCl, $LiAlH_4$ can be used to reduce sulfonyl chloride and prepare aromatic thiols [55].



(1.40)

By Addition to Olefins;

Hydrogen sulfide can be added to an olefin to produce thiol, the structure is predicted by Markovnikov's rule.



(1.41)

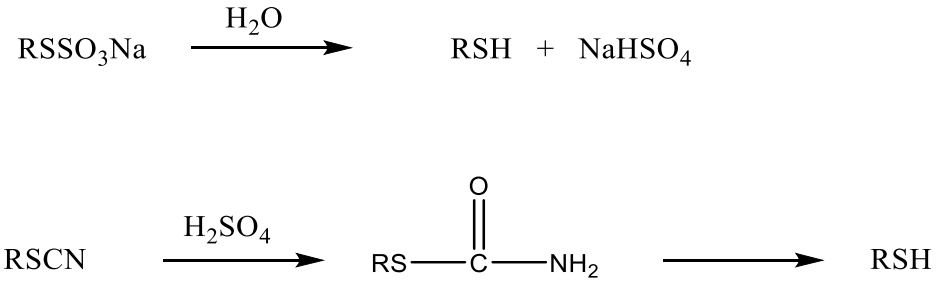
From Organometallics;

Grignard reagent can be used with elemental Sulfur to produce thiols [56].

(1.42)

Miscellaneous Methods;

There are other methods to prepare thiols. For example, thiosulfates and thiocyanates are used to synthesise thiols and in those reactions the functional group separates from the sulfur atom.

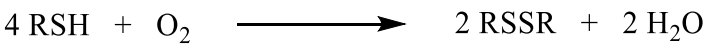


(1.43)

1.1.2.5. Reactions of Thiols

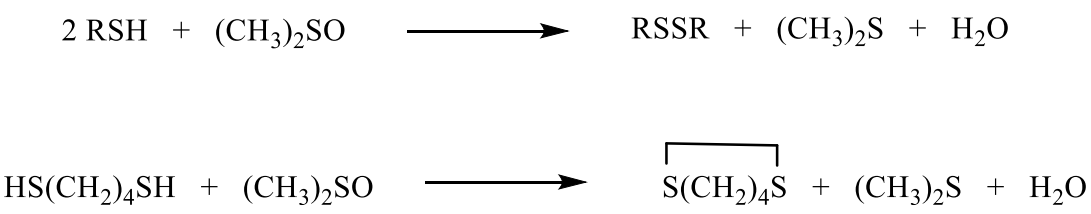
Oxidation:

In the presence of base, thiols can be oxidized to disulfides. This conversion can be done using molecular oxygen at low temperature, and is catalyzed by amines, metals and metal chelates.



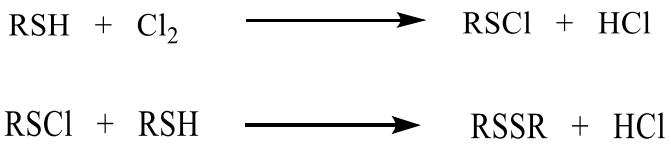
(1.44)

Oxidation to disulfide can be occurred by a variety of other mild oxidizing agents, such as manganese dioxide. When a thiol is heated with dimethyl sulfoxide, it will produce the disulfide and this method is applicable for producing cyclic disulfides from some terminal dithiols [57].



(1.45)

Under controlled conditions chlorine can be added to thiols to give the sulfenyl chloride, RSCl, which is considered to be reactive intermediates.



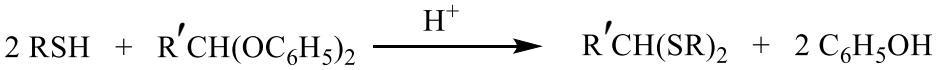
(1.46)

Addition to Carbonyls:

Aldehyde can be reacted with a thiol in an acid catalyzed reaction to produce mercaptals which are analogous to acetals. A hemimercaptal which is the intermediate carbonyl addition product is usually not stable to be isolated.

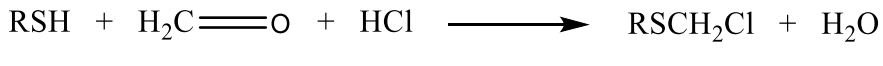
(1.47)

An interchange reaction between a thiol and diphenyl acetal also produce mercaptals.



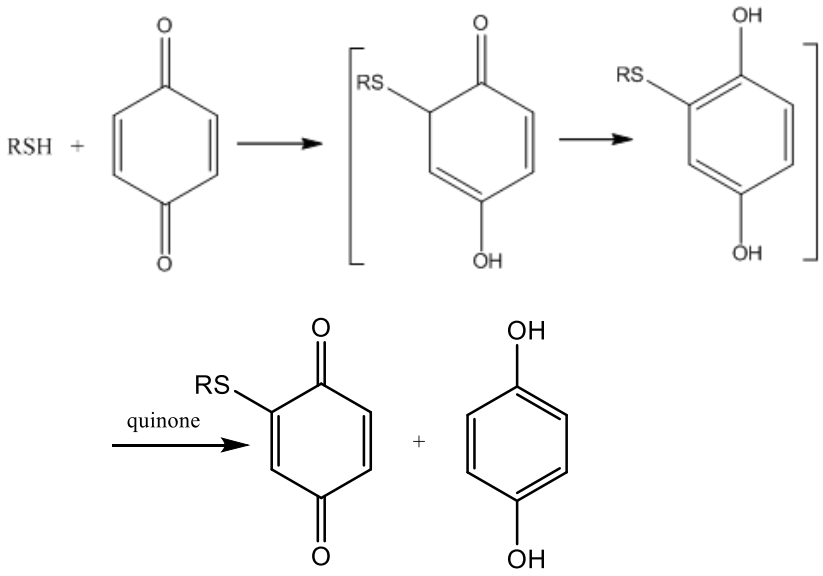
(1.48)

Addition of a hydrogen halide to a thiol-aldehyde mixture results in producing of an α-halothioether, this reaction is considered to be useful for the preparation of reactive chloromethyl sulfides.



(1.49)

Thiol can be added to quinones readily at room temperature to produce the hydroquinone product which is oxidized by the unreacted quinone and normally the product isolated is 2-alkyl (or aryl) thio-1,4-benzoquinone. [58].



(1.50)

Addition to Carbon-Carbon Multiple Bonds:

Thiol can be added to alkene and produce thioether. The adduct is formed through anti-Markownikoff addition under conditions generating free radicals, ie, with an azonitrile or peroxide or with ultraviolet irradiation; eg n-propyl sulfide is produced by the addition reaction of ethanethiol to propylene.

$$(C_2H_5SH \longrightarrow C_2H_5S\cdot) + CH_3CH{=}CH_2 \longrightarrow CH_3\dot{C}HCH_2SC_2H_5$$

$$CH_3\dot{C}HCH_2SC_2H_5 + C_2H_5SH \longrightarrow CH_3CH_2CH_2SC_2H_5 + C_2H_5S\cdot$$

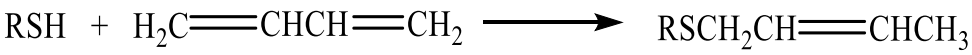
(1.51)

In the presence of elemental sulfur, benzenethiol is heated with propylene and a normal Markownikoff addition occurs.

$$C_6H_5SH + CH_2{=}CHCH_3 \xrightarrow{S} C_6H_5SCH(CH_3)_2$$

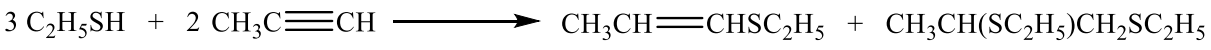
(1.52)

Thiols can react with butadiene through free-radical addition and give the 1,4-adduct exclusively.



(1.53)

Under conditions generating free radicals, thiols can be added to acetylenes. The anti-Markownikoff mono adduct and the 1,2-adduct are produced by the addition reaction of a thiol with an alkylacetylene [59].

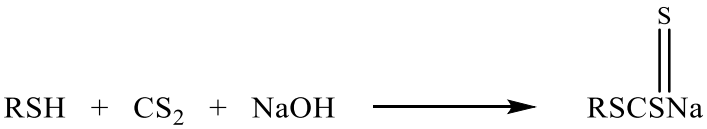


(1.54)

Miscellaneous Reactions:

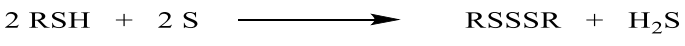
Thiols are considered to be strong nucleophiles and this class of compounds undergo many types of other reactions. Some examples among many types of reactions are the following [23]:

(a) With carbon disulfide and sodium hydroxide to give trithiocarbonate ester;



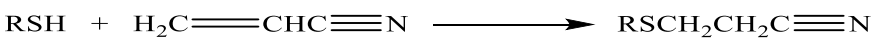
(1.55)

(b) With elemental sulfur in NaOH to give trisulfides;



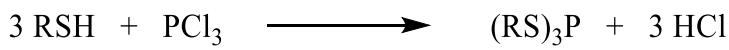
(1.56)

(c) With acrylonitrile in the presence of base, to give the substituted thioethers;



(1.57)

(d) With phosphorus trichloride to give phosphorotrithioite esters;



(1.58)

(e) With isocyanates (catalyzed by tertiary amine) to give thiourethans;

(1.59)

1.1.2.6. Uses of Thiols

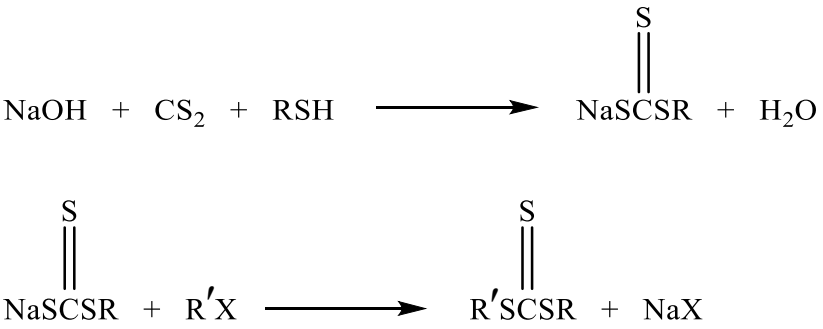
Generally, one of the main uses for aliphatic thiols is in emulsion polymerization systems as polymerization modifiers. Their role is to control the length of the polymer chain within the range needed to provide a product with the required qualities. In the Second World War the production of natural rubber was considerably reduced and this led to the rapid development of processes for manufacturing large quantities of synthetic rubber. The first modifier used was 1-dodecanethiol. Currently, tertiary thiols are used as modifiers in the production of styrene-butadiene rubber while straight-chain thiols are used in the production of chloroprene.

In the gas industry, special blends of alkanethiols are used as odorants. They serve as warning agents in case of leaks and for protectection against fires, explosions and other dangers.

Alkanethiols with low molecular weight such as ethanethiol and propanethiol are used as intermediates in the production of many agricultural chemicals including herbicides, acaricides, insecticides, and defoliants. For example, β-thionaphthol is moderately effective against mosquito larvae. Also, Butyl mercaptan proved to be a repellant for white rats. It repels flies and is fumigant against weevils [60].

In permanent-wave formulations, ammonium or alkanolamine salts of thioglycolic acid (mercaptoacetic acid) are used to soften hair. A reductive cleavage of disulfide cross-linkage occurs in the reaction which is involved in the softening process, ie, a thiol-disulfide interchange between the cystine units of the keratin and the sulfhydryl group of mercaptoacetic acid . Another thiol which is used as an anti-dandruff agent in shampoo is the zinc salt of 2-pyridinethiol-1-oxide.

A potentially widespread market for thiols is the use of alkanethiols and alkanethiol derivatives in the mining industry. Dialkyl trithiocarbonates, sodium alkyl trithiocarbonates and 1-dodecanethiol proved to be excellent collectors for sulfide minerals. The following reactions illustrates how sodium alkyl trithiocarbonates and dialkyl trithiocarbonates are obtained.



(1.60)

In resin stabilization, alkanethiols and mercaptoacid esters are used as intermediates in the preparation of organotin sulfides which are used for stabilization of the resin. The most effective thermal stabilizer known for poly(vinyl chloride) resins is dibutyltin S,S′-(isooctylmercaptoacetate).

Thiols can be used in the medical field: ethanethiol is used for the preparation of ″sulfonal‟, 2,2-bis-(ethylsulfonyl)propane, and related hypnotics. o-Mercaptobenzoic acid is used for the preparation of the well known sterilizing agent Merthiolate, which is ethylmercurithiosalicylate. Also, 2-mercaptoethylamine is used as anti- radiation drug which is effective with less toxicity. It provides some protection for animals against the effects of ionizing radiation [17].

1.1.3. Piperazines

1.1.3.1. General Information about Piperazines

Piperazine consists of a six-membered ring possessing two nitrogen atoms located opposite to each other in the para position. It can also be called hexahydropyrazine, hexahydro-1,4-diazine or diethylenediamine. As a matter of convenience its formula can be written $HN(CH_2CH_2)_2NH$. Figure 1.8 illustrates the structure of piperazine.

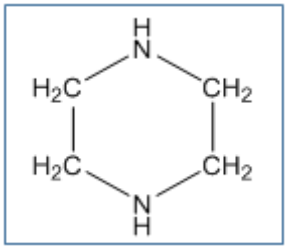
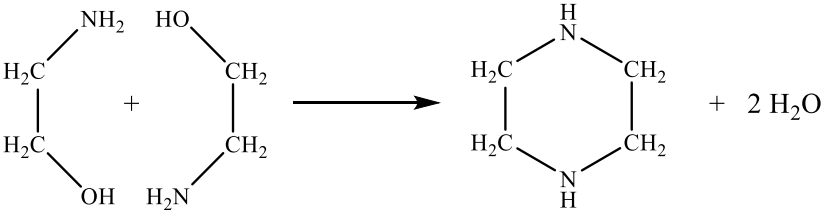


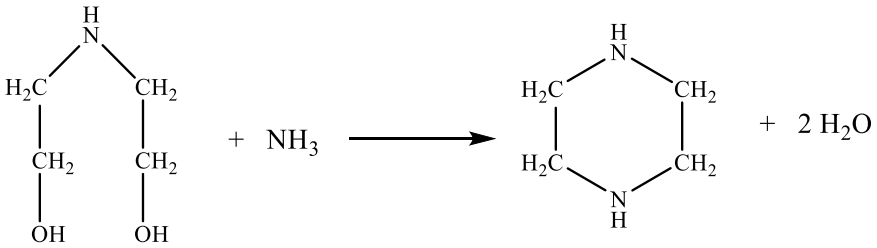
Figure 1.8: Piperazine structure.

Its odor is typical of amines. In the pure state it is a hygroscopic crystalline white solid. According to the solubility, it is soluble in glycerol and water, partially soluble in alcohol, and insoluble in ether.

Piperazine can be prepared from monoethanolamine, diethanolamine or triethanolamine.



monoethanolamine

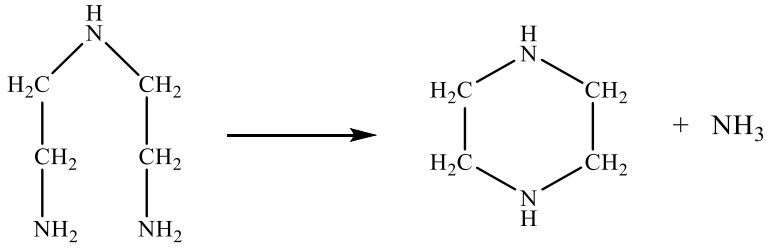


diethanolamine

(1.61)

In these reactions hydrogenation catalysts (cobalt, copper and nickel, and their oxides) may be used.

Piperazine can also be produced from ethylenediamine, diethylenetriamine, or similar higher amines.



(1.62)

This reaction can be done using a hydrogenation catalyst that contains a metal from the group consisting of cobalt, copper, platinum or nickel.

1.1.3.2. Uses of Piperazines

The first applications of piperazine was in the medical field for the treatment of gout [61] and rheumatism. However, this early use has now faded because of its popularity as an anthelmintic [62]. Nowadays, it is the most used product in the treatment of intestinal worms in animals [23].

In fact, piperazine and its derivatives show some biological properties: anti-hypertensive, antibacterial, anticancer [63], antimalaryal [64], antipsychotic [65], antimicrobial [66], antifungal, anti-inflammatory, and antieczematic activity [67].

Piperazine also can be used as antihistaminic. $CH_3N(CH_2CH_2)_2NCH(C_6H_5)_2$ and 1-methyl-4-(substituted benzhydryl)piperazines are the most widely used derivatives for this purpose [68]. The chemical structures of biolgically active compounds containing 1,4-piperazine-ring are shown in Figure 1.9.

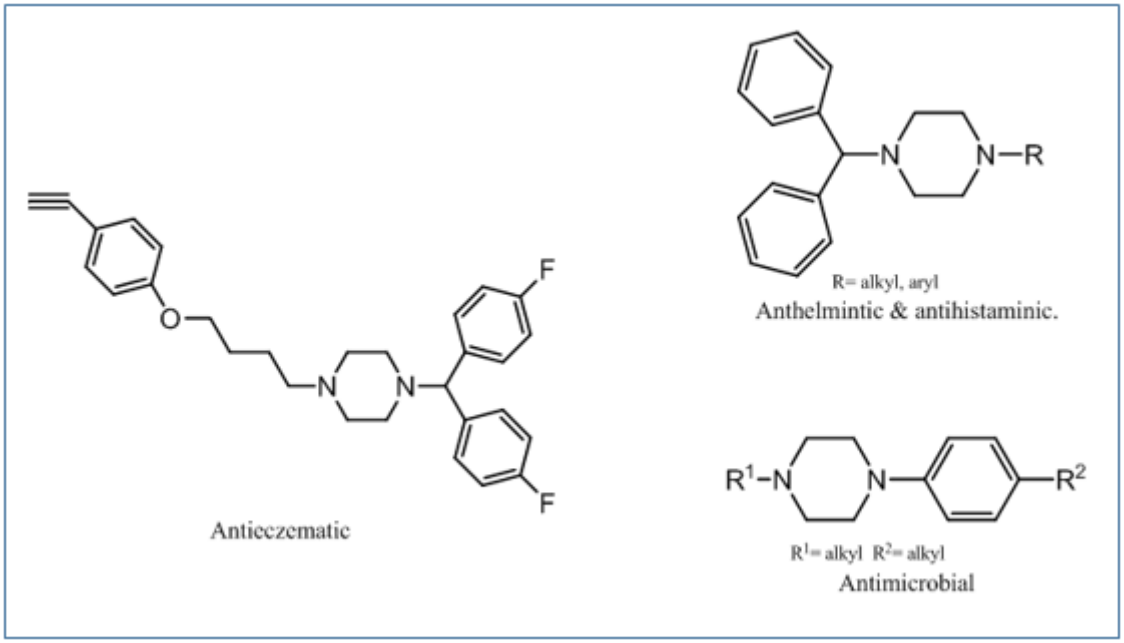


Figure 1.9: Structures of biologically active compounds containing the 1,4-piperazine ring.

Beside these important applications, many of piperazine derevatives have been used as rubber antioxidants, surface-active agents, corrosion inhibitors, and as sedatives.

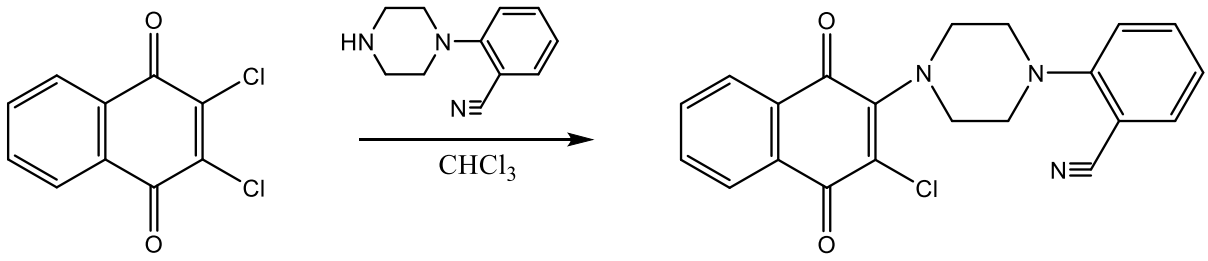
Piperazine can be used in preparing dyes. It protects printed fabrics from being faded. Piperazine, together with caprolactam which is a dibasic acid, are used to prepare copolyamide fibers with dye affinity and efficient water absorption [23].

2. MATERIALS AND METHODS

2.1. SYNTHESIS OF NEW 2,3- DI(SUBSTITUTED)NAPHTHOQUINONE COMPOUNDS

2.1.1. Synthesis of new 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ compound (2)

2,3-Dichloro-1,4-NQ **(1)** was reacted with 1-(2-cyanophenyl)piperazine in chloroform at room temperature, and new 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ compound **(2)** was obtained. The product was separated by column chromatography.



1 2

In the IR spectrum of compound **2**; stretching bands for C-$H_{arom.}$, C-H_{aliph}, cyano group CN, carbonyl group and carbon-carbon double bond were seen at ν = 2979 cm^{-1}, ν = 2903 cm^{1}, ν = 2220 cm^{-1} , ν = 1652 cm^{-1}, ν = 1590, 1557 cm^{-1}, respectively.

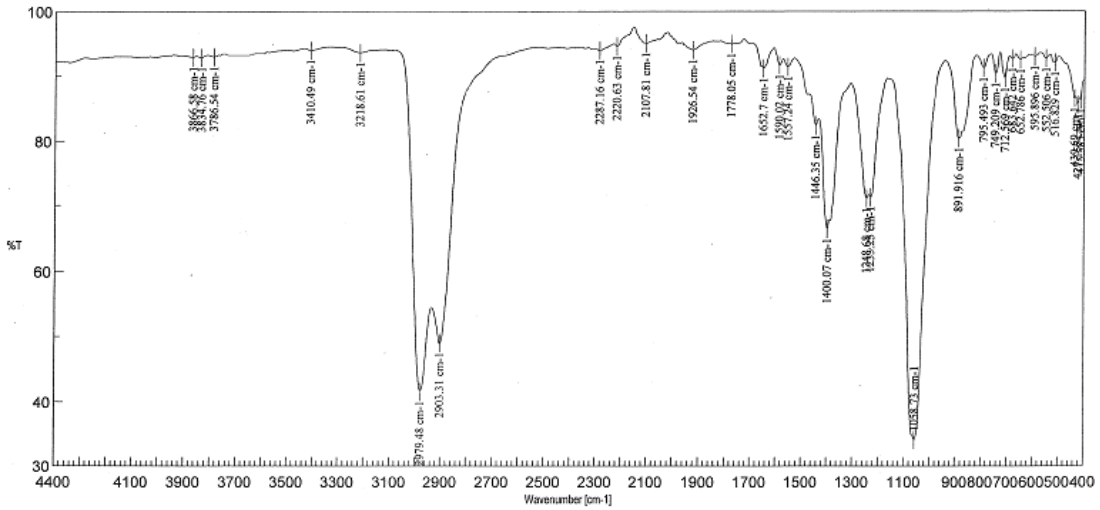


Figure 2.1: IR (KBr) spectrum of compound 2.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **2**; protons of piperazine ring appeared at δ = 3.40-3.42 and 3.82-3.84 ppm as triplet. Protons of phenyl ring appeared at δ = 7.07-7.10, 7.52-7.56 and 7.62-7.63 ppm as multiplet. Protons of NQ appeared at δ = 7.69-7.75, 8.05-8.07 and 8.15-8.17 ppm as multiplet.

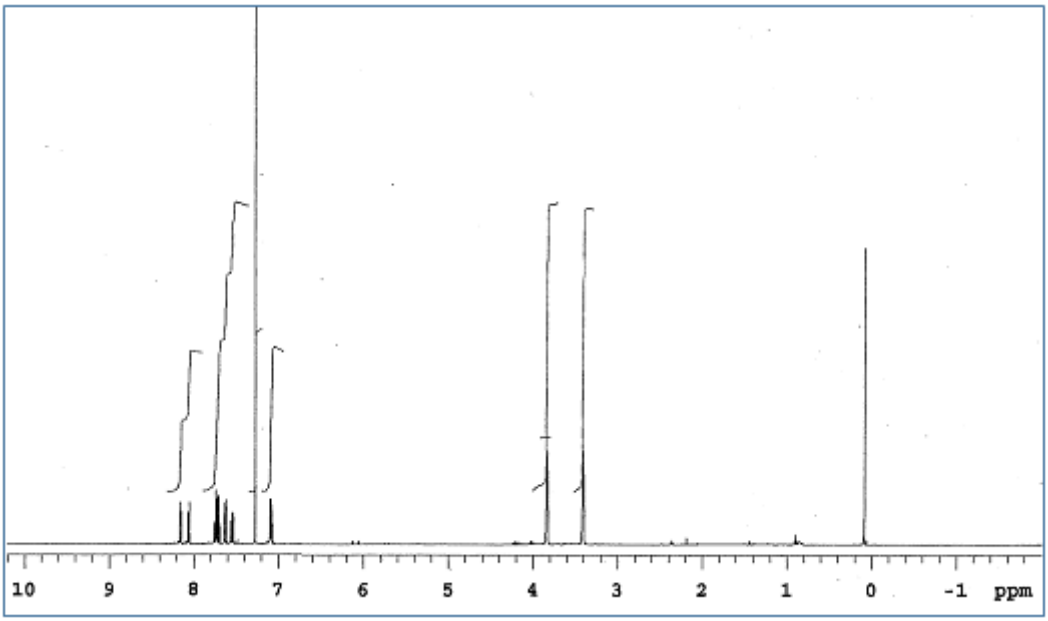


Figure 2.2: ^{1}H NMR ($CDCl_3$) spectrum of compound 2.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **2**; piperazine carbons gave two signals at δ = 51.44, 52.42 ppm. Carbon of the CN group was observed at δ = 106.62 ppm. Ar-C's at δ = 118.23, 119.07, 126.69, 126.98, 131.46, 131.61, 133.25, 133.89, 133.93, 134.18, 134.38, 134.41 ppm. =C-N at δ = 149.94, 155.42 ppm and the carbonyl groups gave two signals at δ = 178.15, 181.85 ppm.

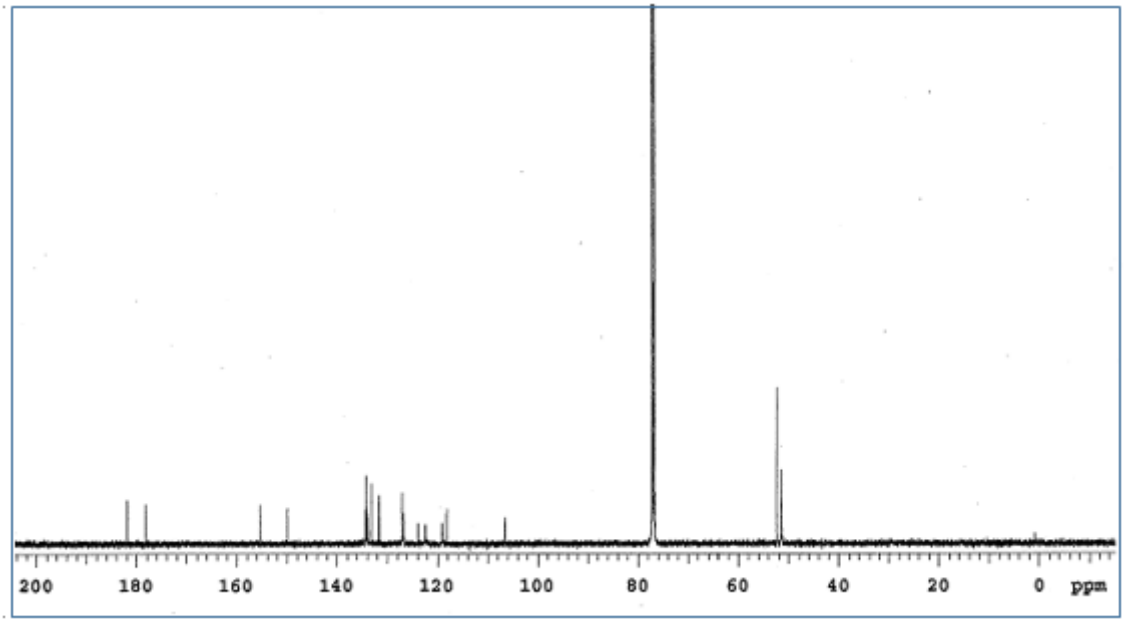


Figure 2.3: ^{13}C ($CDCl_3$) spectrum of compound 2.

The mass spectrum of compound **2** which has the formula $C_{21}H_{16}CN_3O_2$ (M= 377.83 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **2** in the MS spectrum is *m/z*: (%) (100) 378 $[M+H]^+$. Figure 2.4.

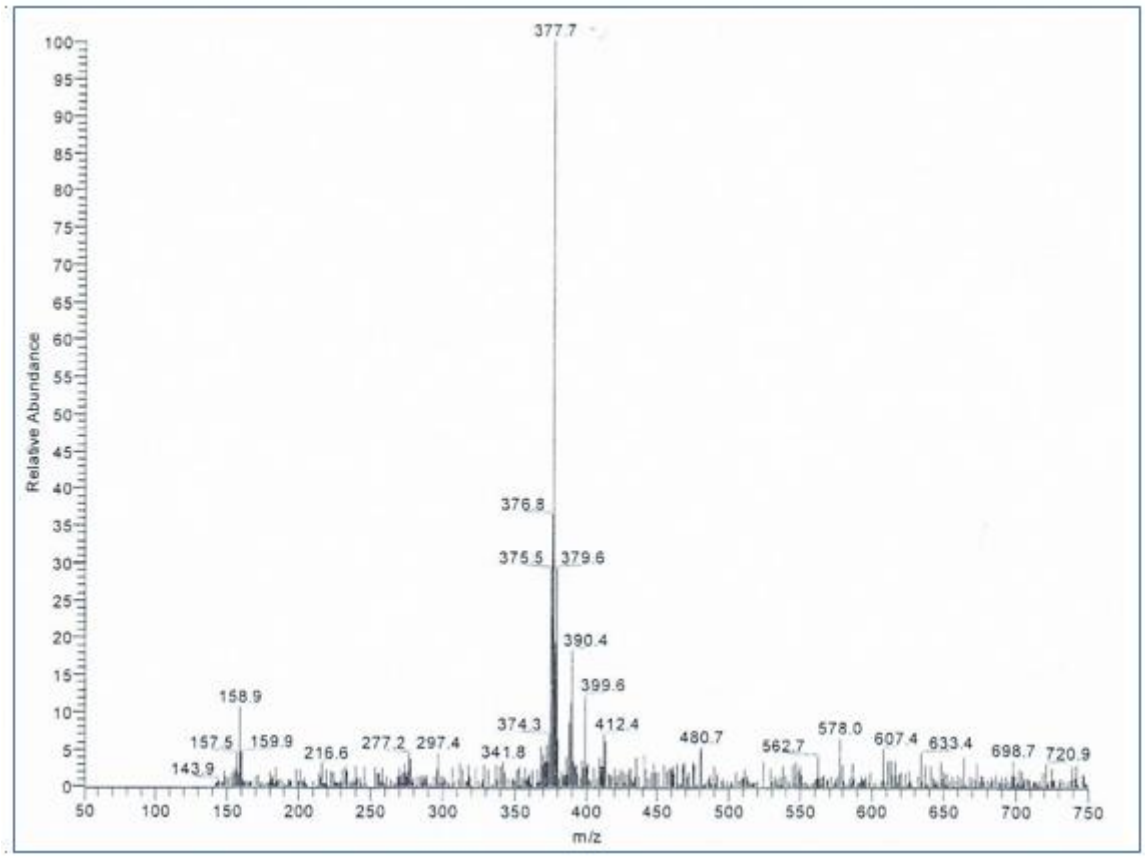
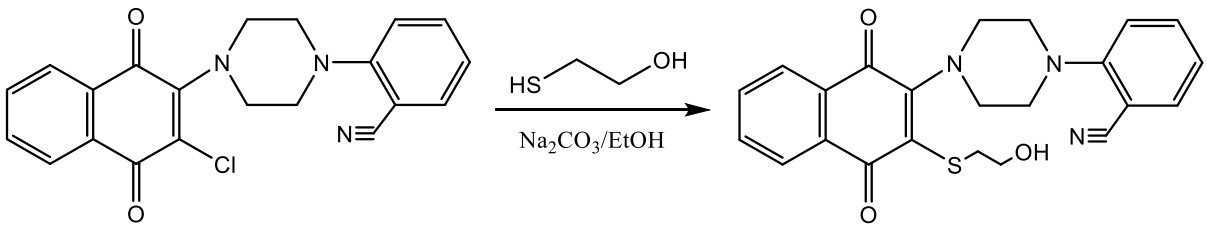


Figure 2.4: MS [+ESI] spectrum of compound 2.

2.1.2. Synthesis of new 2-(1-(2-cyanophenyl)piperazinyl)-3-(2-hydroxyethylthio)-1,4-NQ compound (3)

2-(1-(2-Cyanophenyl)piperazinyl)-3-chloro-1,4-NQ **(2)** was reacted with 2-mercaptoethanol, and new 2-(1-(2-cyanophenyl)piperazinyl)-3-(2-hydroxyethylthio)-1,4-NQ compound **(3)** was obtained. The product was separated by column chromatography.



2 3

In the IR spectrum of compound **3**; hydroxyl band (-OH) was seen at ν = 3390 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, cyano group CN, carbonyl group and carbon-carbon double bond were seen at ν = 3066, 2971 cm^{-1}, ν = 2908 cm^{-1}, ν = 2216 cm^{-1}, ν = 1662 cm^{-1}, ν = 1589, 1523 cm^{-1}, respectively.

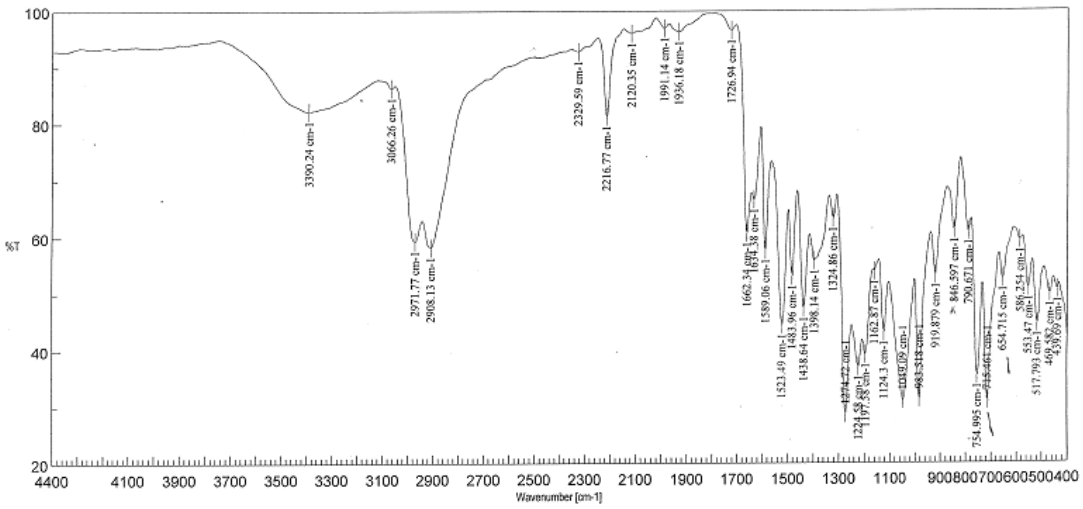


Figure 2.5: IR (film) spectrum of compound 3.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **3**; -OH proton appeared at δ = 1.52 ppm as singlet. -SCH_2 protons appeared at δ = 2.99-3.01 ppm as triplet. Protons of piperazine ring appeared at δ = 3.33-3.35 and 3.75-3.77 ppm as triplet. Methylene protons bonded to hydroxyl group appeared at δ = 3.63-3.66 ppm as triplet. Protons of phenyl ring appeared at δ = 6.98-7.01, 7.43-7.47 and 7.53-7.55 ppm as multiplet. Protons of NQ appeared at δ = 7.58-7.65, 7.93-7.95 and 8.01-8.02 ppm as multiplet.

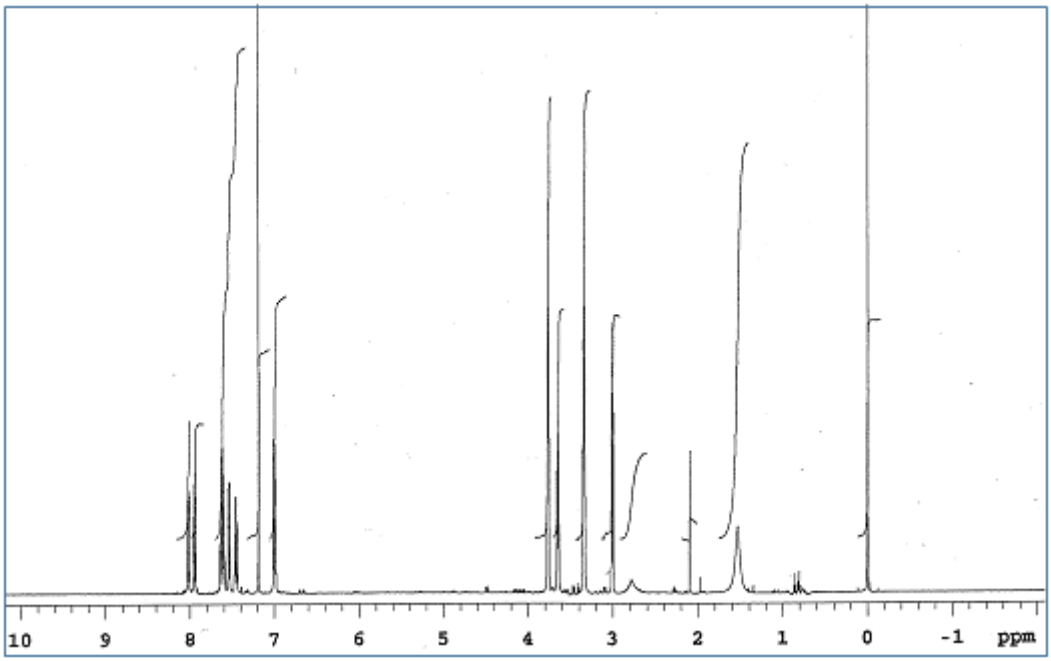


Figure 2.6: ^{1}H NMR ($CDCl_3$) spectrum of compound 3.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **3**; S-CH_2 was observed at δ = 38.67 ppm. The piperazine carbons gave two signals at δ = 52.40, 52.69 ppm. CH_2-OH at δ = 60.88 ppm. Carbon of the CN group at δ = 106.52 ppm. Ar-C's at δ= 118.26, 118.98, 122,36, 124.28, 126.59, 126.77, 132.05, 132.71, 133.12, 133.89, 133.95, 134.43 ppm. =C-N were observed at δ = 155.40, 155.64 ppm and the carbons of carbonyl groups gave two signals at δ = 181.81, 182.40 ppm.

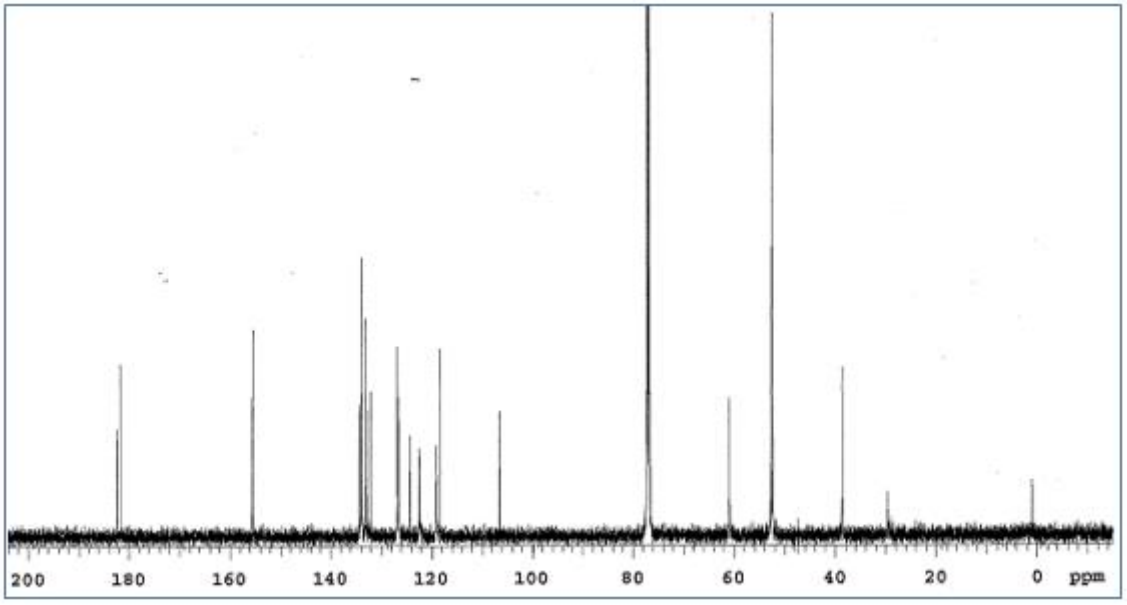


Figure 2.7: ^{13}C NMR ($CDCl_3$) spectrum of compound 3.

The mass spectrum of compound **3** which has the formula $C_{23}H_{21}N_3O_3S$ (M= 419.50 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **3** in the MS spectrum is *m/z*: (%) (100) 420 $[M+H]^+$. Figure 2.8.

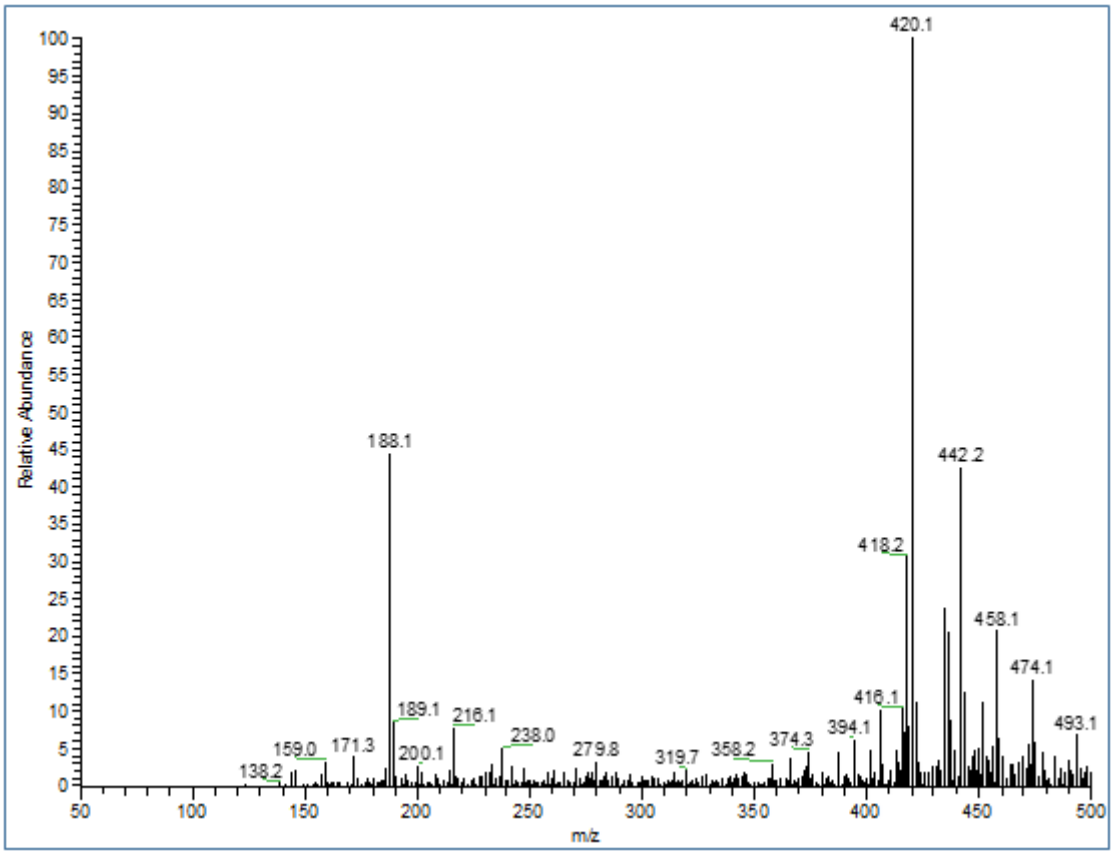
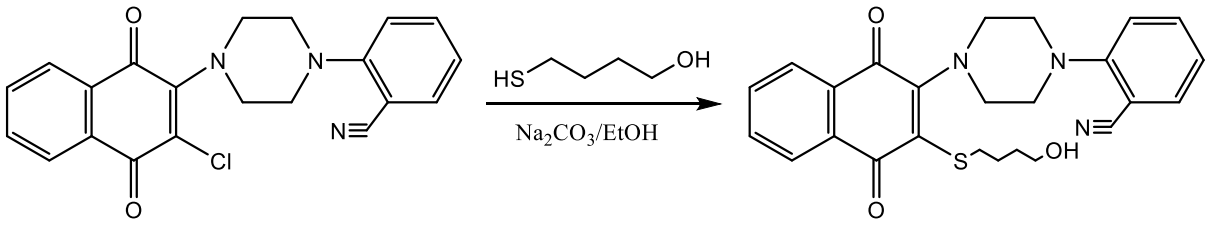


Figure 2.8: MS [+ESI] spectrum of compound 3.

2.1.3. Synthesis of new 2-(1-(2-cyanophenyl)piperazinyl)-3-(4-hydroxybutylthio)-1,4-NQ compound (4)

2-(1-(2-Cyanophenyl)piperazinyl)-3-chloro-1,4-NQ **(2)** was reacted with 4-mercapto-1-butanol and new 2-(1-(2-cyanophenyl)piperazinyl)-3-(4-hydroxybutylthio)-1,4-NQ compound **(4)** was obtained. The product was separated by column chromatography.



2 4

In the IR spectrum of compound **4**; hydroxyl band (-OH) was seen at ν = 3415 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, cyano group CN, carbonyl and carbon-carbon double bond were seen at ν = 3066, 2970 cm^{-1}, ν = 2905 cm^{-1}, ν = 2216 cm^{-1}, ν = 1661 cm^{-1}, and ν = 1589, 1524 cm^{-1}, respectively.

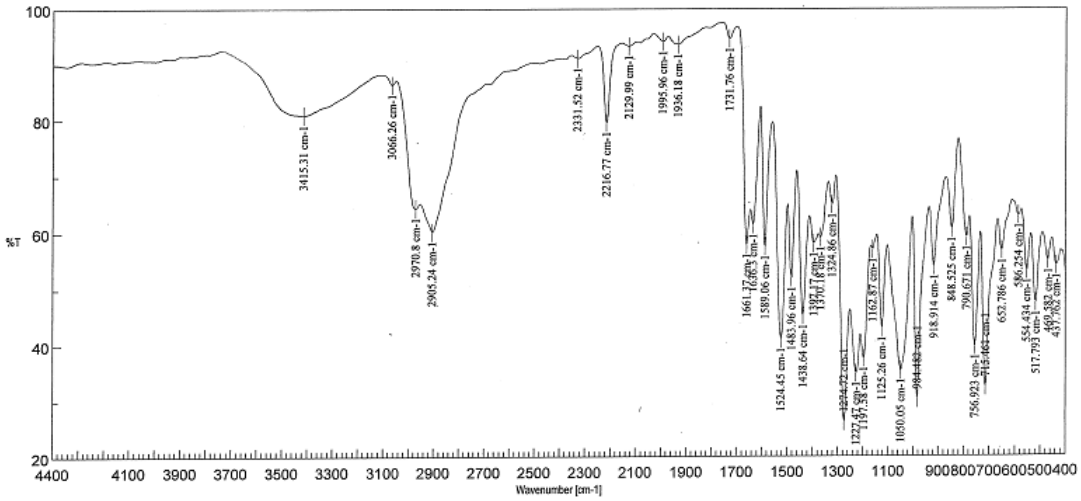


Figure 2.9: IR (film) spectrum of compound 4.

In the ^1H NMR ($CDCl_3$) spectrum of compound **4**; the signal at δ = 1.58-1.65 ppm which appeared as multiplet is belonging to $SCH_2C\mathbf{H_2}$, $C\mathbf{H_2}CH_2OH$ and OH protons. S-CH_2 at δ = 2.89-2.92 ppm as triplet. Protons of piperazine ring at δ = 3.31-3.33 and 3.68-3.70 ppm as triplet. $C\mathbf{H_2}$-OH at δ = 3.56-3.59 ppm as triplet. Protons of phenyl ring appeared at δ = 6.97-7.01, 7.43-7.46 and 7.52-7.54 ppm as multiplet . Protons of NQ appeared at δ= 7.57-7.62, 7.92-7.94 and 7.97-7.99 ppm as multiplet.

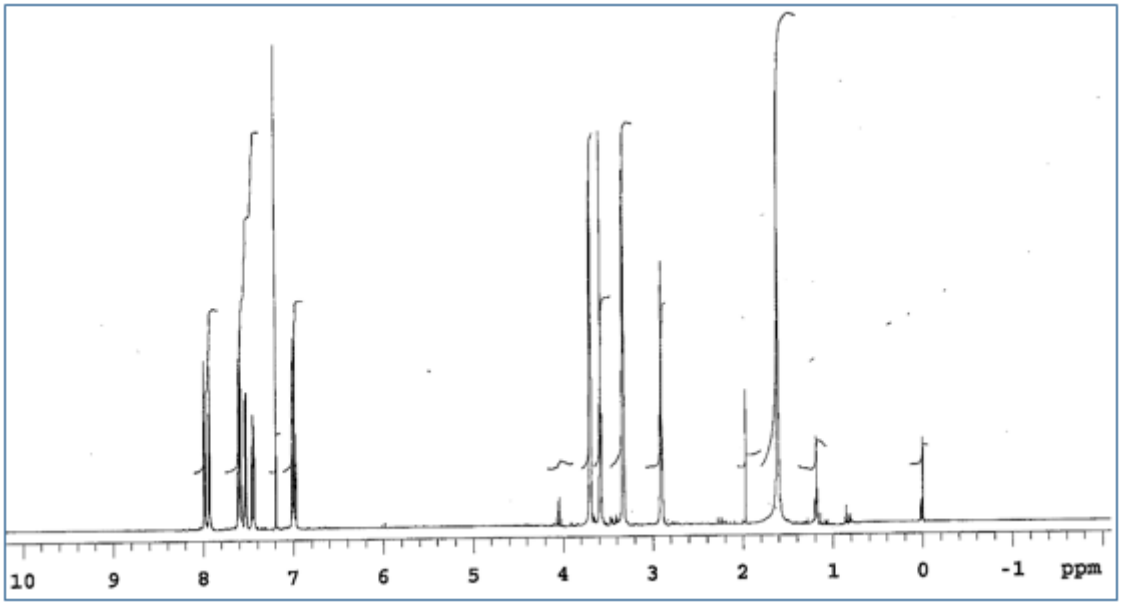


Figure 2.10: ^{1}H NMR ($CDCl_3$) spectrum of compound 4.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **4**; $SCH_2\boldsymbol{C}H_2$ was observed at δ = 26.09 ppm while $SCH_2CH_2\boldsymbol{C}H_2$ at δ = 31.65 ppm. S-CH_2 at δ = 34.49 ppm. The piperazine carbons gave two signals at δ = 52.12, 52.40 ppm. CH_2-OH at δ = 62.20 ppm. Carbon of CN group at δ= 106.42 ppm. Ar-C's at δ = 118.31, 119.05, 122,28, 126.34, 126.64, 127.04, 132.12, 132.86, 132.98, 133.70, 133.94, 134.42 ppm. =C-N were observed at δ = 155.80, 155.47 ppm and the carbons of carbonyl groups gave two signals at δ = 181.64, 182.20 ppm.

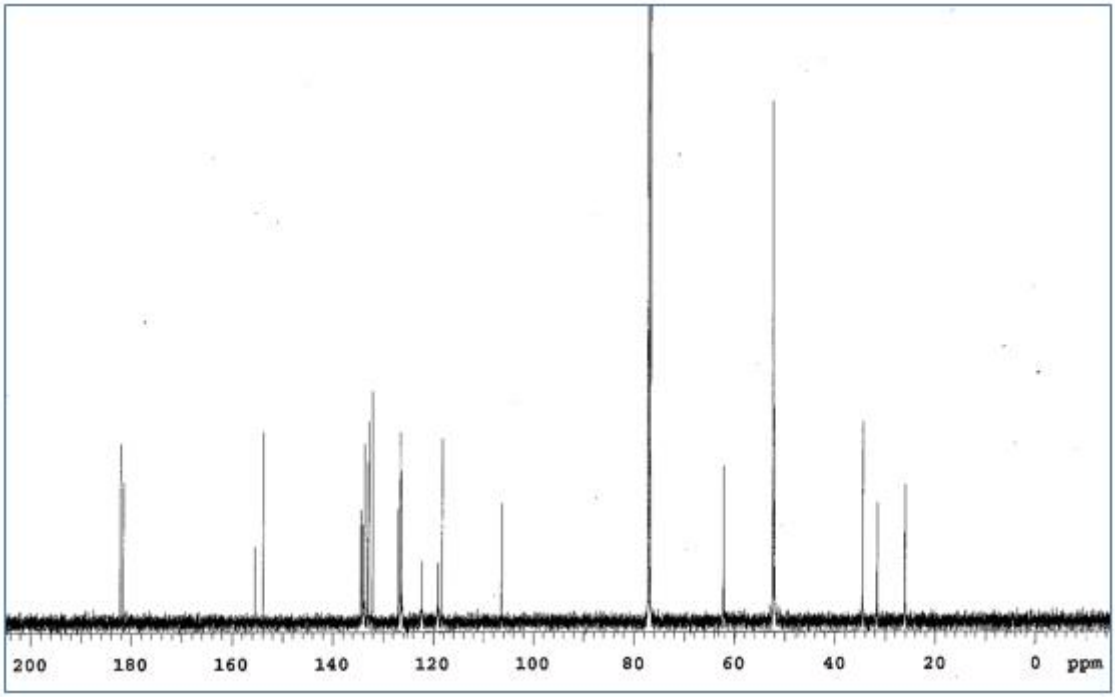


Figure 2.11: ^{13}C NMR ($CDCl_3$) spectrum of compound 4.

The mass spectrum of compound **4** which has the formula $C_{25}H_{25}N_3O_3S$ (M= 447.55 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **4** in the MS spectrum is *m/z*: (%) (100) 486 $[M+K]^+$. Figure 2.12.

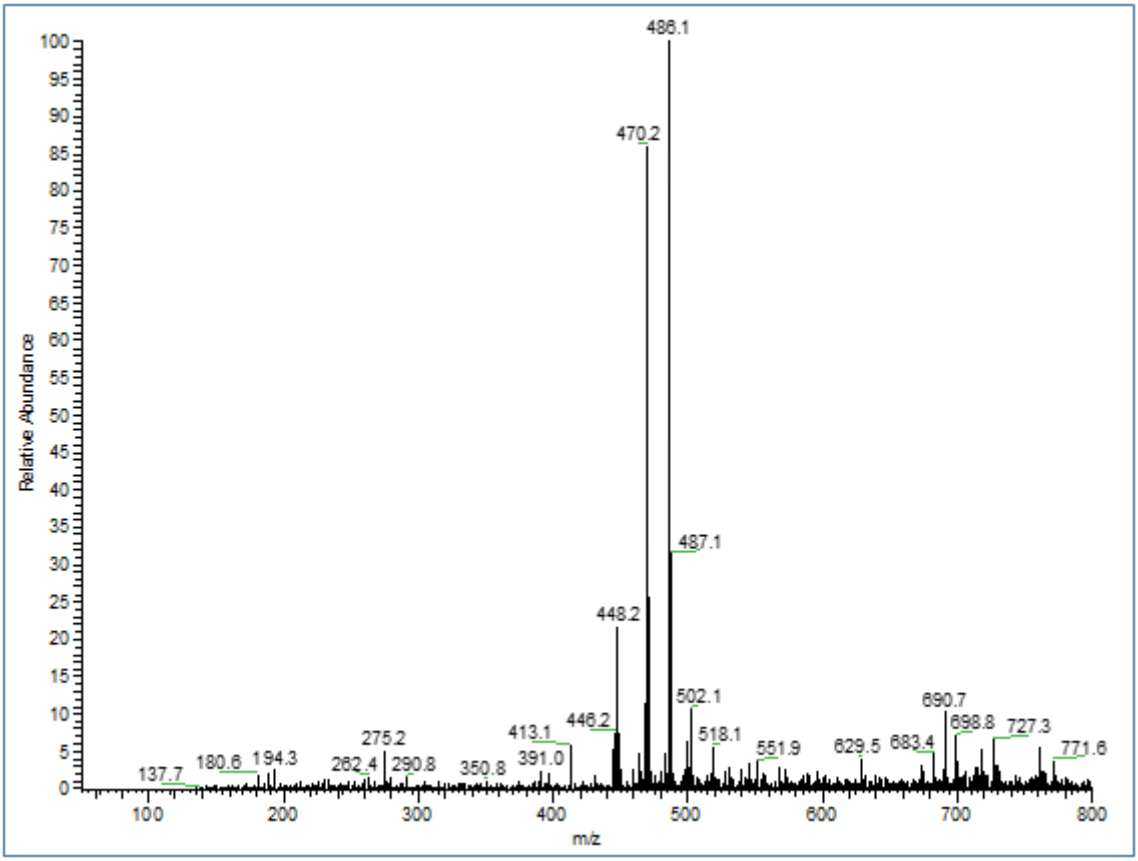
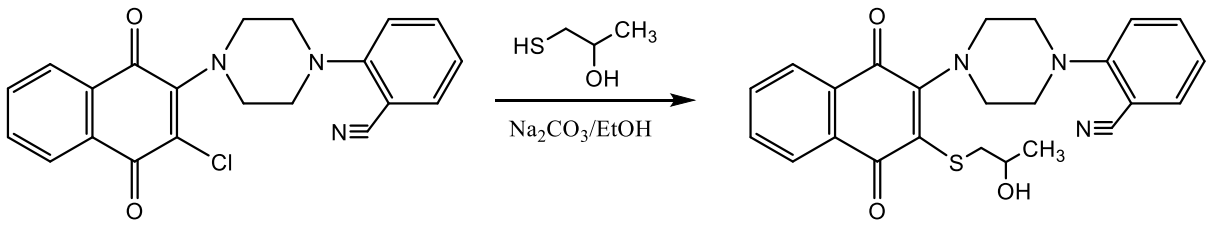


Figure 2.12: MS [+ESI] spectrum of compound 4.

2.1.4. Synthesis of new 2-(1-(2-cyanophenyl)piperazinyl)-3-(2-hydroxy-1-propylthio)-1,4-NQ compound (5)

2-(1-(2-Cyanophenyl)piperazinyl)-3-chloro-1,4-NQ **(2)** was reacted with 1-mercapto-2-propanol and new 2-(1-(2-cyanophenyl)piperazinyl)-3-(2-hydroxy-1-propylthio)-1,4-NQ compound **(5)** was obtained. The product was separated by column chromatography.



2 5

In the IR spectrum of compound **5**; hydroxyl band (-OH) was seen at ν = 3387 cm^{-1}. Stretching bands for the C-$H_{arom.}$, C-$H_{aliph.}$, cyano group CN, carbonyl and carbon-carbon double bond were seen at ν = 3069, 2967 cm^{-1}, ν = 2905, 2841 cm^{-1}, ν = 2217 cm^{-1}, ν = 1663 cm^{-1}, ν = 1590, 1524 cm^{-1}, respectively.

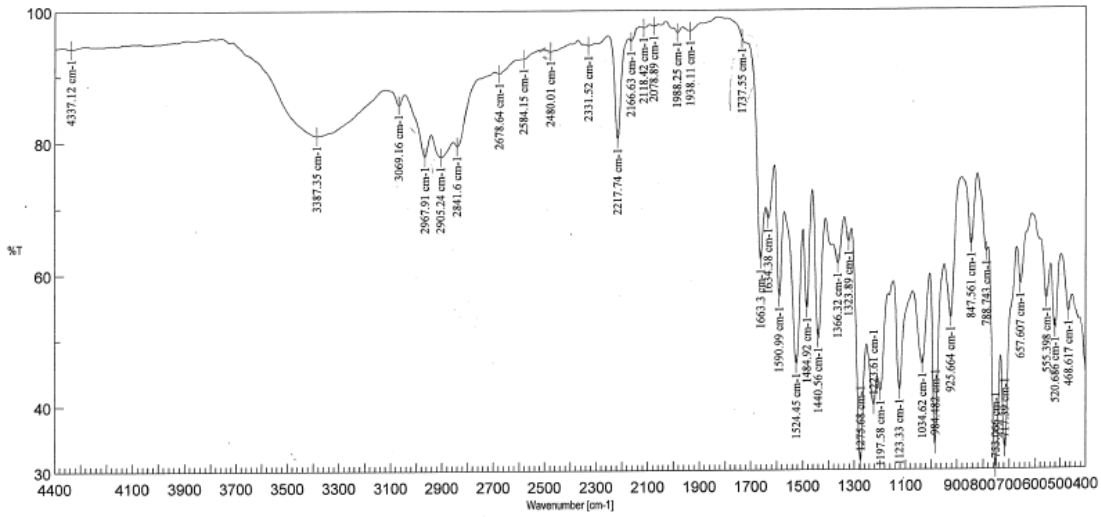


Figure 2.13: IR (film) spectrum of compound 5.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **5**; the signal at δ = 1.15-1.18 ppm which appeared as multiplet is belonging to methyl and hydroxyl protons. S-CH_2 appeared at δ = 2.65-2.70 ppm as multiplet. Protons of piperazine ring appeared at δ = 3.33-3.35 ppm as triplet and the other protons of piperazine appeared with C**H**-OH proton at 3.74-3.76 ppm as multiplet. Protons of phenyl ring appeared at δ = 6.98-7.01, 7.43-7.47 and 7.52-7.54 ppm as multiplet. Protons of NQ appeared at δ = 7.58-7.64, 7.93-7.95 and 8.01-8.03 ppm as multiplet.

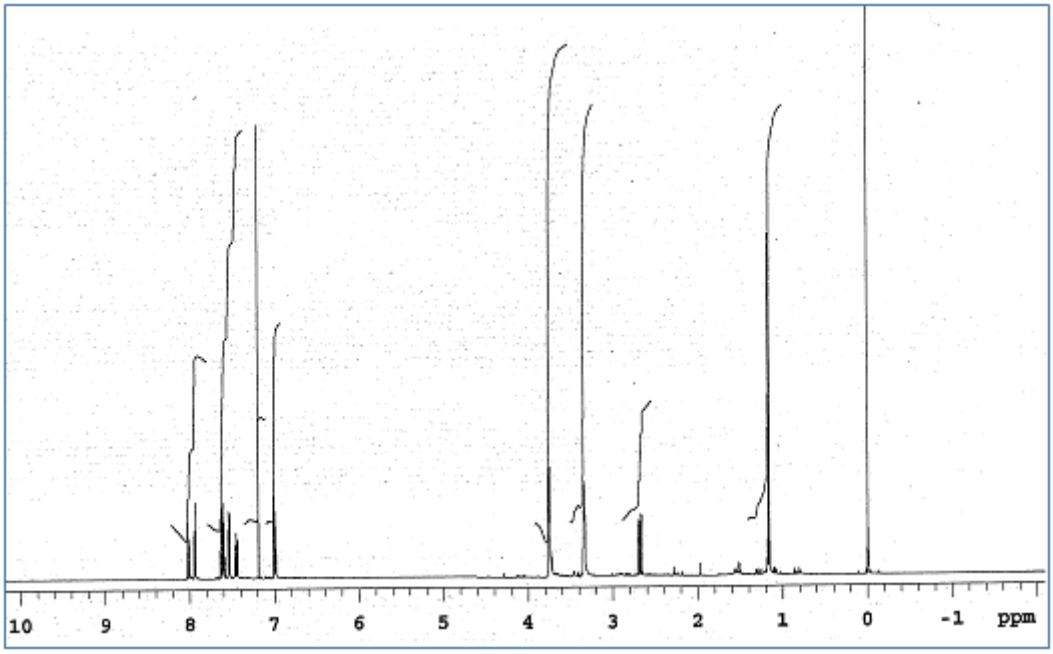


Figure 2.14: ^{1}H NMR ($CDCl_3$) spectrum of compound 5.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **5**; methyl carbon was observed at δ = 20.96 ppm. S-CH_2 at δ = 43.55 ppm. The piperazine carbons gave two signals at δ = 51.39, 51.71 ppm. CH-OH at δ = 65.12 ppm. Carbon of the cyano group at δ = 105.49 ppm. Ar-C's at δ = 117.25, 117.93, 121.44, 123.94, 125.75, 131.03, 131.68, 132.12, 132.94, 132.92, 133.36, 133.42 ppm. =C-N were observed at δ = 154.37, 154.51 ppm and the carbons of carbonyl groups gave two signals at δ = 180.79, 181.29 ppm.

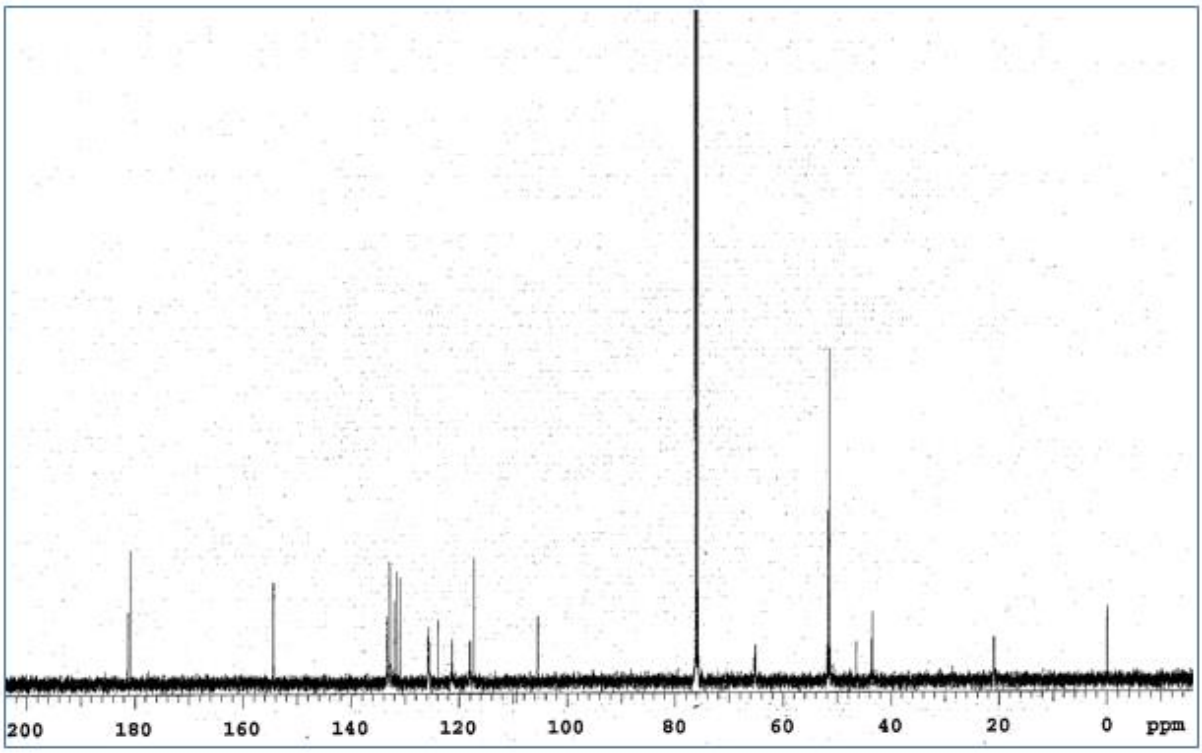


Figure 2.15: ^{13}C NMR ($CDCl_3$) spectrum of compound 5.

The mass spectrum of compound **5** which has the formula $C_{24}H_{23}N_3O_3S$ (M= 433.52 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **5** in the MS spectrum is *m/z*: (%) (100) 434 $[M+H]^+$. Figure 2.16.

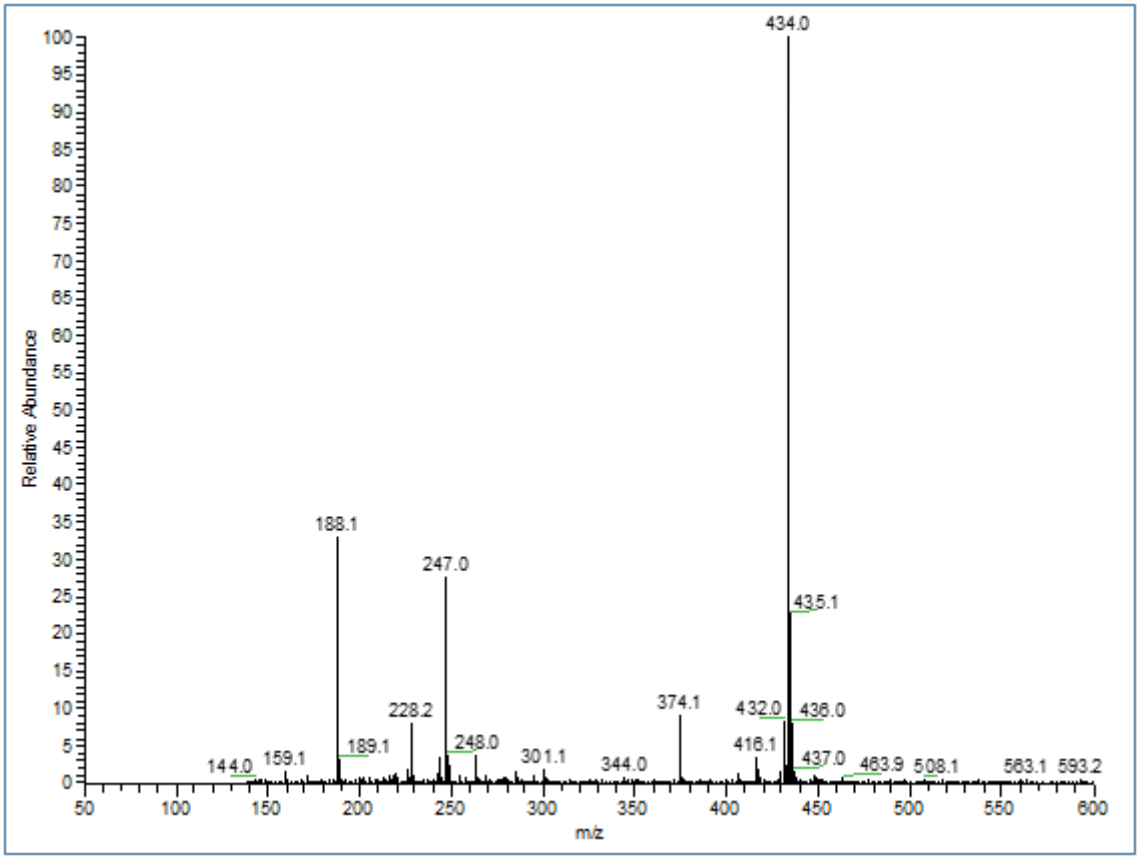
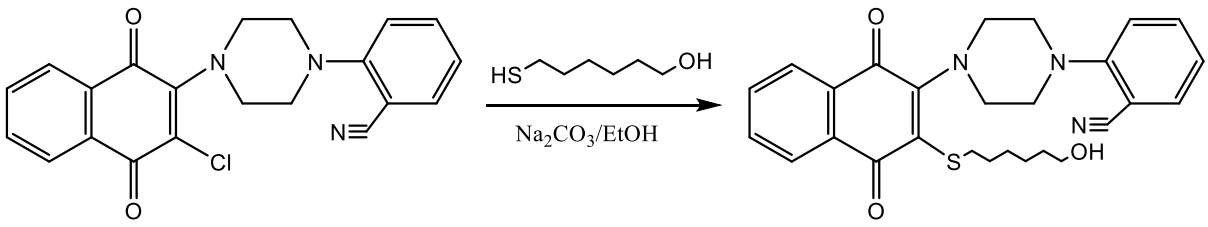


Figure 2.16: MS [+ESI] spectrum of compound 5.

2.1.5. Synthesis of new 2-(1-(2-cyanophenyl)piperazinyl)-3-(6-hydroxyhexylthio)-1,4-NQ compound (6)

2-(1-(2-Cyanophenyl)piperazinyl)-3-chloro-1,4-NQ **(2)** was reacted with 6-mercapto-1-hexanol and new 2-(1-(2-cyanophenyl)piperazinyl)-3-(6-hydroxyhexylthio)-1,4-NQ compound **(6)** was obtained. The product was separated by column chromatography.



2 6

In the IR spectrum of compound **6**; hydroxyl band (-OH) was seen at ν = 3402 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, cyano group CN, carbonyl and carbon-carbon double bond were seen at ν = 2978 cm^{-1}, ν = 2906 cm^{-1}, ν = 2216 cm^{-1}, ν = 1662 cm^{-1}, ν = 1589, 1524 cm^{-1}, respectively.

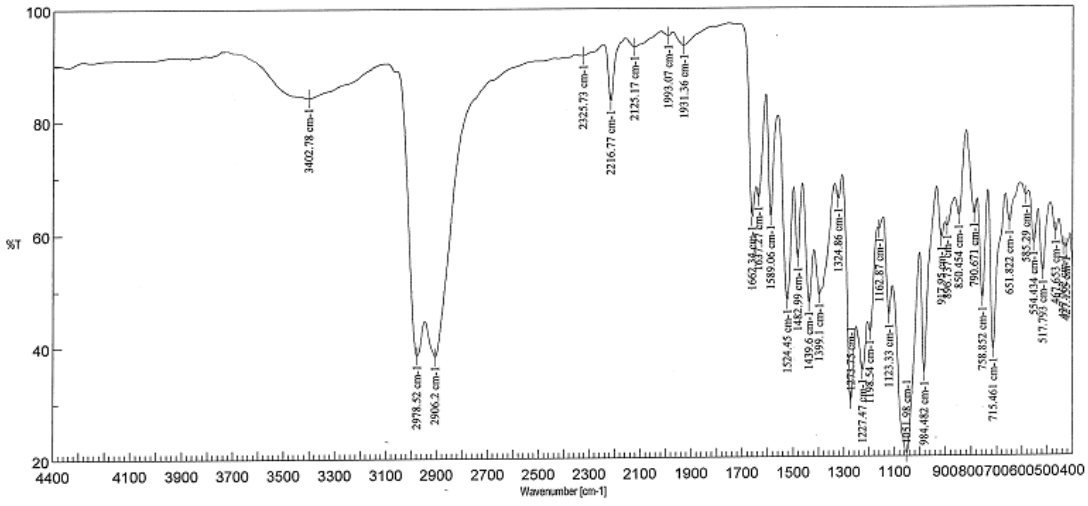


Figure 2.17: IR (film) spectrum of compound 6.

In the ^{1}HNMR ($CDCl_3$) spectrum of compound **6**; C**H₂**CH_2OH protons appeared at δ = 1.28-1.32 ppm as multiplet, SCH_2C**H₂** protons at δ = 1.34-1.40 ppm as multiplet. Aliphatic protons CH_2-CH_2 appeared at δ =1.45-1.55 ppm as multiplet. –OH proton at δ = 1.61 as singlet. -SCH_2 at δ = 2.84-2.87 ppm as triplet. Protons of piperazine ring appeared at δ = 3.32-3.34 and 3.69-3.71 ppm as triplet. C**H₂**-OH at δ = 3.53-3.55 ppm as triplet. Protons of phenyl ring appeared at δ = 6.98-7.03, 7.44-7.47 and 7.52-7.55 ppm as multiplet. Protons of NQ appeared at δ = 7.57-7.63, 7.93-7.95 and 7.98-8.00 ppm as multiplet.

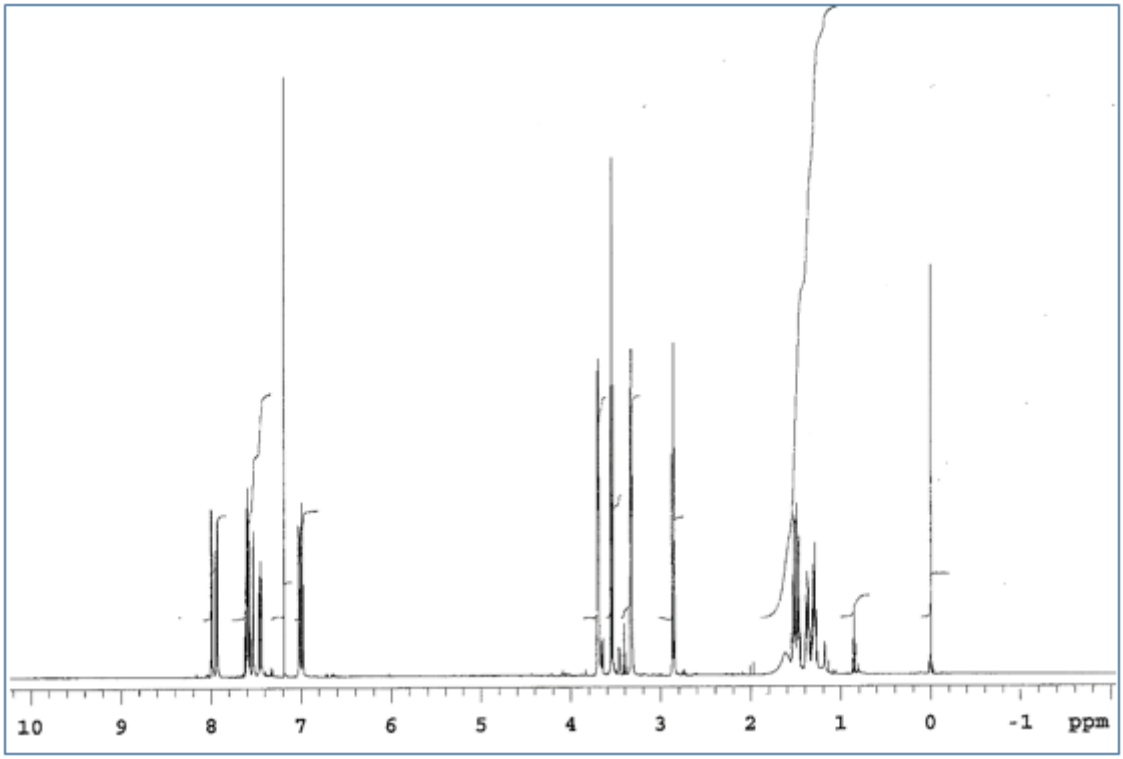


Figure 2.18: ^{1}H NMR ($CDCl_3$) spectrum of compound 6.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **6**; $SCH_2CH_2CH_2\boldsymbol{C}H_2$ was observed at δ = 25.24 ppm while $SCH_2\boldsymbol{C}H_2$ at δ = 28.39 ppm and $SCH_2CH_2\boldsymbol{C}H_2$ at δ = 29.56 ppm. $\boldsymbol{C}H_2CH_2OH$ at δ = 32.58 ppm. S-CH_2 at δ = 34.67 ppm. The piperazine carbons gave two signals at δ = 52.08, 52.44 ppm. CH_2-OH at δ = 62.73 ppm. Carbon of cyano group at δ = 106.44 ppm. Ar-C's at δ = 118.29, 119.07, 119.15, 122.41, 126.34, 126.63, 127.27, 132.13, 132.89, 133.68, 133.96, 134.44 ppm. =C-N were observed at δ = 153.79, 155.47 ppm and the carbonyl groups gave two signals at δ = 181.71, 182.18 ppm.

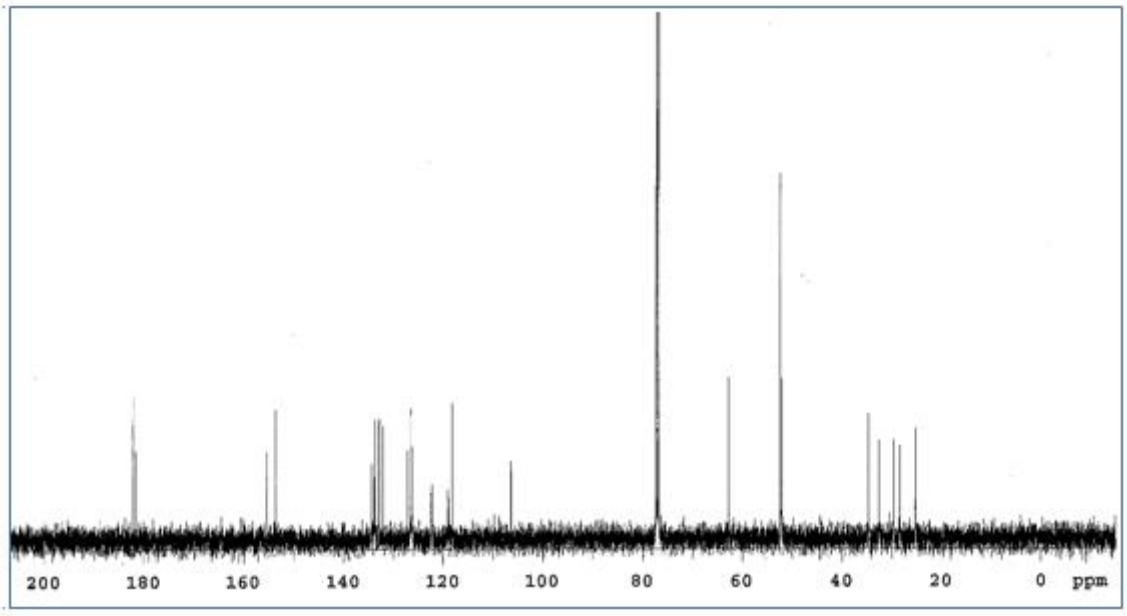


Figure 2.19: ^{13}C NMR ($CDCl_3$) spectrum of compound 6.

The mass spectrum of compound **6** which has the formula $C_{27}H_{29}N_3O_3S$ (M= 475.60 g/mole), was measured using the - ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **6** in the MS spectrum is *m/z*: (%) (100) 474 $[M-H]^+$. Figure 2.20.

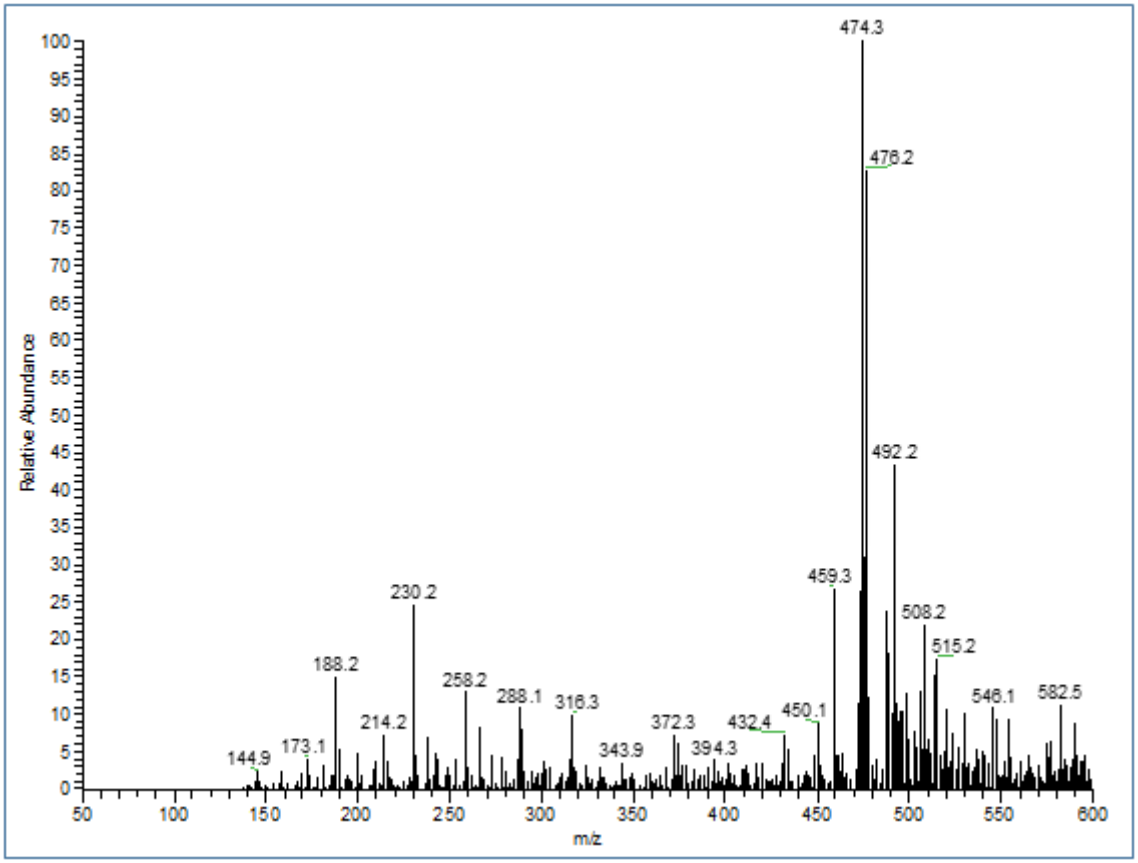
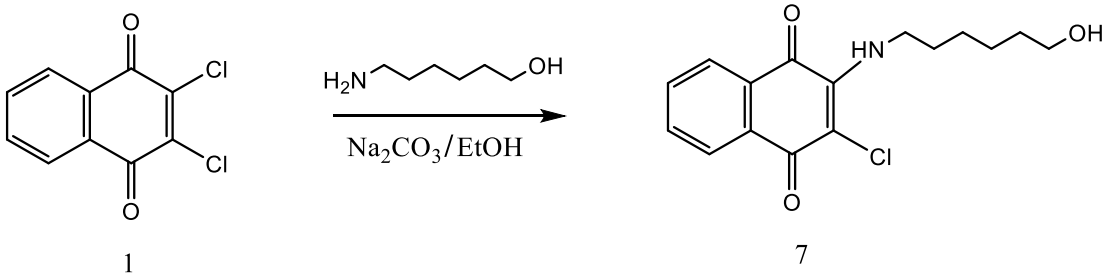


Figure 2.20: MS [-ESI] spectrum of compound 6.

2.1.6. Synthesis of 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ compound (7)

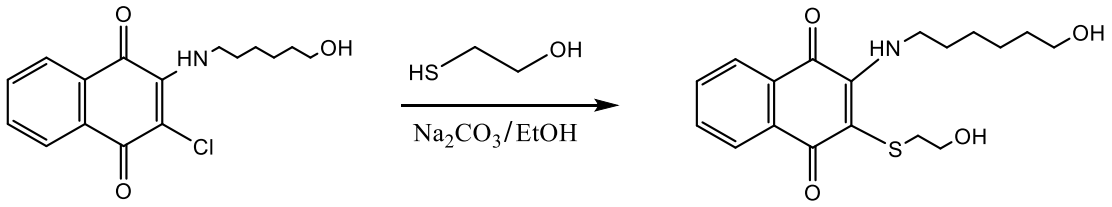
2,3-Dichloro-1,4-NQ **(1)** was reacted with 6-amino-1-hexanol, and known 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ compound **(7)** was obtained. This compound is not new one. It was prepared in a previous work [69]. It was prepared in this study to be used as starting material for other reactions. The product was separated by column chromatography.



1 7

2.1.7. Synthesis of new 2-(6-aminohexyl-1-ol)-3-(2-hydroxyethylthio)-1,4-NQ compound (8)

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** was reacted with 2-mercaptoethanol, and new 2-(6-aminohexyl-1-ol)-3-(2-hydroxyethylthio)-1,4-NQ compound **(8)** was obtained. The product was separated by column chromatography.



7 8

In the IR spectrum of compound **8**; characteristic stretching bands for (-NH and -OH) were seen at ν = 3341, 3227 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 2980 cm^{-1}, ν = 2919, 2852 cm^{-1}, ν = 1686 cm^{-1}, ν = 1590, 1536 cm^{-1}, respectively.

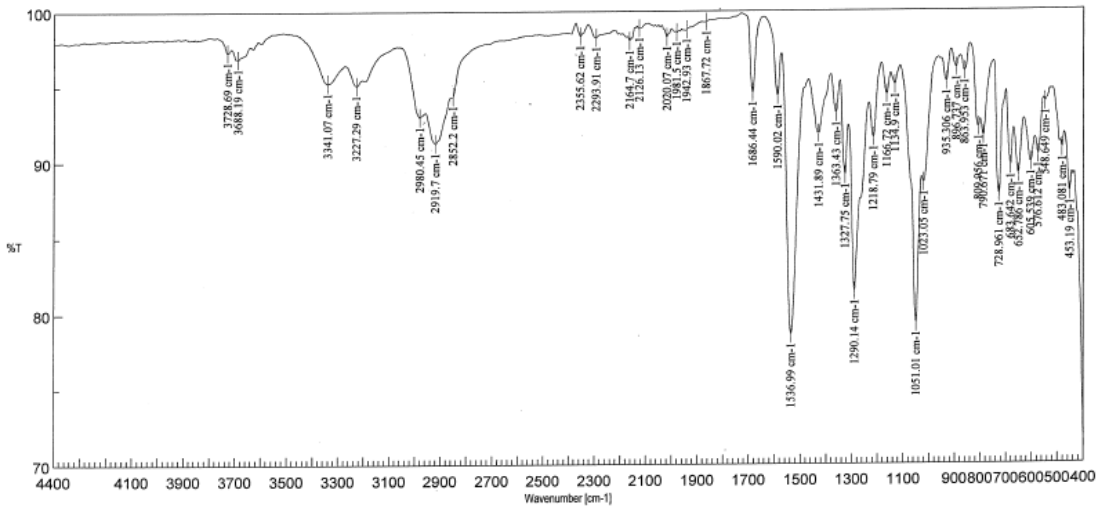


Figure 2.21: IR (KBr) spectrum of compound 8.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **8**; -OH protons appeared at δ = 1.26 ppm as singlet. $NH(CH_2)_2C\mathbf{H_2}C\mathbf{H_2}$ protons at δ = 1.46-1.50 ppm as multiplet. $NH(CH_2)_4C\mathbf{H_2}CH_2OH$ protons at δ = 1.61-1.63 ppm as quintet. $NHCH_2C\mathbf{H_2}$ protons at δ = 1.72-1.77 ppm as quintet. NH-$C\mathbf{H_2}$ at δ = 2.84-2.86 ppm as triplet. The signal at δ = 3.64-3.69 ppm which appeared as multiplet is belonging to $NH(CH_2)_5C\mathbf{H_2}OH$ and -SCH_2 protons. $SCH_2C\mathbf{H_2}OH$ protons at δ = 3.98-4.01 ppm as triplet. Protons of NQ group appeared at δ = 7.62-7.65, 7.73-7.76, 8.03-8.05 and 8.17-8.19 ppm as multiplet.

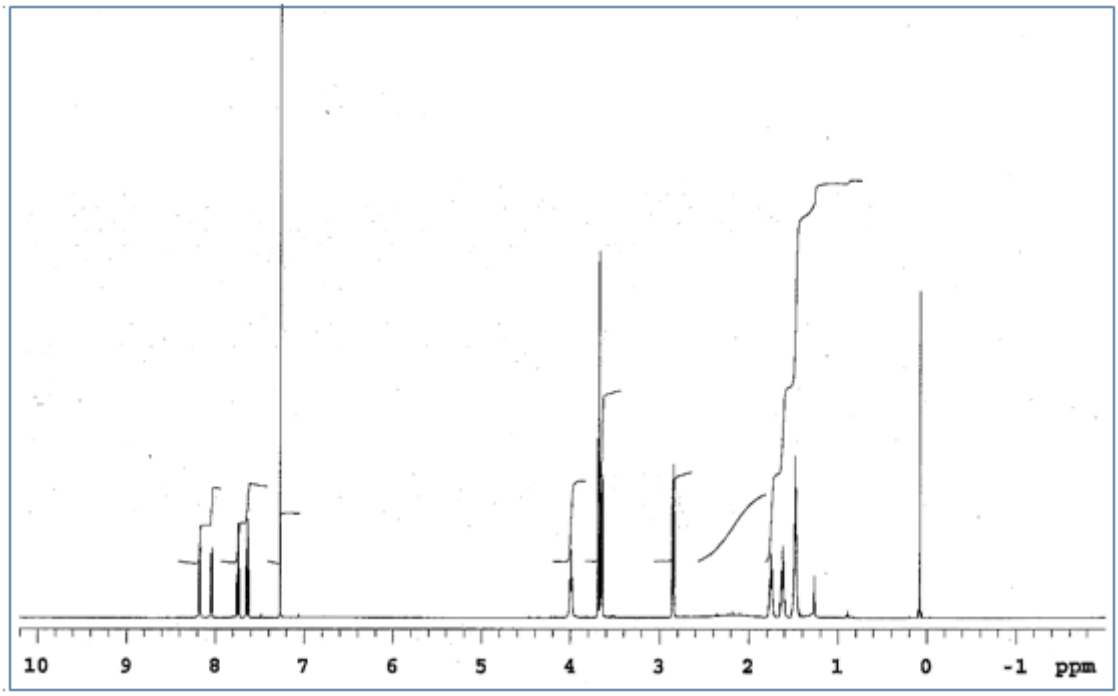


Figure 2.22: ^{1}H NMR ($CDCl_3$) spectrum of compound 8.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **8**; the aliphatic carbons were observed at δ = 25.44, 26.54, 30.49, 32.49 ppm. S-CH_2 carbon was observed at δ = 45.91 ppm. NH-CH_2 carbon at δ = 47.50 ppm. $SCH_2\boldsymbol{C}H_2OH$ at δ = 59.91 ppm. $NH(CH_2)_5\boldsymbol{C}H_2OH$ at δ = 62.73 ppm. Ar-C's at δ = 126.66, 127.08, 132.29, 133.65, 134.97 ppm and the carbonyl groups gave a signal at δ = 181.36 ppm.

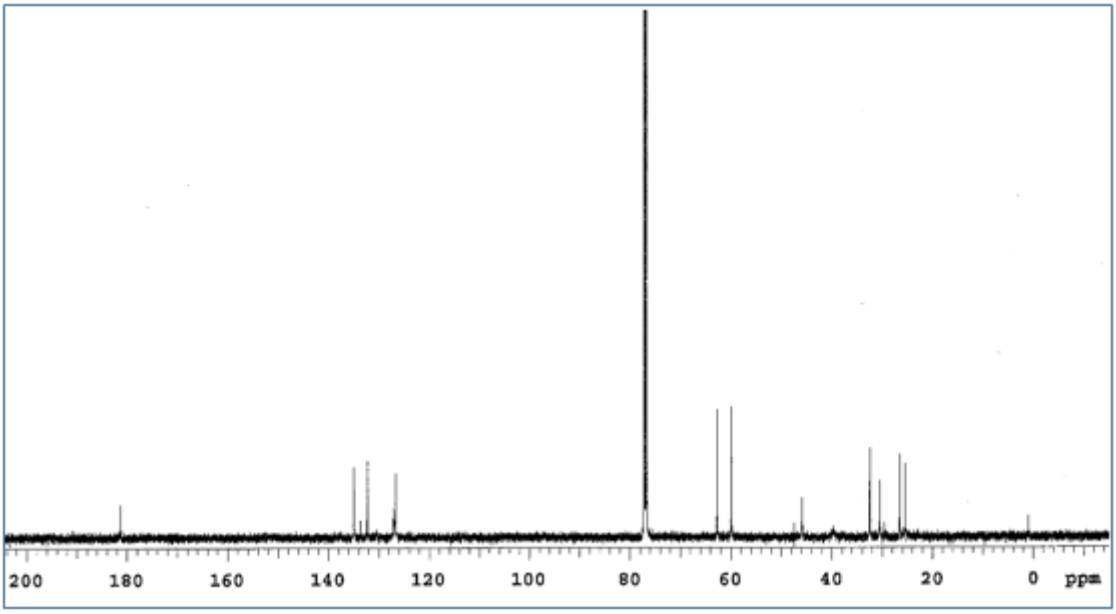


Figure 2.23: ^{13}C NMR ($CDCl_3$) spectrum of compound 8.

The mass spectrum of compound **8** which has the formula $C_{18}H_{23}NO_4S$ (M= 349.44 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **8** in the MS spectrum is *m/z*: (%) (100) 350 $[M+H]^+$. Figure 2.24.

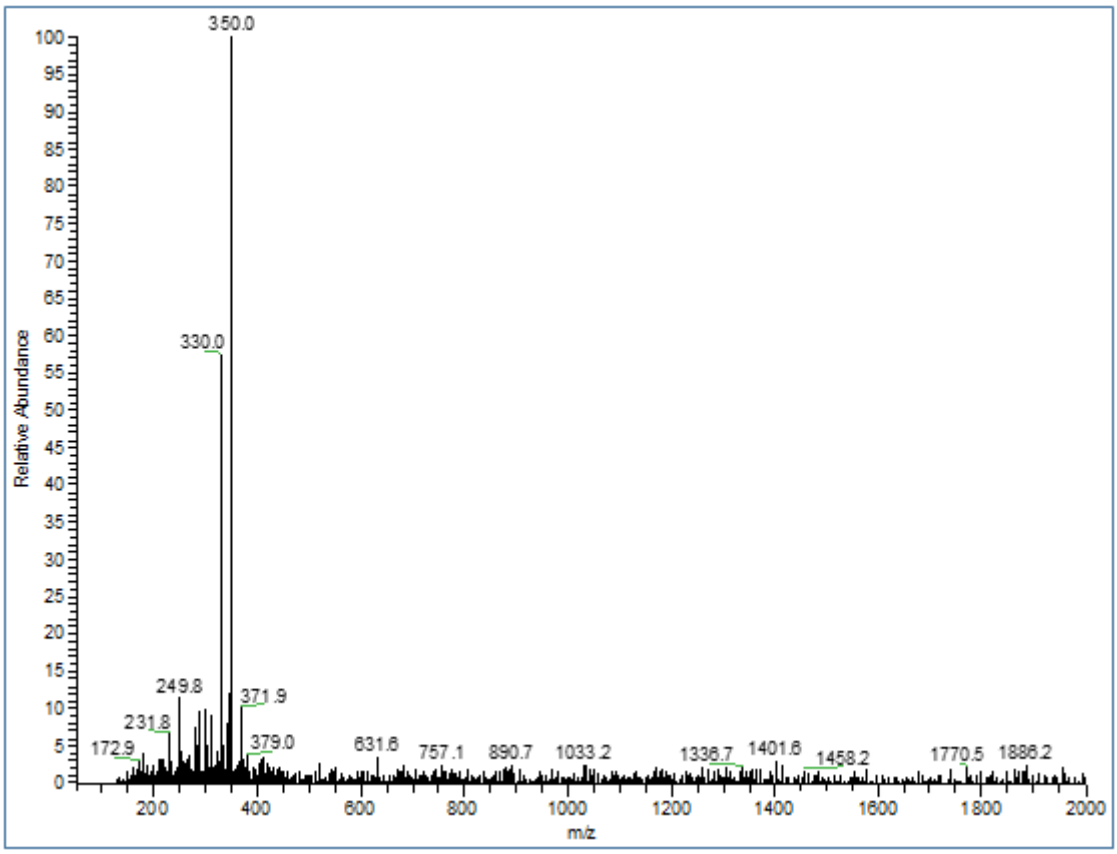
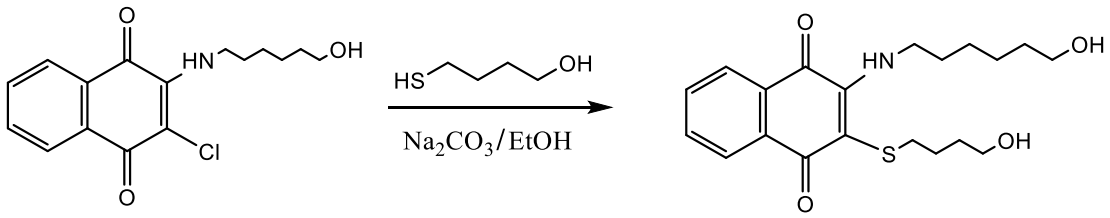


Figure 2.24: MS [+ESI] spectrum of compound 8.

2.1.8. Synthesis of new 2-(6-aminohexyl-1-ol)-3-(4-hydroxybutylthio)-1,4-NQ compound (9)

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** was reacted with 4-mercapto-1-butanol and new 2-(6-aminohexyl-1-ol)-3-(4-hydroxybutylthio)-1,4-NQ compound **(9)** was obtained. The product was separated by column chromatography.



7 9

In the IR spectrum of compound **9**; stretching band for (-NH and -OH) was seen at ν = 3285 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 3013 cm^{-1}, ν = 2929, 2853 cm^{-1}, ν = 1668 cm^{-1}, ν = 1588, 1549 cm^{-1}, respectively.

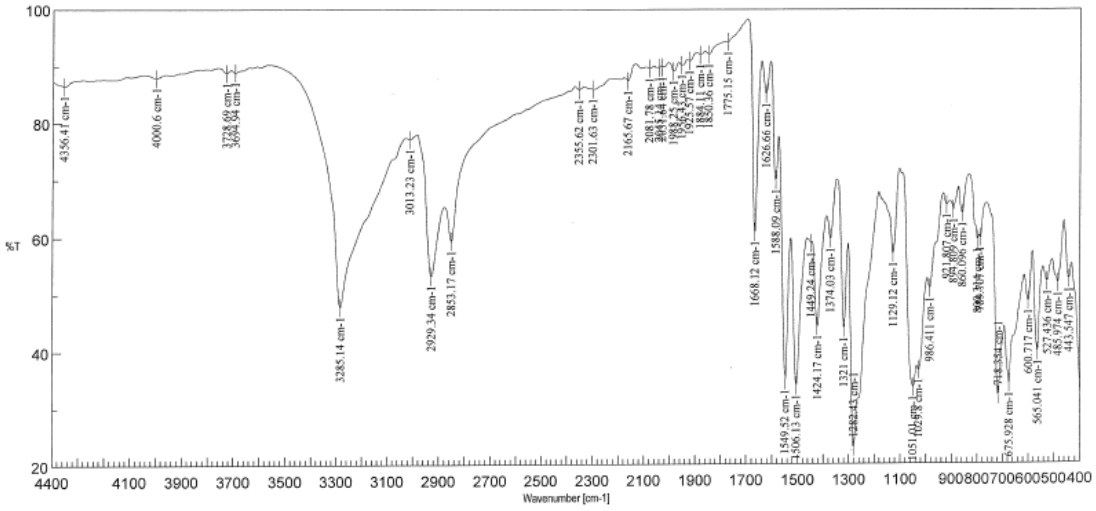


Figure 2.25: IR (KBr) spectrum of compound 9.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **9**; -OH protons appeared at δ = 1.26 ppm as singlet. Aliphatic CH_2 protons at δ = 1.45-1.74 ppm as multiplet. NH-C**H**$_2$ at δ = 2.83-2.86 ppm as triplet. The signal at δ = 3.65-3.69 ppm which appeared as multiplet is belonging to $NH(CH_2)_5C\mathbf{H}_2OH$ and -SCH_2 protons. $S(CH_2)_3C\mathbf{H}_2OH$ protons at δ = 3.91-3.94 ppm as triplet. Protons of NQ appeared at δ = 7.60-7.63, 7.70-7.74, 8.02-8.04 and 8.13-8.15 ppm as multiplet.

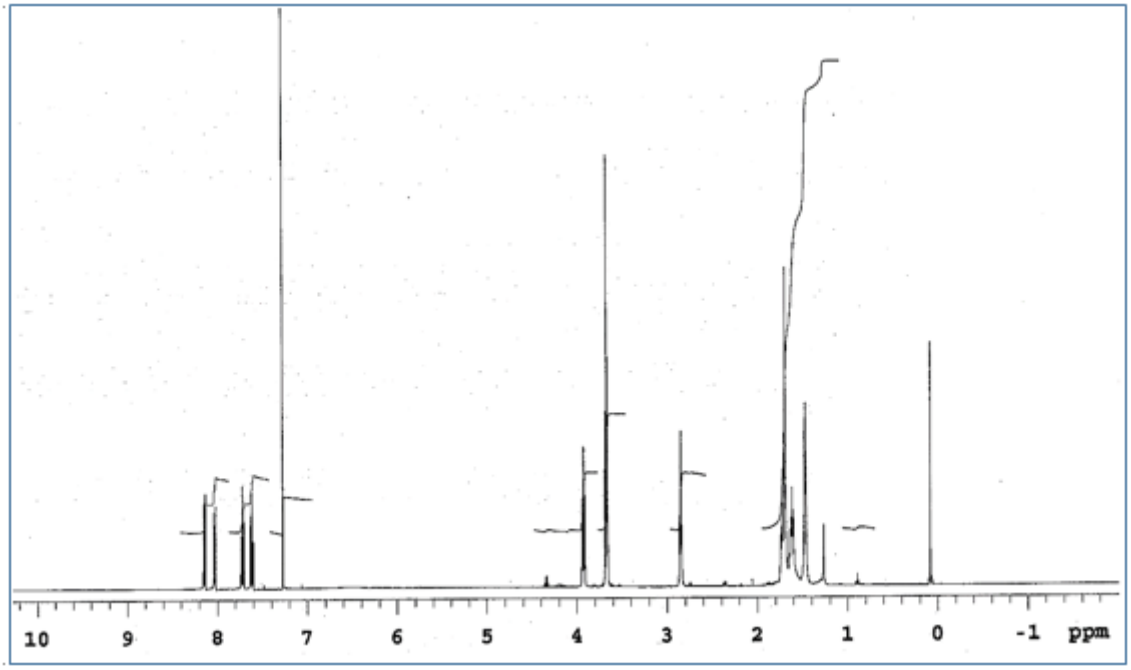


Figure 2.26: ^{1}H NMR ($CDCl_3$) spectrum of compound 9.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **9**; aliphatic carbons were observed at δ = 25.43, 26.53, 30.56, 31.84, 32.52, 34.92 ppm. S-CH_2 carbon was observed at δ = 45.96 ppm. NH-CH_2 carbon at δ = 47.51 ppm. $S(CH_2)_3\boldsymbol{C}H_2OH$ at δ = 62.28 ppm. $NH(CH_2)_5\boldsymbol{C}H_2OH$ at δ = 62.72 ppm. Ar-C's at δ = 126.47, 126.59, 126.68, 130.61, 132.06, 133.86, 134.67 ppm and the carbonyl groups gave two signals at δ = 180.23, 181.45 ppm.

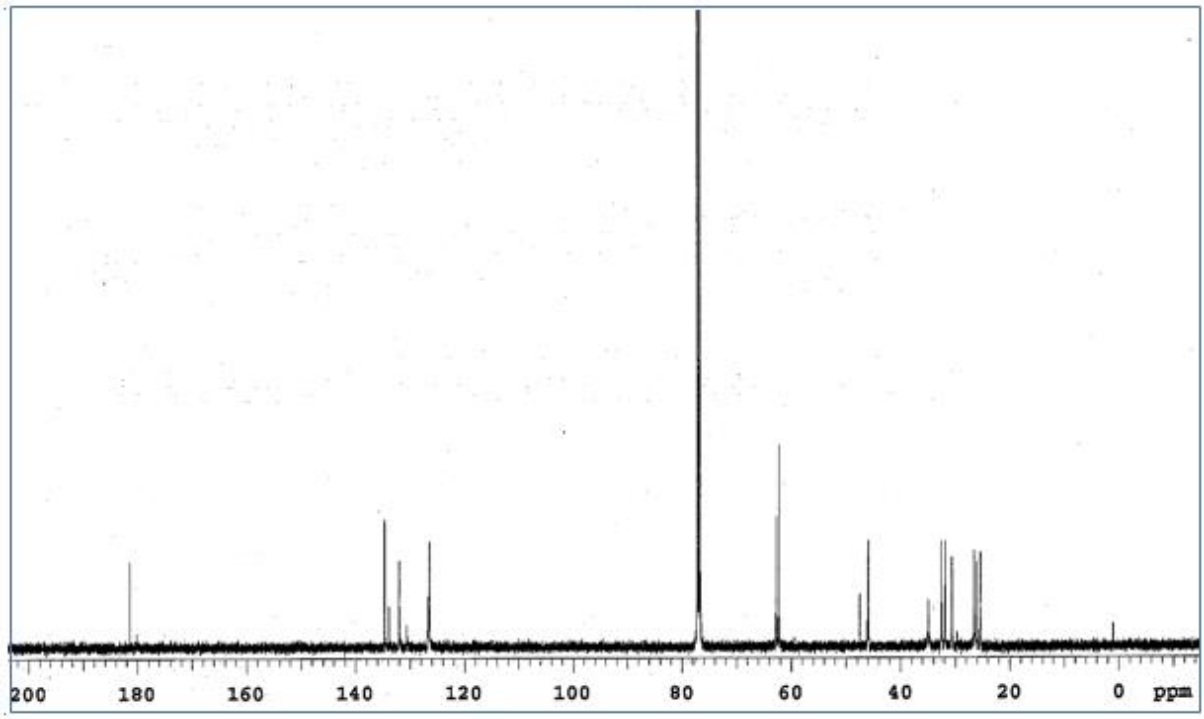


Figure 2.27: ^{13}C NMR ($CDCl_3$) spectrum of compound 9.

The mass spectrum of compound **9** which has the formula $C_{20}H_{27}NO_4S$ (M= 377.50g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **9** in the MS spectrum is *m/z*: (%) (100) 378 $[M+H]^+$. Figure 2.28.

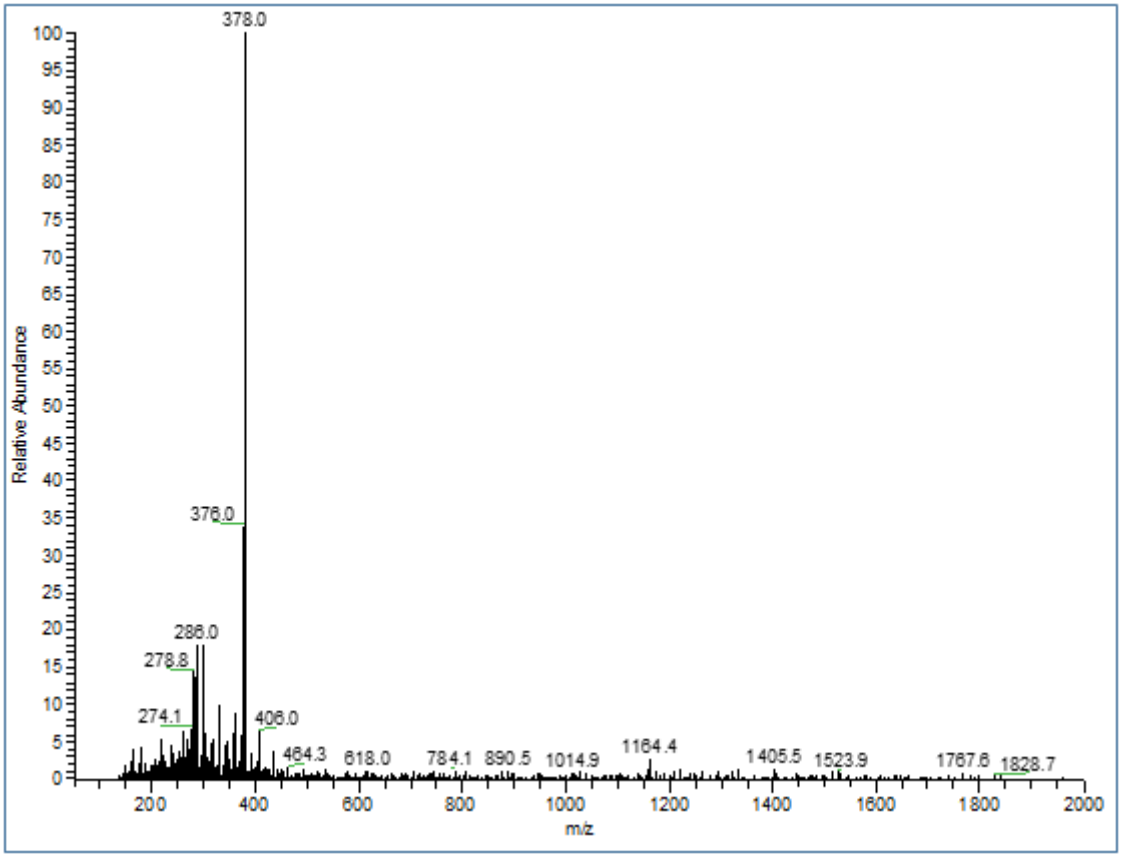
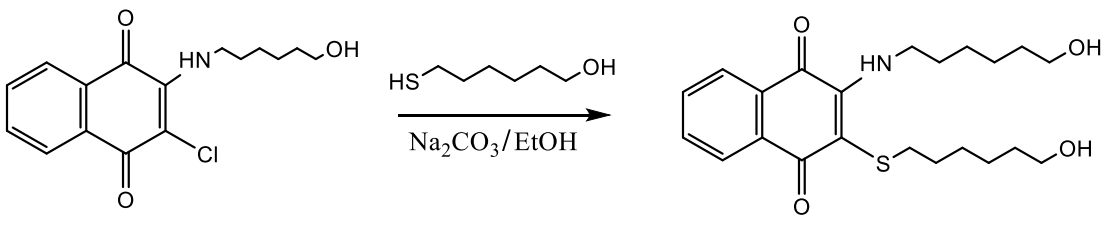


Figure 2.28: MS [+ESI] spectrum of compound 9.

2.1.9. Synthesis of new 2-(6-aminohexyl-1-ol)-3-(6-hydroxyhexylthio)-1,4-NQ compound (10)

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** was reacted with 6-mercapto-1-hexanol and new 2-(6-aminohexyl-1-ol)-3-(6-hydroxyhexylthio)-1,4-NQ compound **(10)** was obtained. The product was separated by column chromatography.



7 10

In the IR spectrum of compound **10**; stretching band for (-NH and -OH) was seen at ν = 3276 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 3070, 3012 cm^{-1}, ν = 2925, 2852 cm^{-1}, ν = 1669 cm^{-1}, ν = 1588, 1549 cm^{-1}, respectively.

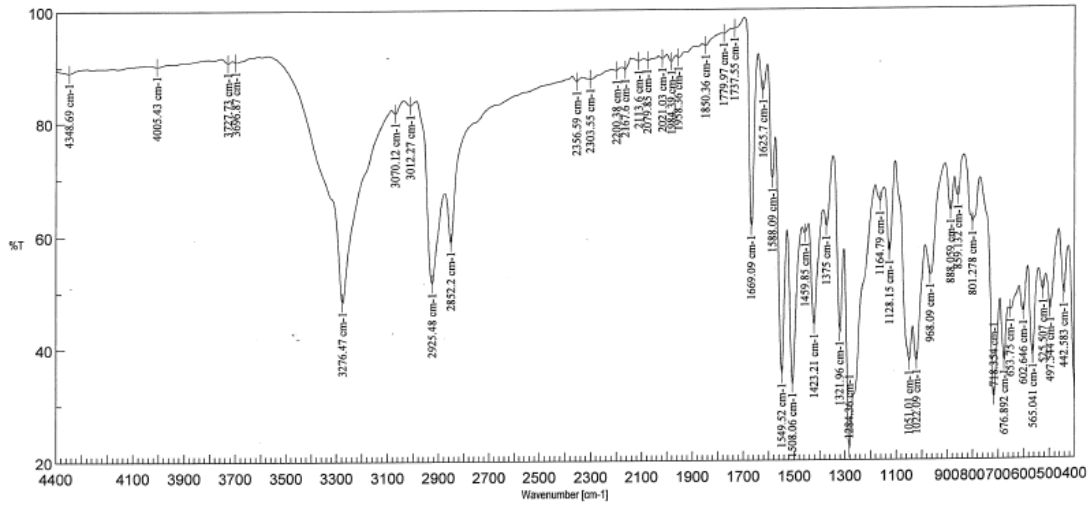


Figure 2.29: IR (KBr) spectrum of compound 10.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **10**; -OH protons appeared at δ = 1.26 ppm as singlet. Aliphatic CH_2 protons appeared as multiplet at δ = 1.35-1.74 ppm. -SCH_2 at δ = 2.80-2.84 ppm as triplet. The signal at δ = 3.62-3.68 ppm which appeared as multiplet is belonging to $NH(CH_2)_5C\mathbf{H_2}OH$ and NH-C$\mathbf{H_2}$protons. $S(CH_2)_5C\mathbf{H_2}OH$ protons at δ = 3.90-3.93 ppm as triplet. –NH proton appeared at δ = 6.49 ppm as singlet. Protons of NQ appeared at δ = 7.60-7.63, 7.70-7.73, 8.02-8.04 and 8.13-8.15 ppm as multiplet.

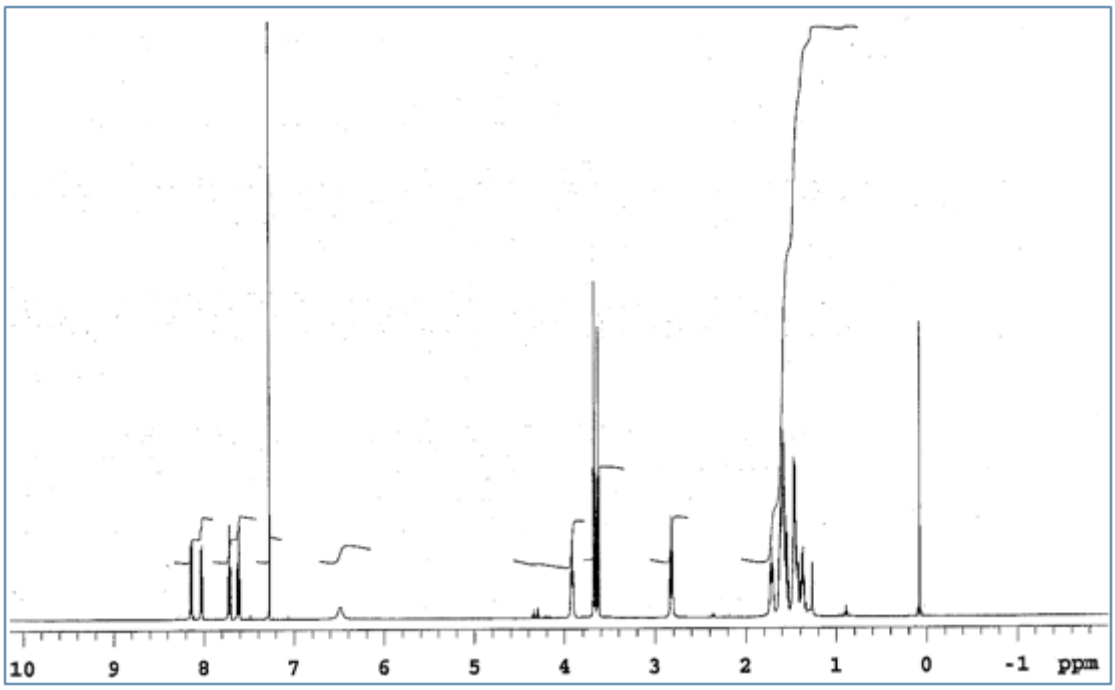


Figure 2.30: ^{1}H NMR ($CDCl_3$) spectrum of compound 10.

^{13}C NMR ($CDCl_3$) spectrum of compound **10**; the aliphatic carbons were observed at δ = 25.31, 25.49, 26.59, 28.55, 29.79, 30.62, 32.57, 34.97 ppm. S-CH_2 carbon was observed at δ = 46 ppm. NH-CH_2 carbon at δ = 47.51 ppm. $S(CH_2)_5\boldsymbol{C}H_2OH$ at δ = 62.78 ppm. $NH(CH_2)_5\boldsymbol{C}H_2OH$ at 62.85 ppm. Ar-C's at δ = 126.45, 126.65, 130.64, 132.03, 133.86, 134.63 ppm and the carbonyl groups gave two signals at δ = 180.11, 181.48 ppm.

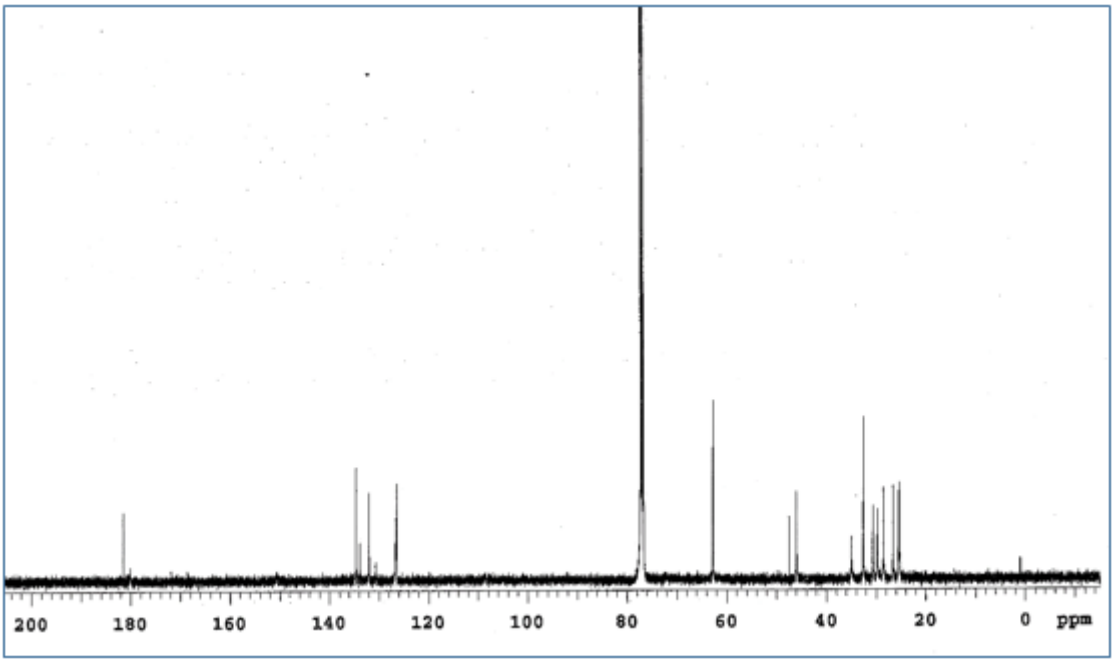


Figure 2.31: ^{13}C NMR ($CDCl_3$) spectrum of compound 10.

The mass spectrum of compound **10** which has the formula $C_{22}H_{31}NO_4S$ (M= 405.55 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **10** in the MS spectrum is *m/z*: (%) (100) 406 $[M+H]^+$. Figure 2.32.

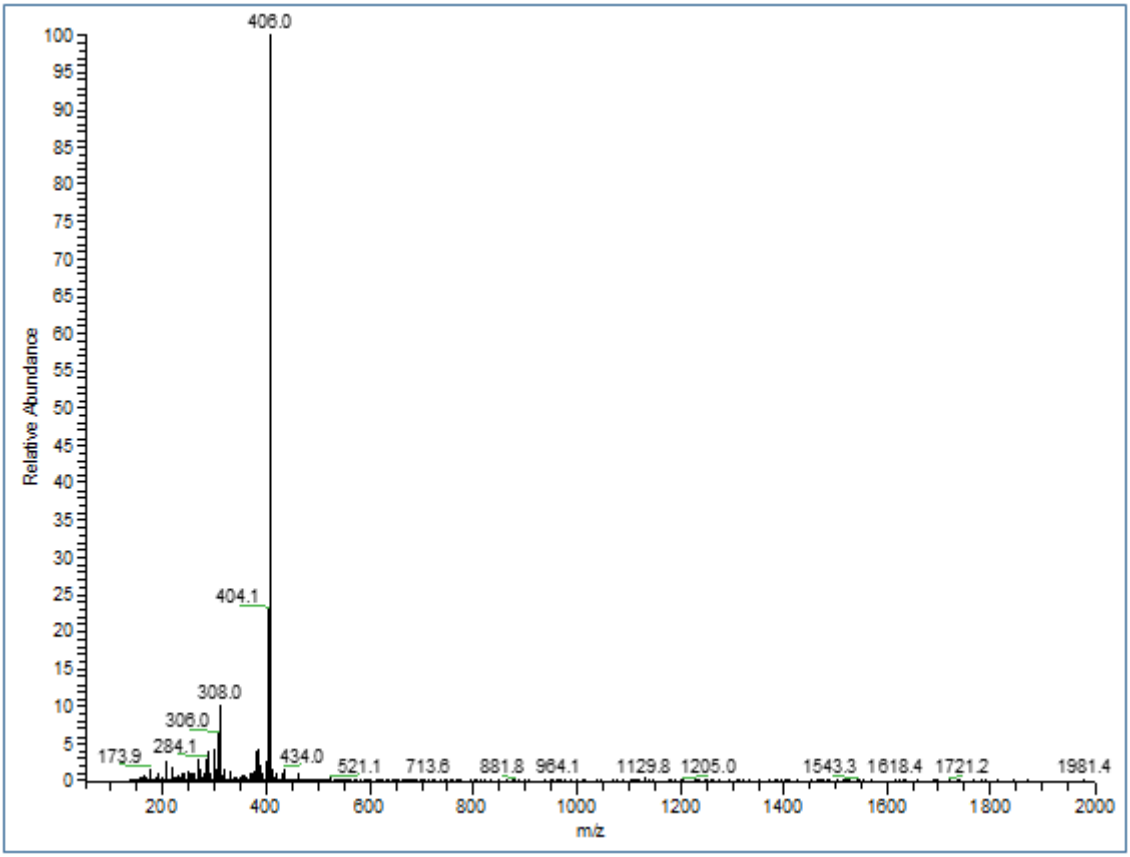
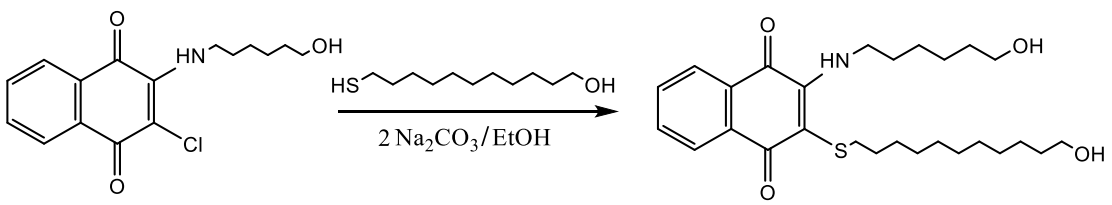


Figure 2.32: MS [+ESI] spectrum of compound 10.

2.1.10. Synthesis of new 2-(6-aminohexyl-1-ol)-3-(11-hydroxyundecylthio)-1,4-NQ compound (11)

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** was reacted with 11-mercapto-1-undecanol in ethanol, and new 2-(6-aminohexyl-1-ol)-3-(11-hydroxyundecylthio)-1,4-NQ compound **(11)** was obtained. The product was separated by column chromatography.



7 11

In the IR spectrum of compound **11**; stretching bands for (-NH and -OH) were seen at ν = 3427, 3372, 3294 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 3069 cm^{-1}, ν = 2923, 2850 cm^{-1}, ν = 1668 cm^{-1}, ν = 1589, 1549 cm^{-1}, respectively.

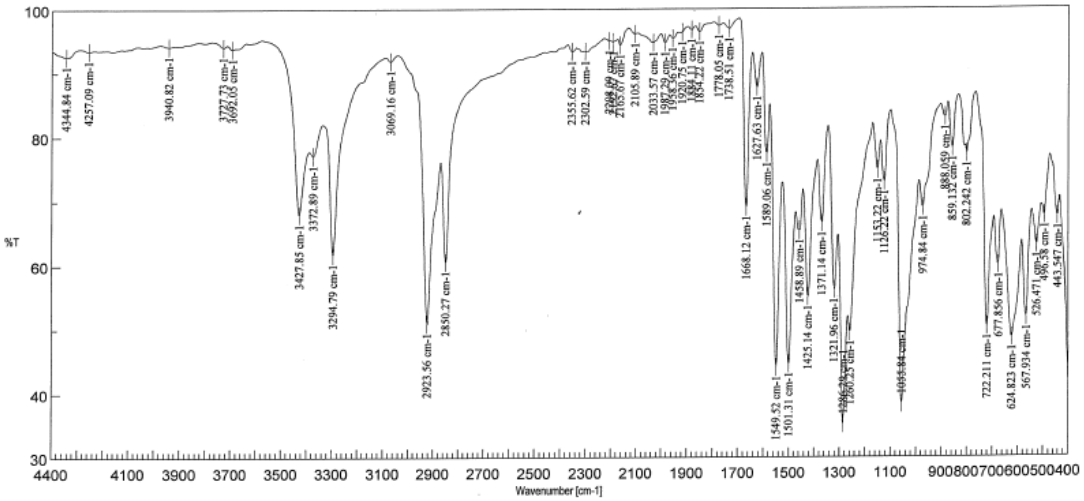


Figure 2.33: IR (KBr) spectrum of compound 11.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **11**; aliphatic CH_2 protons with -OH protons appeared as multiplet at δ = 1.16-1.67 ppm. -SCH_2 at δ = 2.71-2.74 ppm as triplet. The signal at δ = 3.54-3.60 ppm which appeared as multiplet is belonging to $S(CH_2)_{10}C\mathbf{H_2}OH$ and NH-$C\mathbf{H_2}$ protons. $NH(CH_2)_5C\mathbf{H_2}OH$ protons at δ = 3.81-3.85 ppm as triplet. Protons of NQ appeared at δ = 7.51-7.54, 7.61-7.65, 7.93-7.95 and 8.05-8.07 ppm as multiplet.

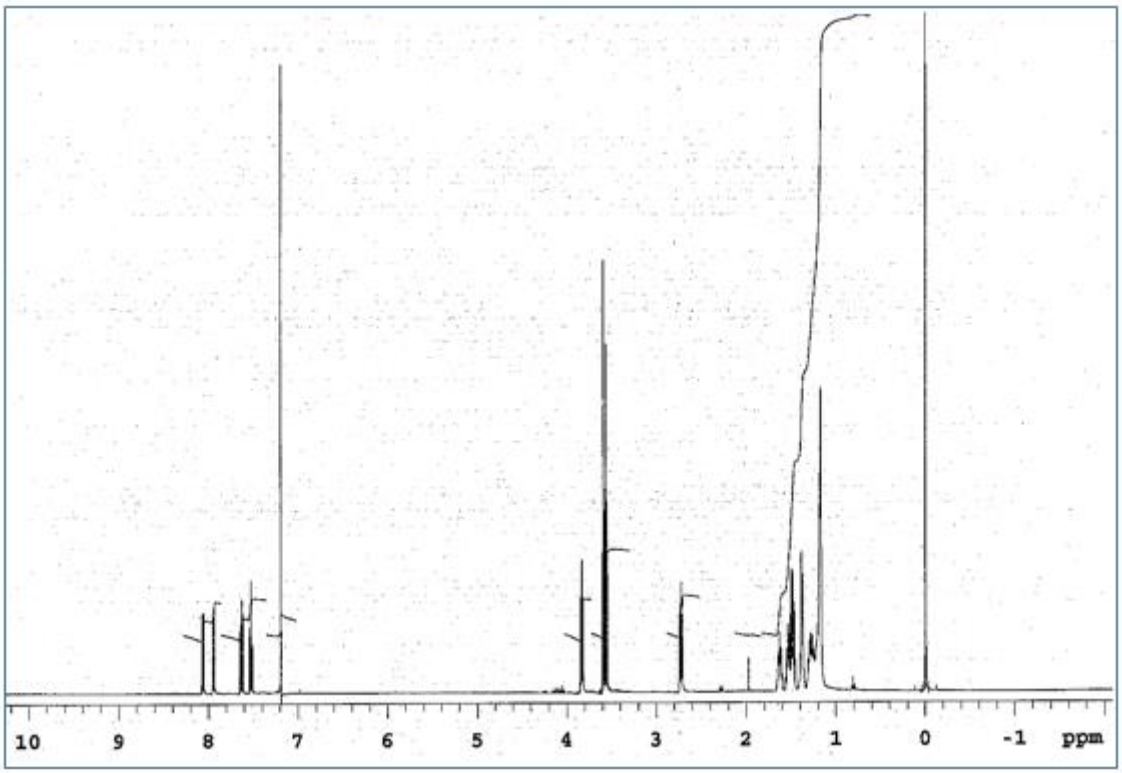


Figure 2.34: ^{1}H NMR ($CDCl_3$) spectrum of compound 11.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **11**; aliphatic carbons were observed at δ = 24.49, 24.68, 25.60, 27.85, 28.34, 28.43, 28.45, 28.50, 28.84, 29.62, 31.58, 31.74, 34.06 ppm. S-CH_2 carbon was observed at δ = 44.99 ppm. NH-CH_2 carbon at δ = 46.49 ppm. $S(CH_2)_{10}\mathbf{C}H_2OH$ at δ = 61.75 ppm. $NH(CH_2)_5\mathbf{C}H_2OH$ at δ = 62.03 ppm. Ar-C's were observed at δ = 125.39, 125.50, 129.64, 130.95, 132.86, 133.58 ppm and the carbonyl groups gave two signals at δ = 179.05, 180.49 ppm.

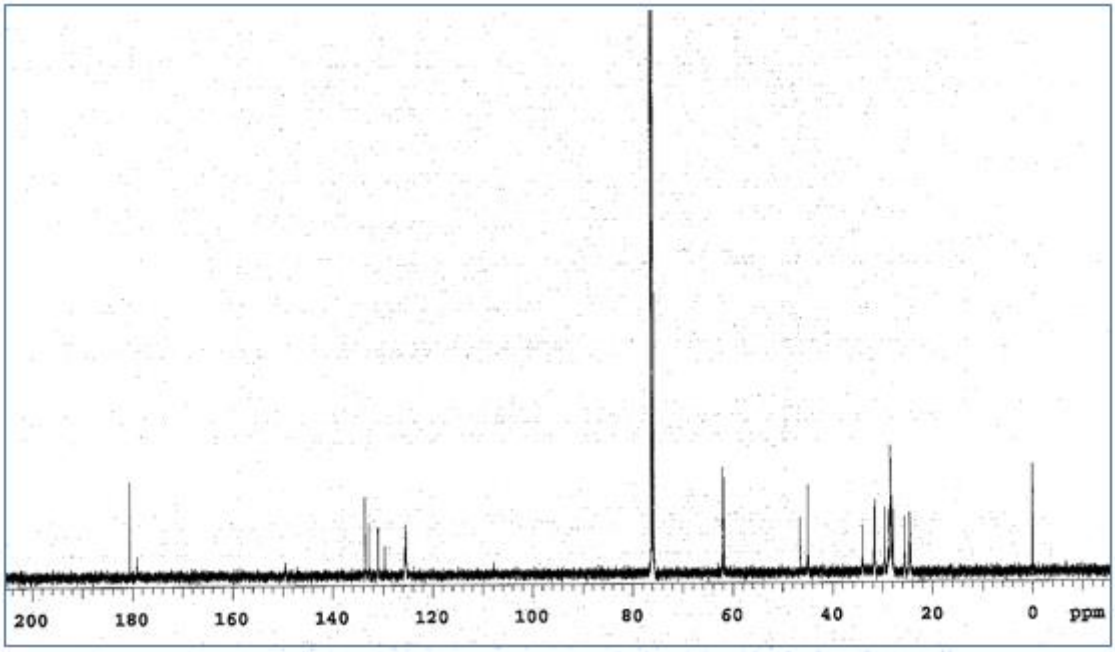


Figure 2.35: ^{13}C NMR ($CDCl_3$) spectrum of compound 11.

The mass spectrum of compound **11** which has the formula $C_{27}H_{41}NO_4S$ (M= 475.68 g/mole), was measured using the - ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **11** in the MS spectrum is *m/z*: (%) (100) 474 $[M-H]^+$. Figure 2.36.

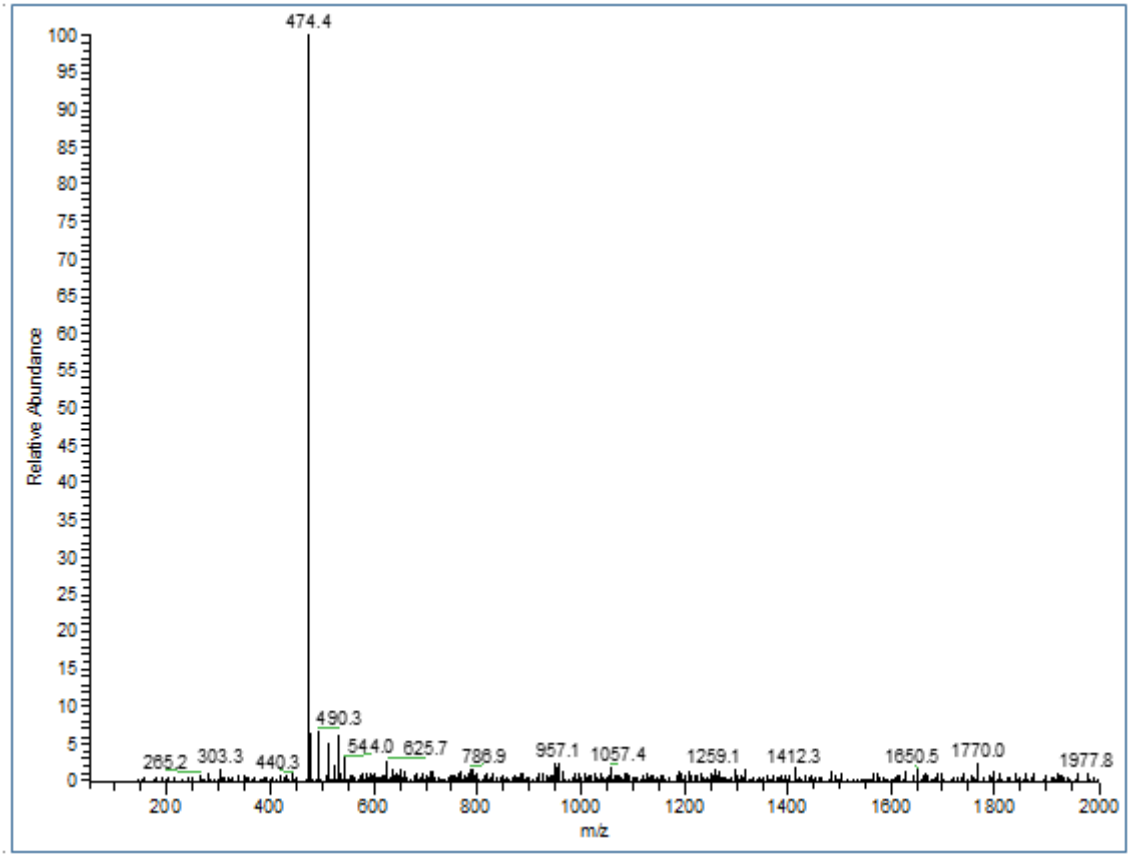
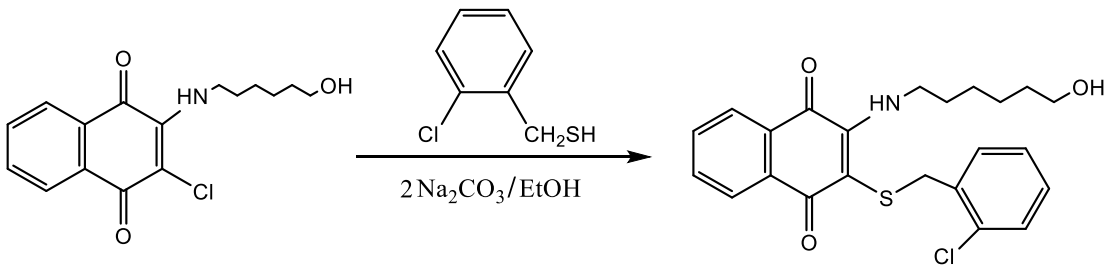


Figure 2.36: MS [-ESI] spectrum of compound 11.

2.1.11. Synthesis of new 2-(6-aminohexyl-1-ol)-3-(2-chlorobenzenemethylthio)-1,4-NQ compound (12)

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** was reacted with 2-chlorobenzyl mercaptan, and new 2-(6-aminohexyl-1-ol)-3-(2-chlorobenzenemethylthio)-1,4-NQ compound **(12)** was obtained. The product was separated by column chromatography.



7 12

In the IR spectrum of compound **12**; stretching bands for (-NH and -OH) were seen at ν = 3423, 3321 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 3063 cm^{-1}, ν = 2927, 2856 cm^{-1}, ν = 1672 cm^{-1}, ν = 1590, 1548 cm^{-1}, respectively.

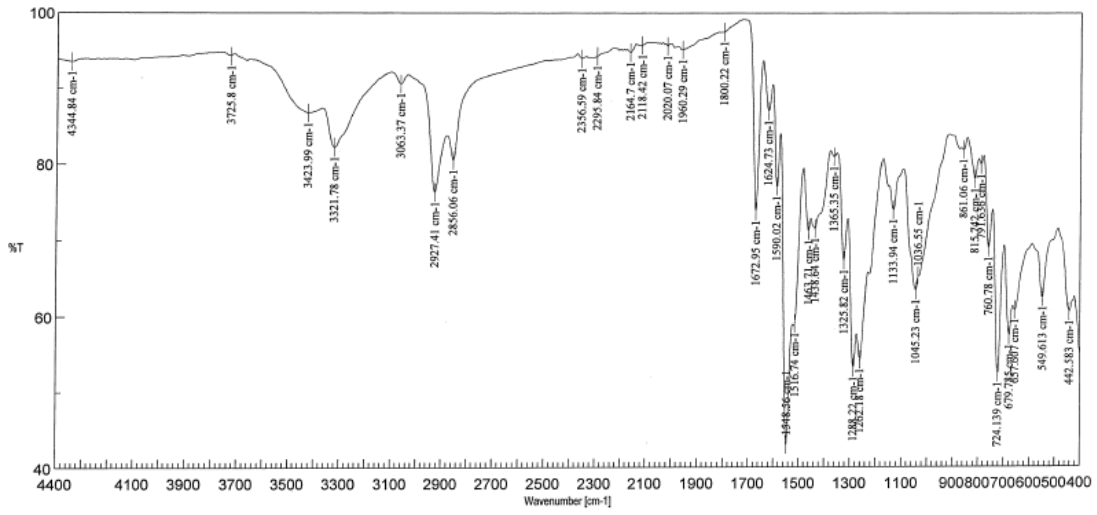


Figure 2.37: IR (film) spectrum of compound 12.

In the ^1H NMR ($CDCl_3$) spectrum of compound **12**; -OH proton appeared at δ = 1.18 ppm as singlet. Aliphatic CH_2 protons appeared as multiplet at δ = 1.23-1.33 ppm. $NHCH_2C\mathbf{H_2}$ protons at δ = 1.36-1.42 ppm as quintet. $C\mathbf{H_2}CH_2OH$ protons at δ = 1.47-1.53 ppm as quintet. NH-$C\mathbf{H_2}$ at δ = 3.41-3.44 ppm as triplet. $C\mathbf{H_2}$-OH at δ = 3.57-3.59 ppm as triplet. -SCH_2 at δ = 4.03 ppm as singlet. Protons of phenyl ring appeared at δ = 6.94-6.98, 7.04-7.07 and 7.24-7.26 ppm as multiplet. Protons of NQ appeared at δ = 7.52-7.55, 7.65-7.68, 7.91-7.92 and 8.11-8.13 ppm as multiplet.

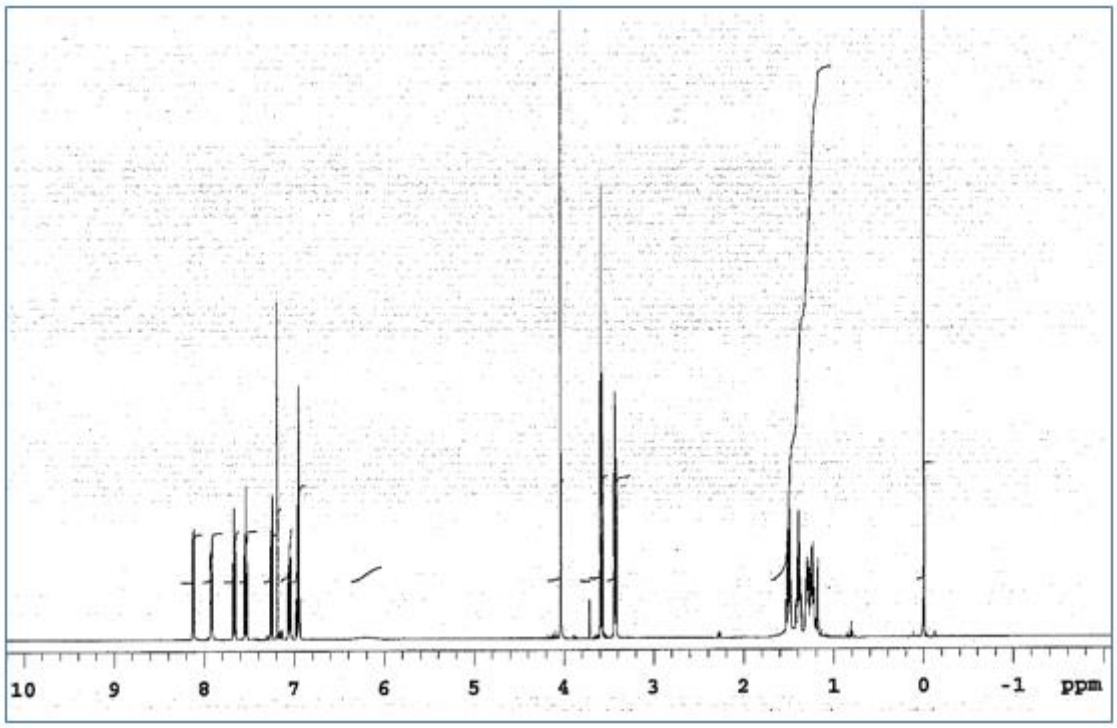


Figure 2.38: ^{1}H NMR ($CDCl_3$) spectrum of compound 12.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **12**; aliphatic carbons were observed as the following: ***C***$H_2CH_2CH_2OH$ at δ = 25.41 ppm, $NHCH_2CH_2$***C***H_2 at δ = 26.47 ppm, $NHCH_2$***C***H_2 at δ = 30.05 ppm, ***C***H_2CH_2OH at δ = 32.56 ppm. S-CH_2 carbon was observed at δ = 36.84 ppm. NH-CH_2 carbon at δ = 45.82 ppm. CH_2-OH carbon was observead at δ = 62.81 ppm. Ar-C's were observed at δ = 126.54, 126.63, 126.67, 128.39, 128.55, 129.47, 129.59, 130.85, 131.00, 132.01, 132.05, 133.81, 134.82, 136.08 ppm and the carbonyl groups gave two signals at δ = 180.18, 181.31 ppm.

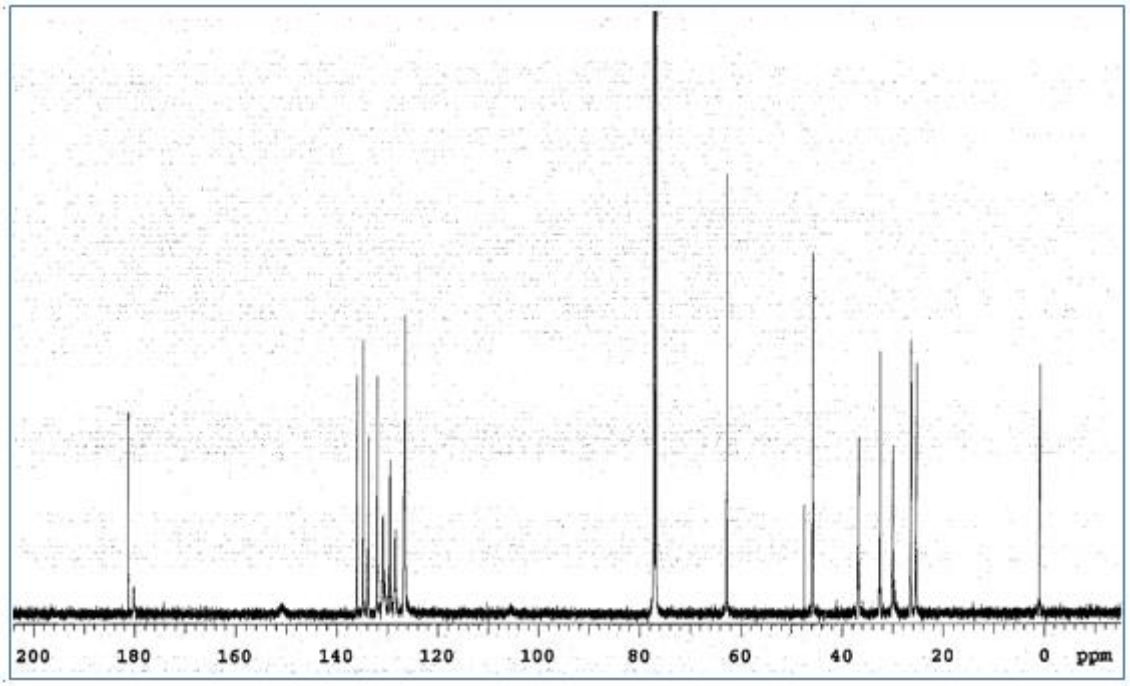


Figure 2.39: ^{13}C NMR ($CDCl_3$) spectrum of compound 12.

The mass spectrum of compound **12** which has the formula $C_{23}H_{24}ClNO_3S$ (M= 429.96 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **12** in the MS spectrum is *m/z*: (%) (100) 452 $[M+Na]^+$. Figure 2.40.

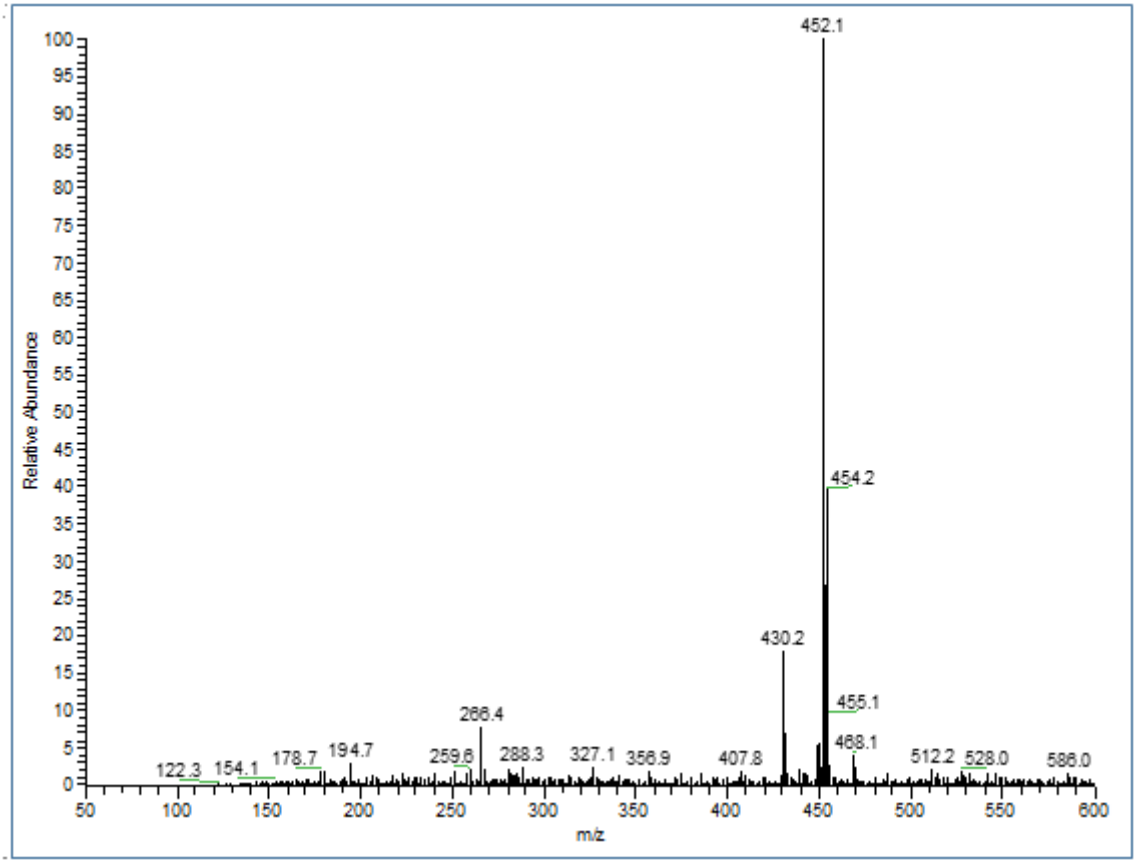
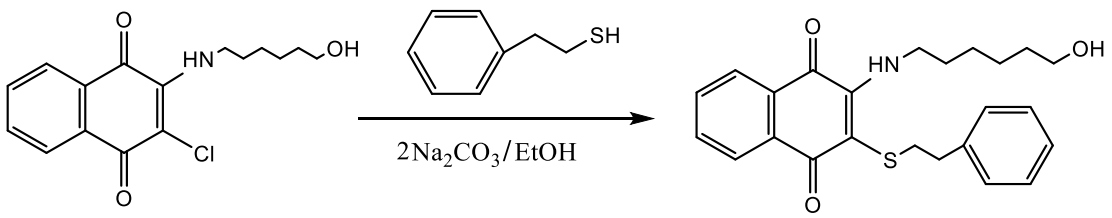


Figure 2.40: MS [+ESI] spectrum of compound 12.

2.1.12. Synthesis of new 2-(6-aminohexyl-1-ol)-3-(2-phenylethylthio)-1,4-NQ compound (13)

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** was reacted with 2-phenylethanethiol, and new 2-(6-aminohexyl-1-ol)-3-(2-phenylethylthio)-1,4-NQ compound **(13)** was obtained. The product was separated by column chromatography.



7 13

In the IR spectrum of compound **13**; stretching bands for (-NH and -OH) were seen at ν = 3423, 3325 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 3061, 3022 cm^{-1}, ν = 2926, 2856 cm^{-1}, ν = 1672 cm^{-1}, ν = 1590, 1548 cm^{-1}, respectively.

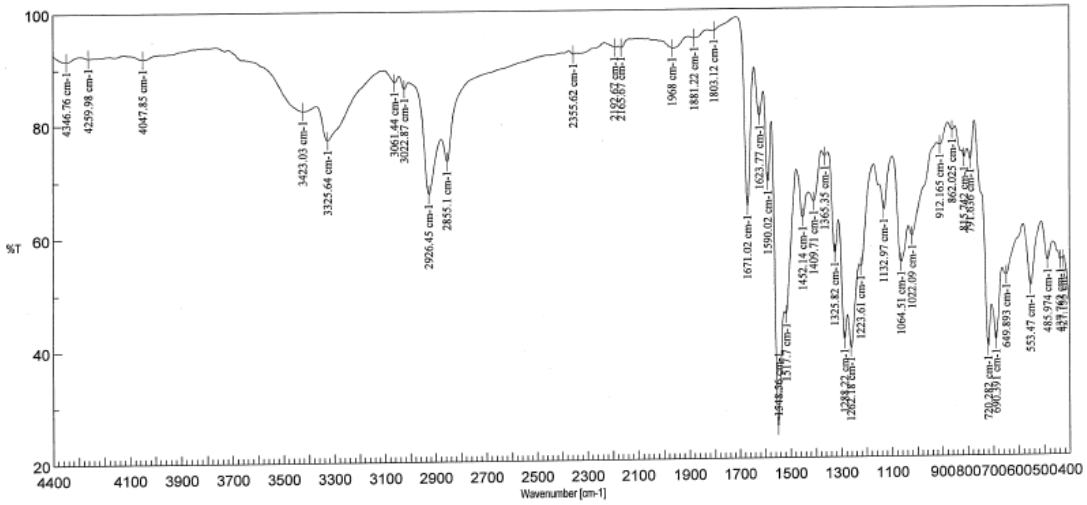


Figure 2.41: IR (film) spectrum of compound 13.

In the ^1H NMR ($CDCl_3$) spectrum of compound **13**; -OH proton appeared at δ = 1.18 ppm as singlet. Aliphatic CH_2 protons appeared as multiplet at δ = 1.30-1.37 ppm. The signal which appeared at δ = 1.49-1.57 ppm as multiplet is belonging to $NHCH_2C\mathbf{H_2}$ and $C\mathbf{H_2}CH_2OH$ protons. -SCH_2 protons appeared at δ = 2.80-2.83 ppm as triplet. NH-$C\mathbf{H_2}$ at δ = 3.03-3.06 ppm as triplet. CH_2-Ph protons at δ = 3.56-3.59 ppm as triplet. $C\mathbf{H_2}$-OH at δ = 3.67-3.70 ppm as triplet. Protons of phenyl ring appeared at δ = 7.03-7.09 and 7.12-7.15 ppm as multiplet. Protons of NQ appeared at δ = 7.50-7.54, 7.61-7.64, 7.91-7.93 and 8.05-8.07 ppm as multiplet.

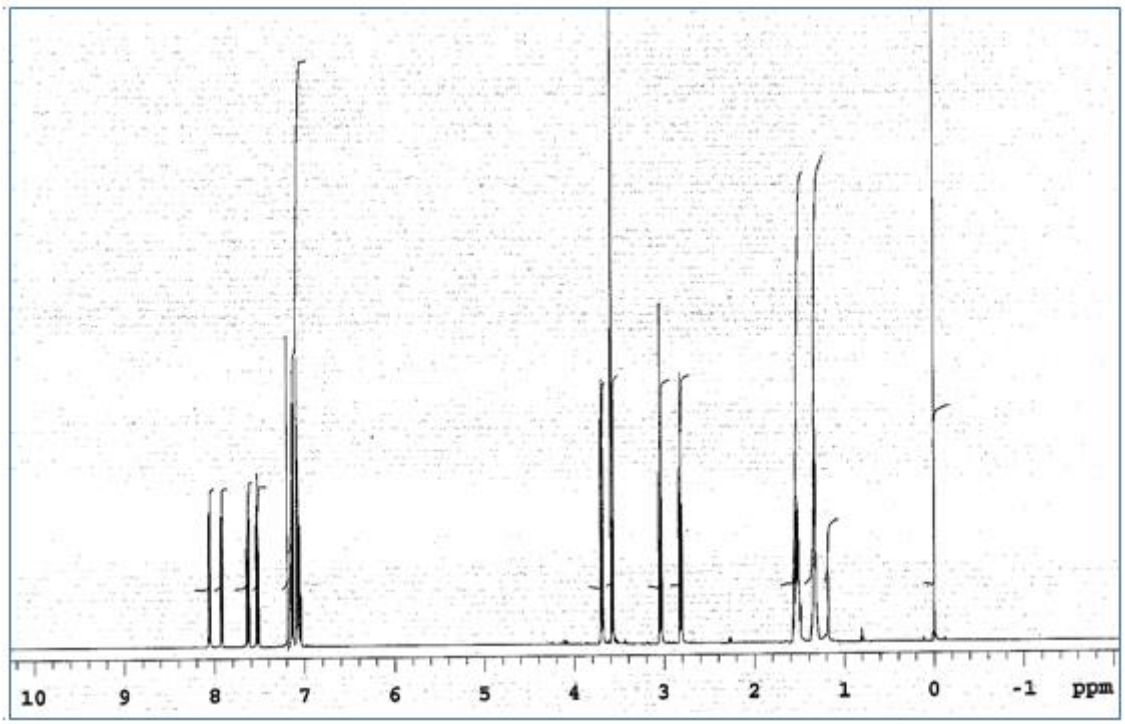


Figure 2.42: ^{1}H NMR ($CDCl_3$) spectrum of compound 13.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **13**; aliphatic carbons were observed as the following: ***C***$H_2CH_2CH_2OH$ at δ = 25.48 ppm, $NHCH_2CH_2$***C***H_2 at δ = 26.55 ppm, $NHCH_2$***C***H_2 at δ = 30.49 ppm, ***C***H_2CH_2OH at δ = 32.57 ppm. S-CH_2 carbon was observed at δ= 35.69 ppm. CH_2-Ph was observed at δ = 36.08 ppm. NH-CH_2 carbon at δ = 46.00 ppm. CH_2-OH carbon was observed at δ = 62.78 ppm. Ar-C's were observed at δ = 126.42, 126.53, 128.25, 128.30, 128.39, 128.43, 128.60, 130.61, 131.99, 131.97, 132.02, 133.86, 134.61, 140.19 ppm and the carbonyl groups gave two signals at δ = 180.06, 181.33 ppm.

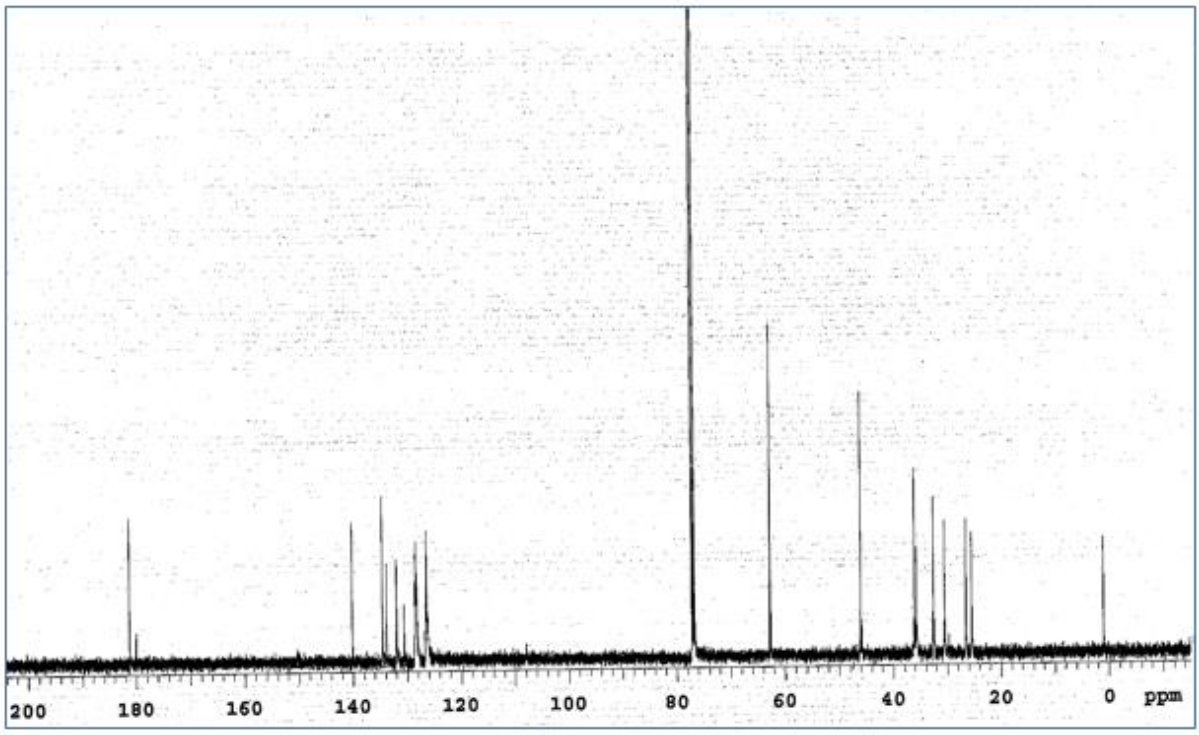


Figure 2.43: ^{13}C NMR ($CDCl_3$) spectrum of compound 13.

The mass spectrum of compound **13** which has the formula $C_{24}H_{27}NO_3S$ (M= 409.54 g/mole), was measured using the - ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **13** in the MS spectrum is *m/z*: (%) (100) 408 $[M-H]^+$. Figure 2.44.

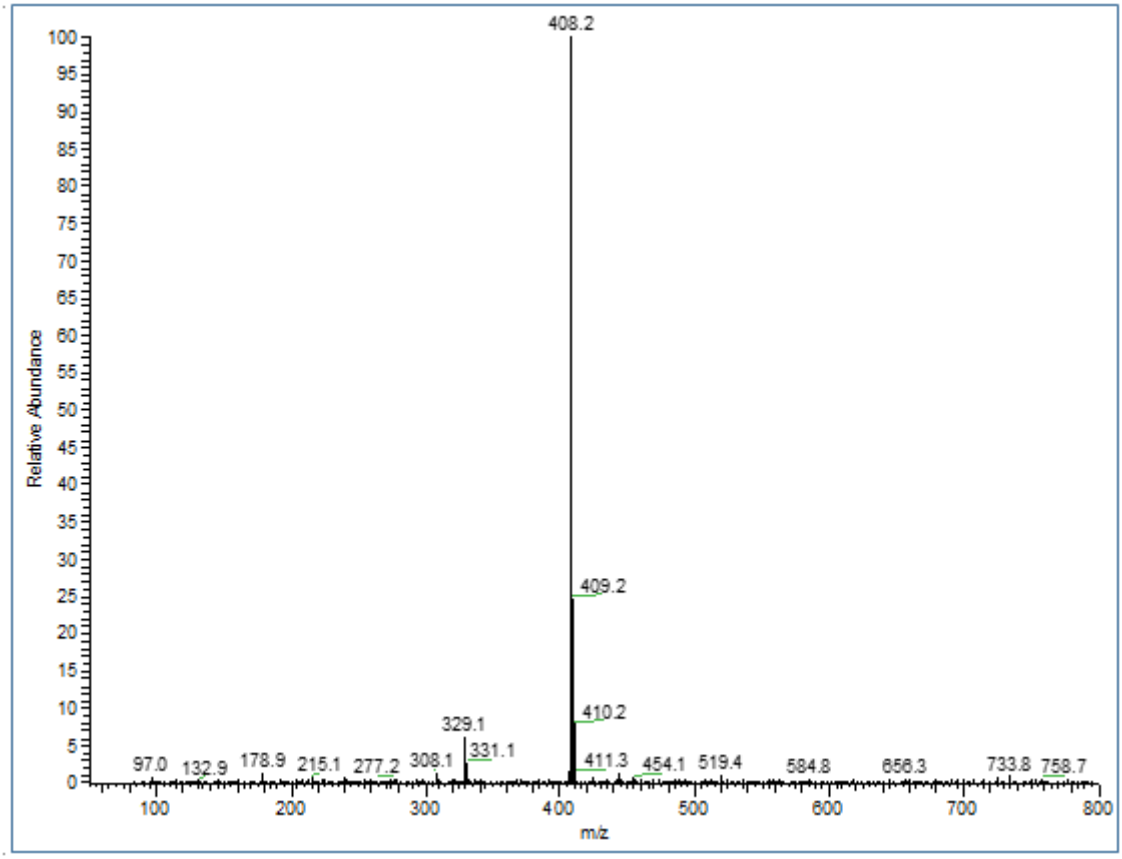
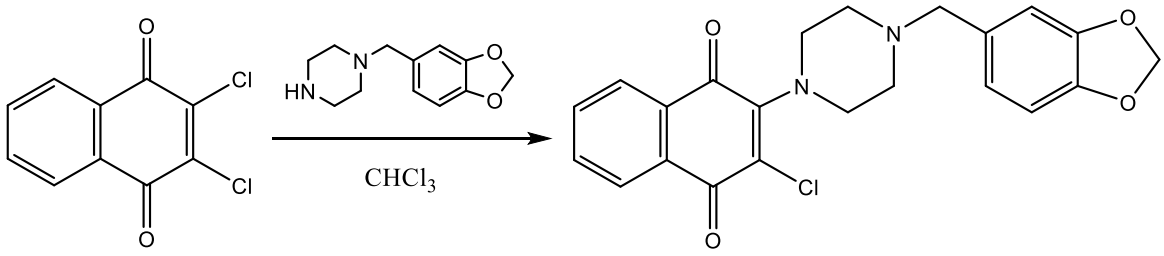


Figure 2.44: MS [-ESI] spectrum of compound 13.

2.1.13. Synthesis of 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ compound (14)

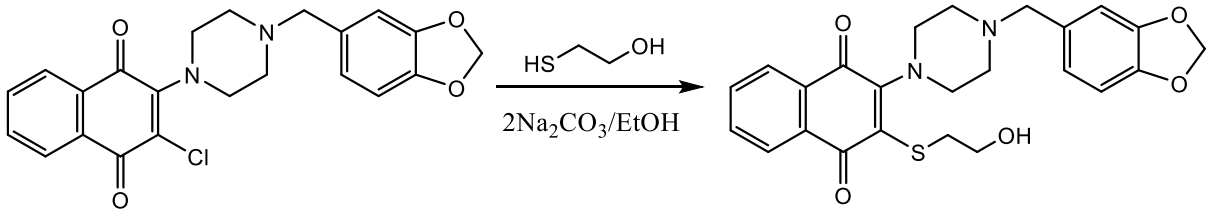
2,3-Dichloro-1,4-NQ **(1)** was reacted with 1-piperonylpiperazine and known 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ compound **(14)** was obtained. This compound is not new one. It was prepared in a previous work [2]. It was prepared in this study to be used as starting material for other reactions. The product was separated by column chromatography.



1 14

2.1.14. Synthesis of new 2-(1-piperonylpiperazin-1-yl)-3-(2-hydroxyethylthio)-1,4-NQ compound (15)

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** was reacted with 2-mercaptoethanol, and new 2-(1-piperonylpiperazin-1-yl)-3-(2-hydroxyethylthio)-1,4-NQ compound **(15)** was obtained. The product was separated by column chromatography.



14 15

In the IR spectrum of compound **15**; hydroxyl band (-OH) was seen at ν = 3300 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 3100 cm^{-1}, ν = 2899, 2809 cm^{-1}, ν = 1650 cm^{-1}, ν = 1587, 1548 cm^{-1}, respectively.

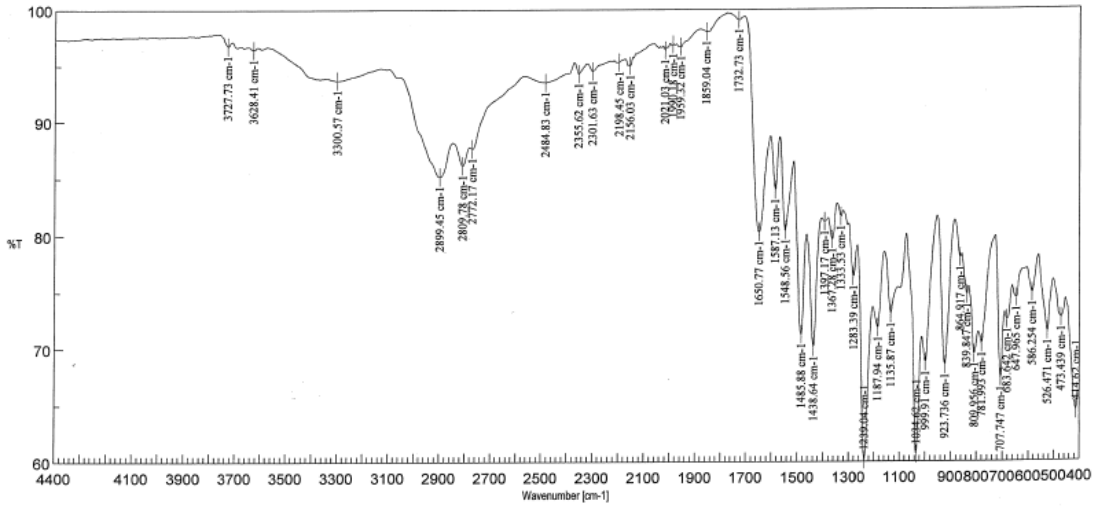


Figure 2.45: IR (film) spectrum of compound 15.

In the ^1H NMR ($CDCl_3$) spectrum of compound **15**; -OH proton appeared at δ = 1.18 ppm as singlet. Protons of piperazine ring at δ = 2.41 ppm as singlet and at 2.80-2.94 ppm as multiplet. -SCH_2 protons appeared at δ = 3.08-3.10 ppm as multiplet. N-CH_2-Ph protons at δ = 3.33-3.40

ppm as multiplet. -C**H**$_2$OH protons appeared at δ = 4.47-4.49 ppm as multiplet. O-CH_2-O protons at δ = 5.86-5.88 ppm as multiplet. Protons of phenyl ring appeared at δ = 6.63-6.69 ppm as multiplet and at 6.76 ppm as singlet. Protons of NQ appeared at δ = 7.60-7.63 and 7.98-8.04 ppm as multiplet.

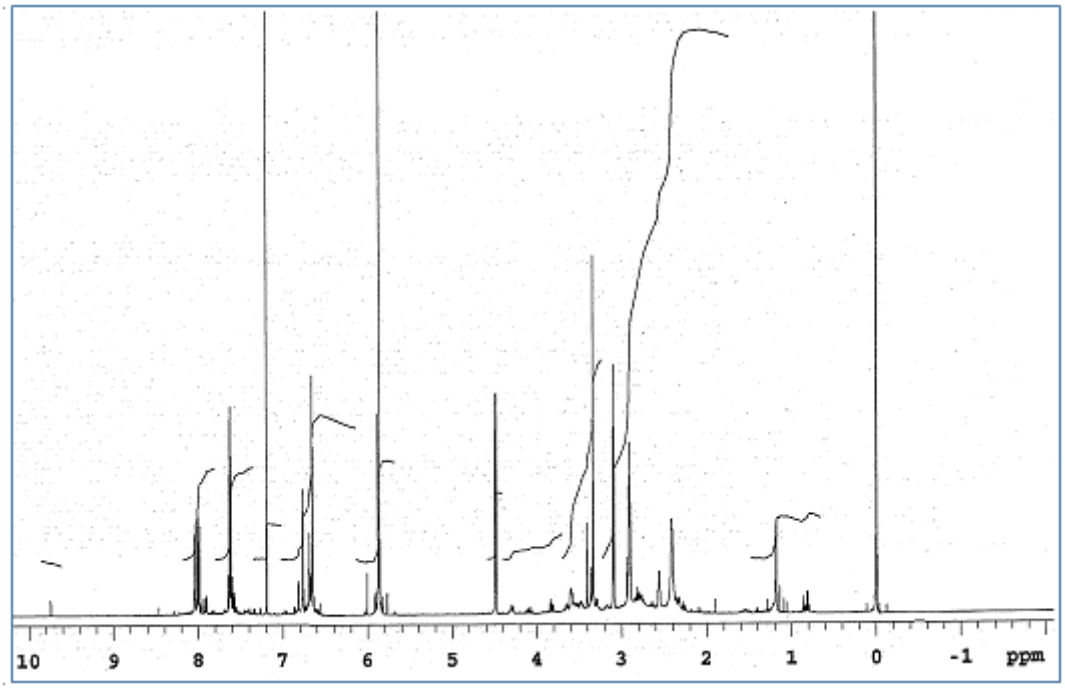


Figure 2.46: ^{1}H NMR ($CDCl_3$) spectrum of compound 15.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **15**; S-CH_2 carbon was observed at δ = 38.82 ppm. The piperazine carbons gave two signals at δ = 52.30, 52.88 ppm. CH_2-OH carbon was observed at δ = 62.88 ppm. N-***C***H_2-Ph at δ = 65.92 ppm. O-CH_2-O at δ = 100.92 ppm. Ar-C's were observed at δ = 107.88, 109.35, 122.24, 124.50, 126.34, 126.88, 130.80, 131.48, 132.73, 133.71, 133.83 ppm. =C-N were observed at δ = 146.73 ppm and =C-O at δ = 147.69, 151.61 ppm. The carbonyl groups gave two signals at δ = 176.48, 181.65 ppm.

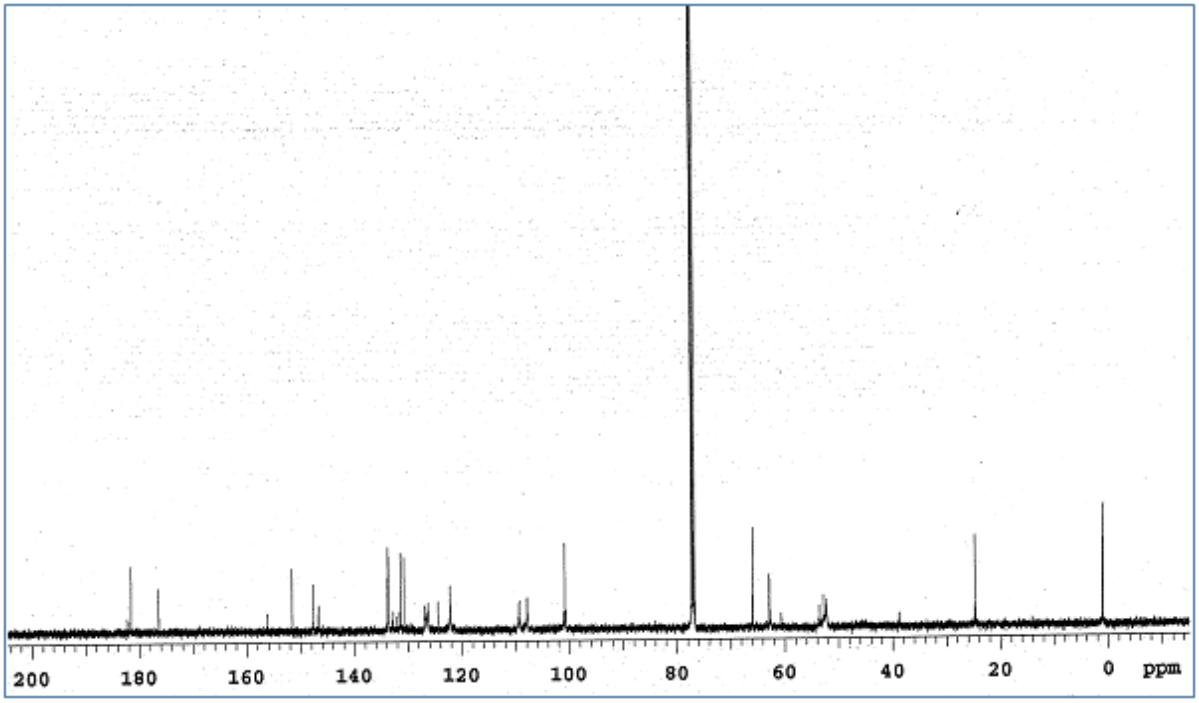


Figure 2.47: ^{13}C NMR ($CDCl_3$) spectrum of compound 15.

The mass spectrum of compound **15** which has the formula $C_{24}H_{24}N_2O_5S$ (M= 452.52 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **15** in the MS spectrum is *m/z*: (%) (100) 453 $[M+H]^+$. Figure 2.48.

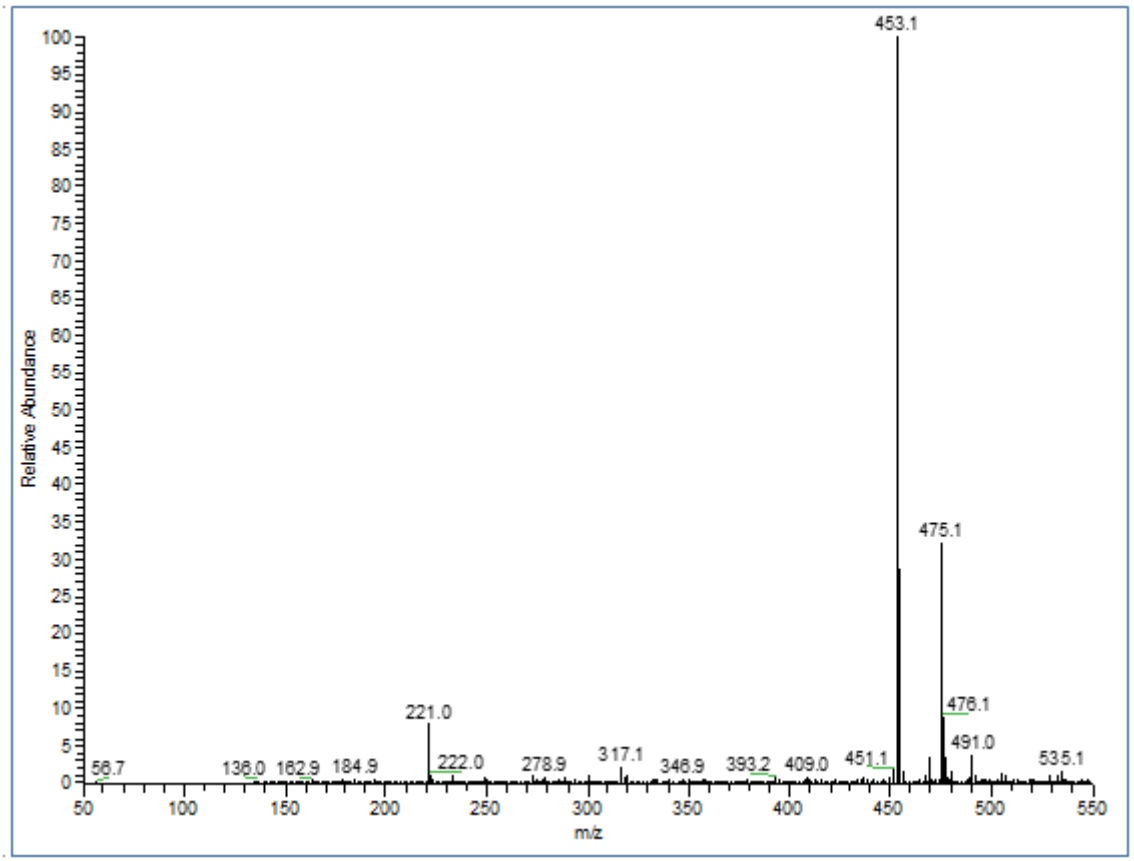
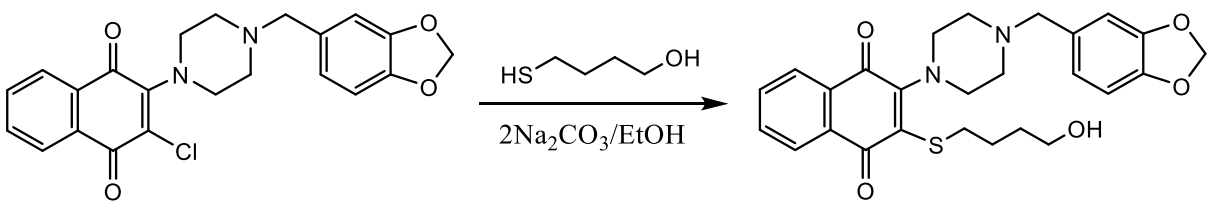


Figure 2.48: MS [+ESI] spectrum of compound 15.

2.1.15. Synthesis of new 2-(1-piperonylpiperazin-1-yl)-3-(4-hydroxybutylthio)-1,4-NQ compound (16)

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** was reacted with 4-mercapto-1-butanol, and new 2-(1-piperonylpiperazin-1-yl)-3-(4-hydroxybutylthio)-1,4-NQ compound **(16)** was obtained. The product was separated by column chromatography.



14 16

In the IR spectrum of compound **16**; hydroxyl band (-OH) was seen at ν = 3364 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 2961 cm^{-1}, ν = 2907 cm^{-1}, ν = 1662 cm^{-1}, ν = 1589, 1525 cm^{-1}, respectively.

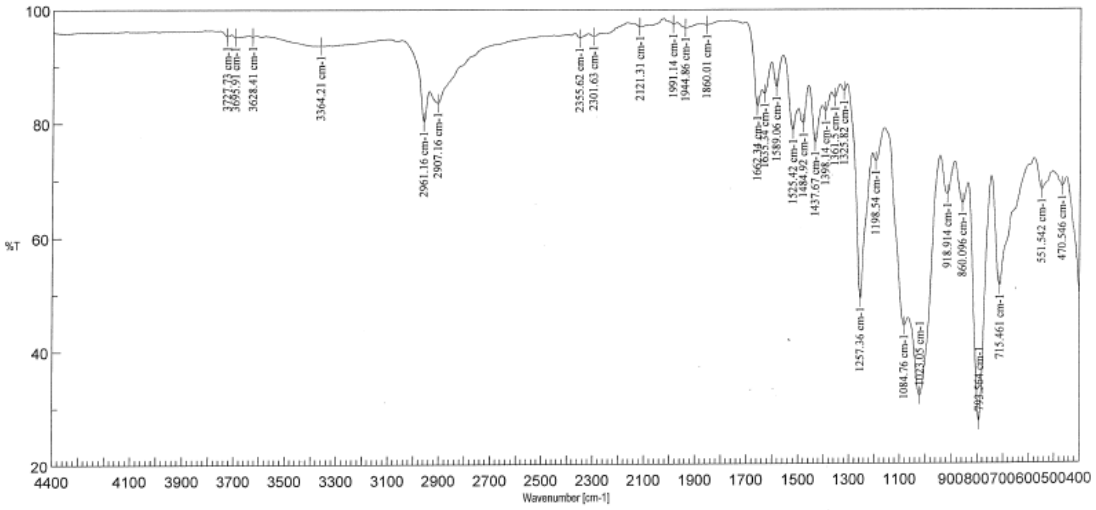


Figure 2.49: IR (film) spectrum of compound 16.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **16**; -OH proton appeared at δ = 1.18 ppm as singlet. Aliphatic CH_2 protons appeared as multiplet at δ = 1.56-1.61 ppm. Protons of piperazine ring at δ = 2.56-2.58 ppm as multiplet. -SCH_2 protons at δ = 2.82-2.85 ppm as triplet. N-CH_2-Ph protons at δ =3.44 ppm as singlet. -C**H_2**OH protons togother with the other protons of piperazine ring appeared at δ = 3.52-3.57 ppm as multiplet. O-CH_2-O protons at δ = 5.88 ppm as singlet. Protons of phenyl ring appeared at δ = 6.68-6.72 ppm as multiplet and at δ = 6.83 ppm as singlet. Protons of NQ appeared at δ = 7.54-7.60 and 7.89-7.97 ppm as multiplet.

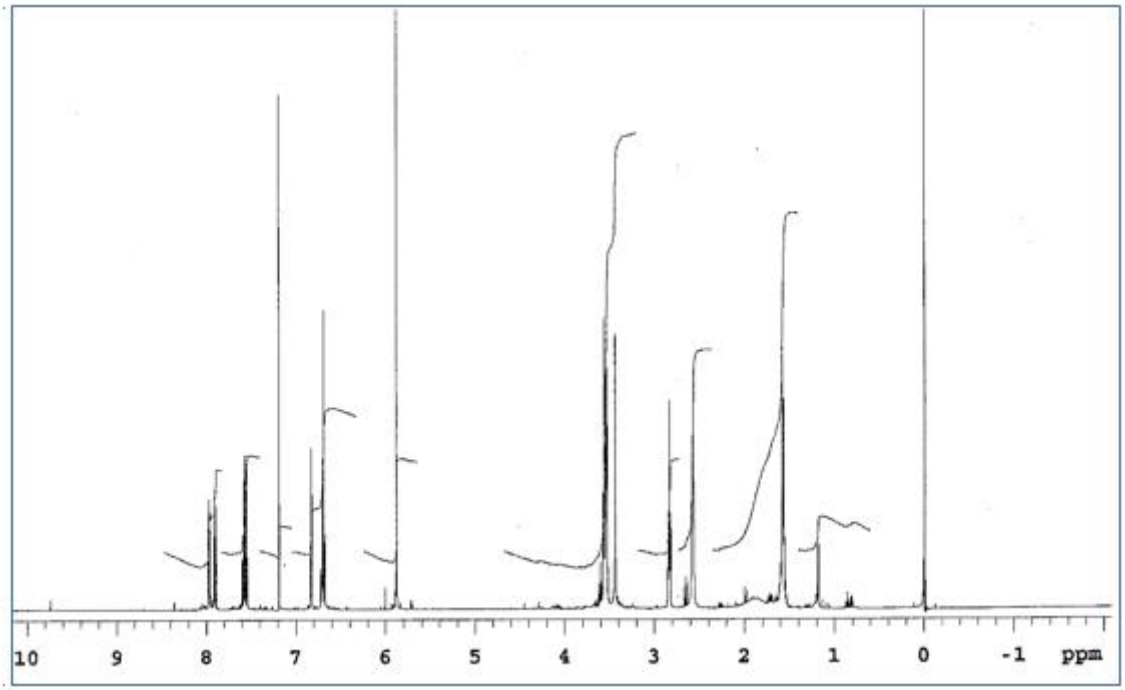


Figure 2.50: ^{1}H NMR ($CDCl_3$) spectrum of compound 16.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **16**; $SCH_2\boldsymbol{C}H_2$ carbon was observed at δ = 25.96 ppm. $SCH_2CH_2\boldsymbol{C}H_2$ at δ = 31.64 ppm. S-CH_2 carbon at δ = 34.46 ppm. The piperazine carbons gave two signals at δ = 52.06, 53.53 ppm. CH_2-OH carbon was observed at δ = 62.20 ppm. N-$\boldsymbol{C}H_2$-Ph at δ = 62.72 ppm. O-CH_2-O at δ = 100.96 ppm. Ar-C's were observed at δ = 107.96, 109.55, 122.54, 125.31, 126.27, 126.57, 132.13, 132.82, 132.88, 133.64 ppm. =C-N were observed at δ = 146.85 ppm and =C-O at δ = 147.74, 154.16 ppm. The carbonyl groups gave two signals at δ = 181.83, 182.11 ppm.

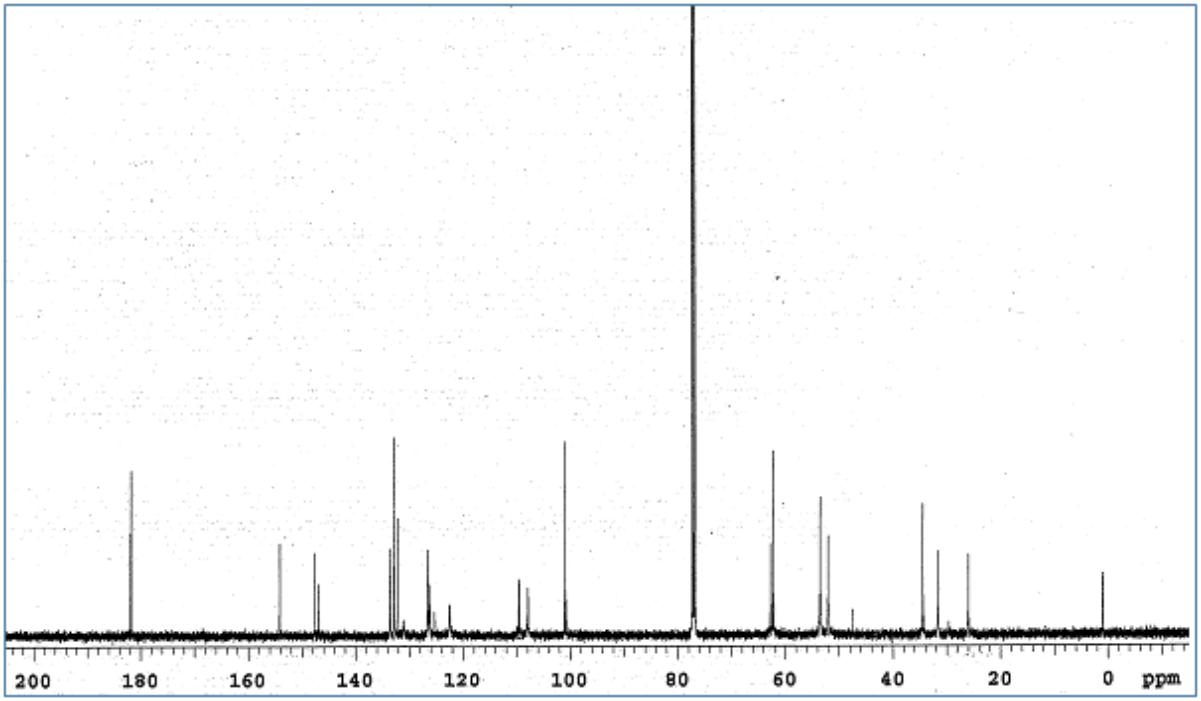


Figure 2.51: ^{13}C NMR ($CDCl_3$) spectrum of compound 16.

The mass spectrum of compound **16** which has the formula $C_{26}H_{28}N_2O_5S$ (M= 480.58 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **16** in the MS spectrum is *m/z*: (%) (100) 481 $[M+H]^+$. Figure 2.52.

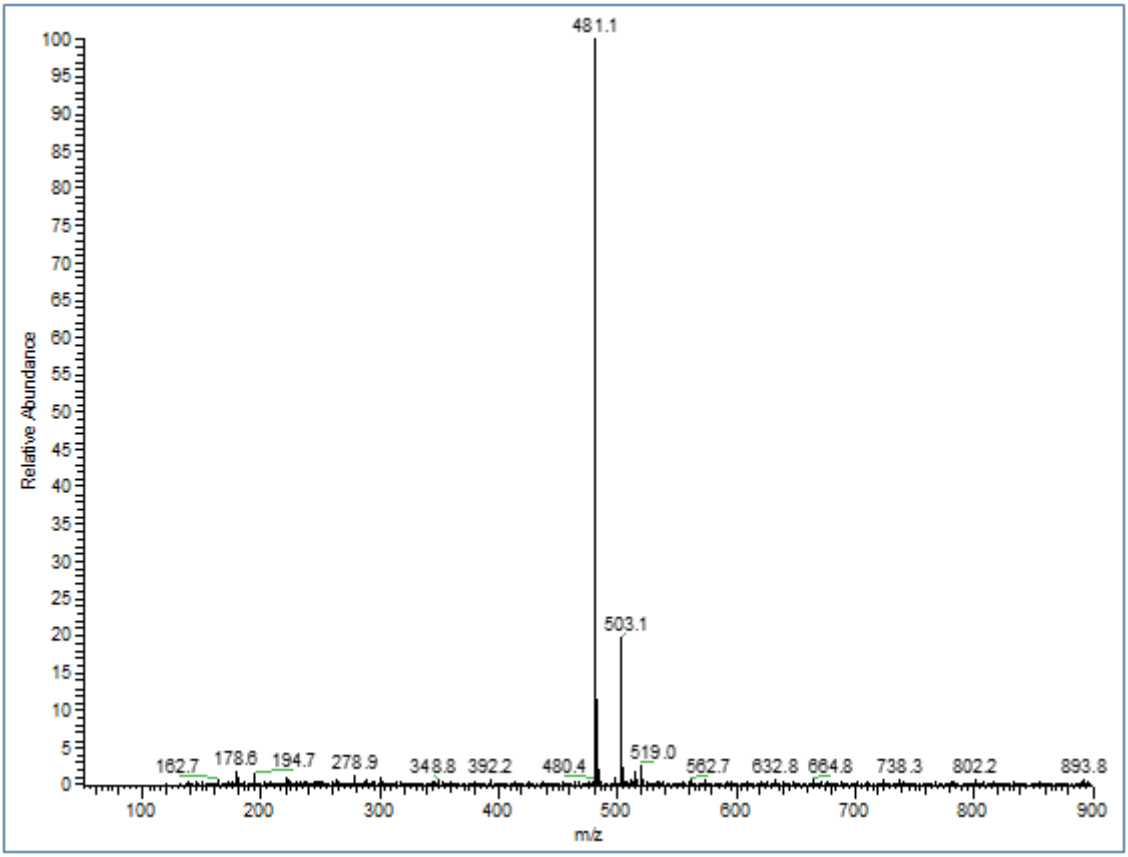
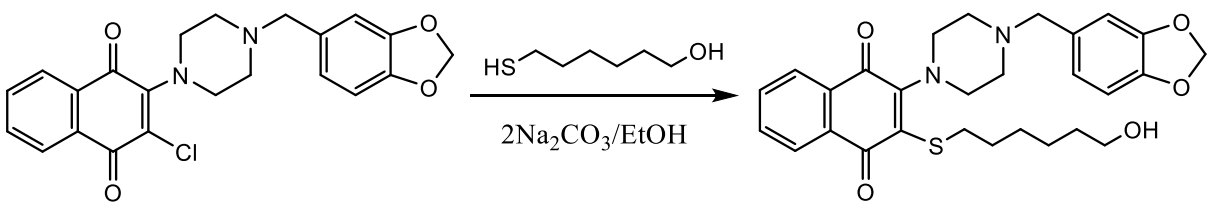


Figure 2.52: MS [+ESI] spectrum of compound 16.

2.1.16. Synthesis of new 2-(1-piperonylpiperazin-1-yl)-3-(6-hydroxyhexylthio)-1,4-NQ compound (17)

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** was reacted with 6-mercaptohexanol, and new 2-(1-piperonylpiperazin-1-yl)-3-(6-hydroxyhexylthio)-1,4-NQ compound **(17)** was obtained. The product was separated by column chromatography.



14 17

In the IR spectrum of compound **17**; hydroxyl band (-OH) was seen at ν = 3397 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 3067 cm^{-1}, ν = 2923, 2857 cm^{-1}, ν = 1663 cm^{-1}, ν = 1589, 1526 cm^{-1}, respectively.

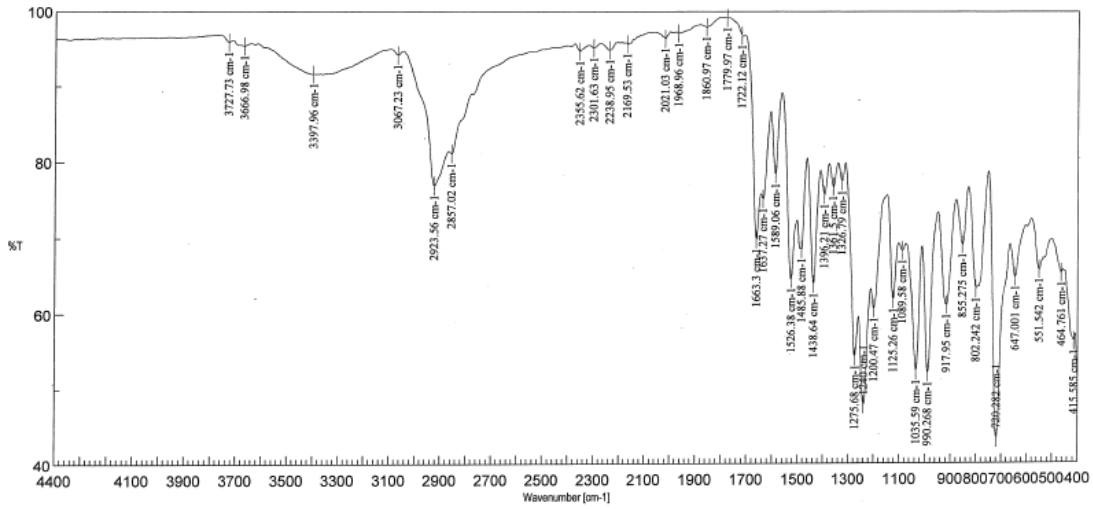


Figure 2.53: IR (film) spectrum of compound 17.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **17**; aliphatic CH_2 protons with -OH proton appeared as multiplet at δ = 1.18-1.48 ppm. Protons of piperazine ring at δ = 2.57-2.59 ppm as triplet. $SCH_2C\mathbf{H_2}$ protons at δ = 2.77-2.80 ppm as multiplet. -SCH_2 protons appeared at δ = 3.44 ppm as singlet. $C\mathbf{H_2}OH$ protons togother with N-CH_2-Ph protons and with the other protons of piperazine ring appeared at δ = 3.53-3.55 ppm as multiplet. O-CH_2-O protons at δ = 5.87 ppm as singlet. Protons of phenyl ring appeared at δ = 6.67-6.70 ppm as multiplet and at δ = 6.83 ppm as singlet. Protons of NQ group appeared at δ = 7.55-7.59 and 7.89-7.97 ppm as multiplet.

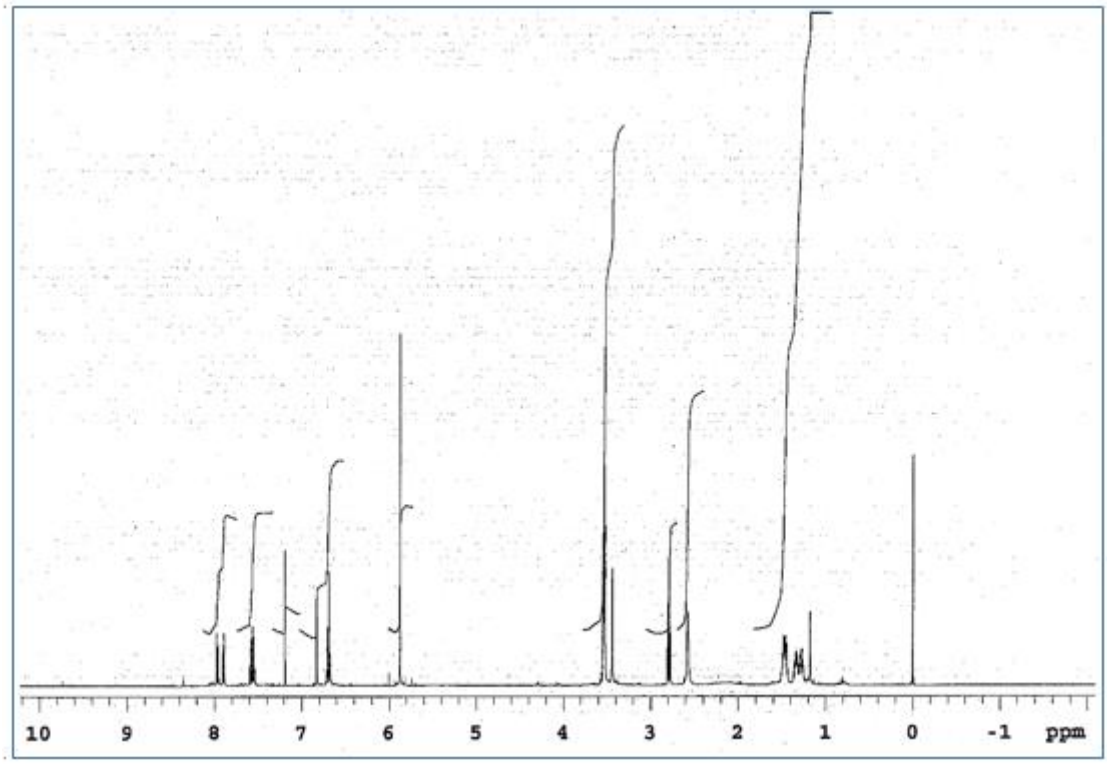


Figure 2.54: ^{1}H NMR ($CDCl_3$) spectrum of compound 17.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **17**; $SCH_2CH_2CH_2\boldsymbol{C}H_2$ was observed at δ = 25.20 ppm, $SCH_2\boldsymbol{C}H_2$ at δ = 28.34 ppm, $SCH_2CH_2\boldsymbol{C}H_2$ at δ = 29.47 ppm, $\boldsymbol{C}H_2CH_2OH$ at δ = 32.53 ppm. S-CH_2 carbon at δ = 34.62 ppm. The piperazine carbons gave two signals at δ = 51.96, 53.52 ppm. N-$\boldsymbol{C}H_2$-Ph was observed at δ = 62.65 ppm. CH_2-OH carbon at δ = 62.72 ppm. O-CH_2-O at δ = 100.96 ppm. Aromatic carbons were observed at δ = 107.96, 109.96, 122.52, 125.68, 126.25, 126.55, 132.14, 132.77, 132.79, 132.89, 133.60 ppm. =C-N were observed at δ = 146.86 ppm and =C-O at δ = 147.73, 154.03 ppm. The carbonyl groups gave two signals at δ = 181.84, 182.09 ppm.

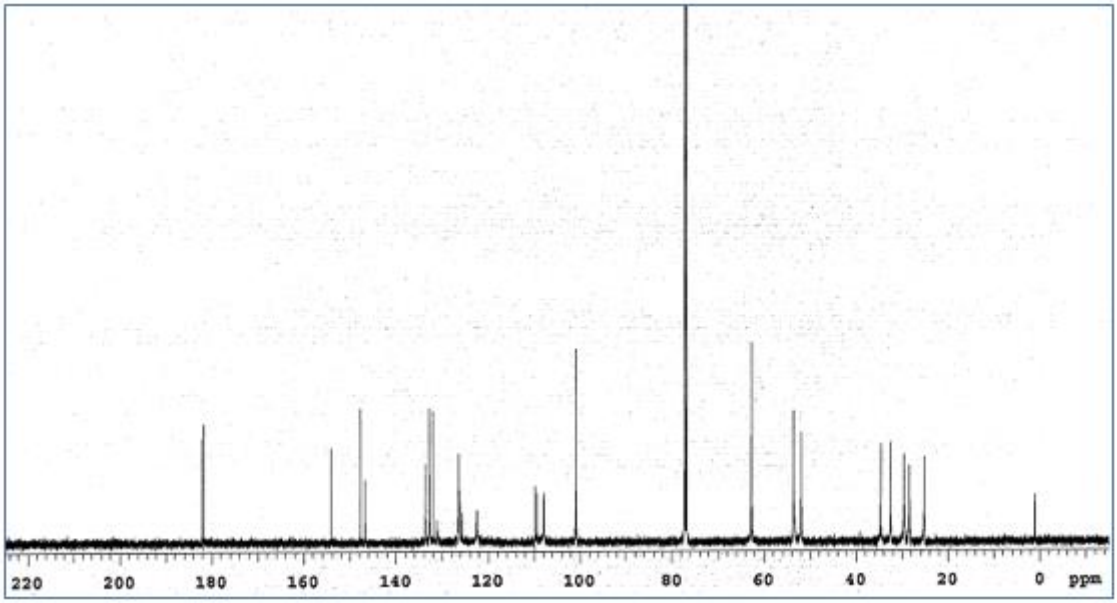


Figure 2.55: ^{13}C NMR ($CDCl_3$) spectrum of compound 17.

The mass spectrum of compound **17** which has the formula $C_{28}H_{32}N_2O_5S$ (M= 508.63 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **17** in the MS spectrum is *m/z*: (%) (100) 509 $[M+H]^+$. Figure 2.56.

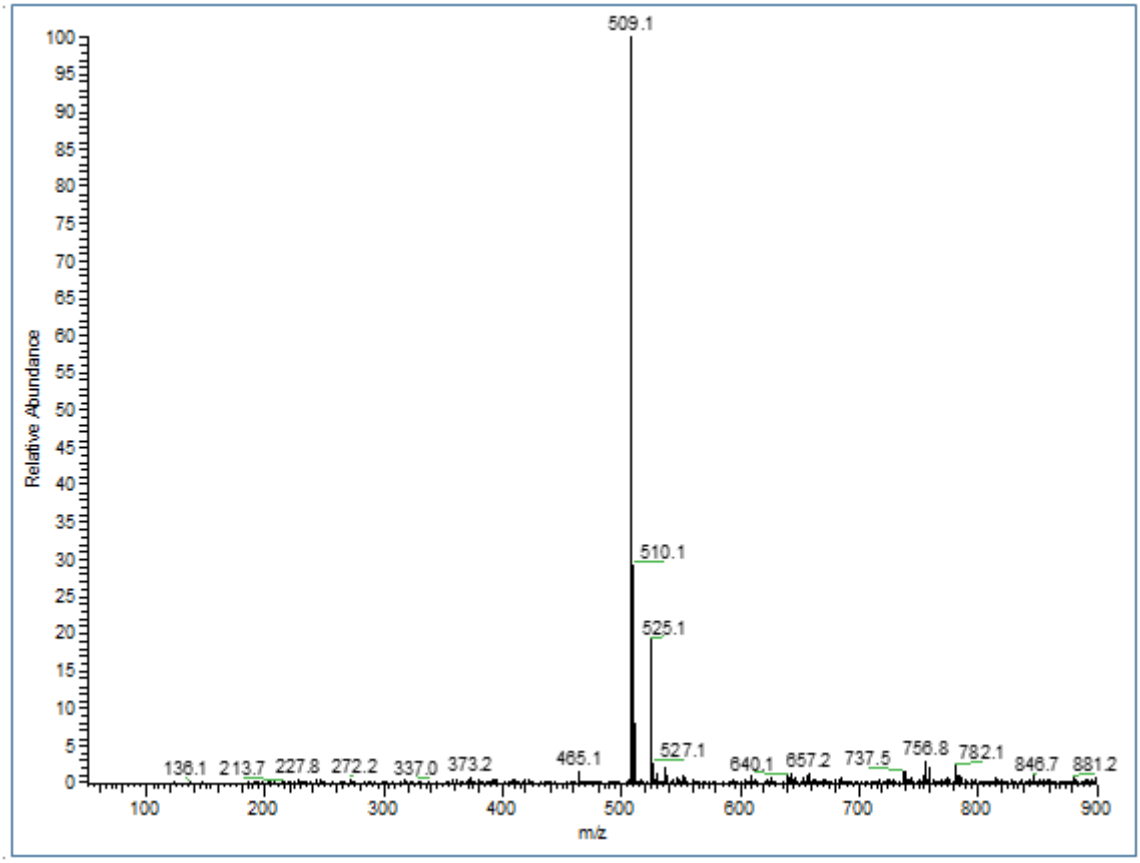
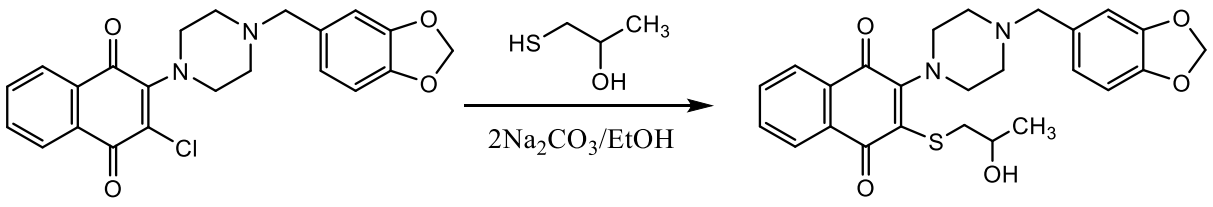


Figure 2.56: MS [+ESI] spectrum of compound 17.

2.1.17. Synthesis of new 2-(1-piperonylpiperazin-1-yl)-3-(2-hydroxy-1-propylthio)-1,4-NQ compound (18)

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** was reacted with 1-mercapto-2-propanol, and new 2-(1-piperonylpiperazin-1-yl)-3-(2-hydroxy-1-propylthio)-1,4-NQ compound **(18)** was obtained. The product was separated by column chromatography.



14 18

In the IR spectrum of compound **18**; hydroxyl band (-OH) was seen at ν = 3358 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 3068, 2961 cm^{-1}, ν = 2915, 2854 cm^{-1}, ν = 1663 cm^{-1}, ν = 1589, 1525 cm^{-1}, respectively.

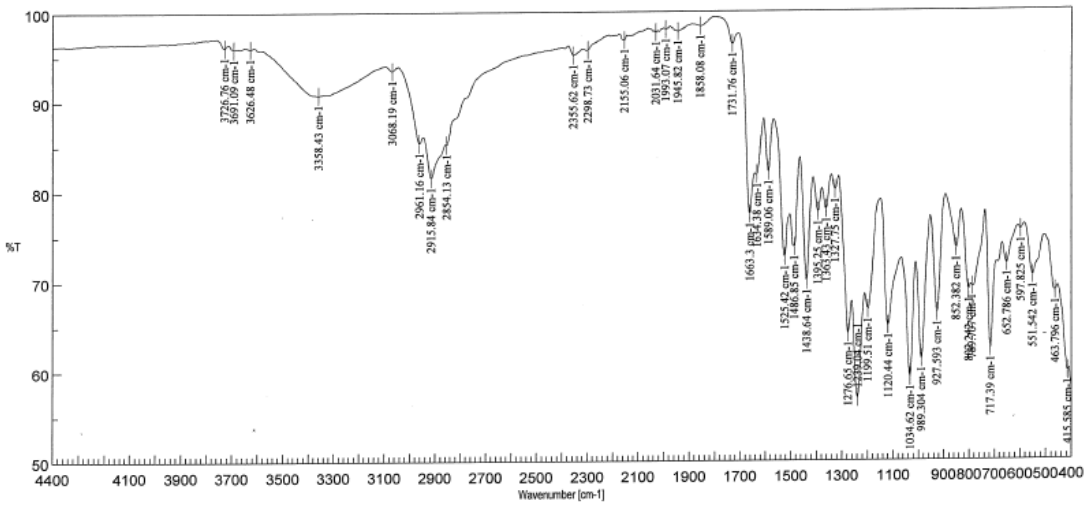


Figure 2.57: IR (film) spectrum of compound 18.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **18**; -CH_3 protons appeared at δ = 1.12-1.13 as doublet. -OH proton appeared δ = 1.17 ppm as singlet. Protons of piperazine ring appeared at δ = 2.57-2.62 and 3.39-3.46 ppm as multiplet. -SCH_2 at δ = 2.96-2.99 ppm as multiplet. N-CH_2-Ph protons at δ = 3.57-3.59 ppm as multiplet. C**H**-OH proton appeared at δ = 3.64-3.70 ppm as multiplet. O-CH_2-O protons at δ = 5.87 ppm as singlet. Protons of phenyl ring appeared at δ = 6.67-6.72 ppm as multiplet and at δ = 6.83 ppm as singlet. Protons of NQ group appeared at δ = 7.54-7.60, 7.89-7.91 and 7.96-7.98 ppm as multiplet.

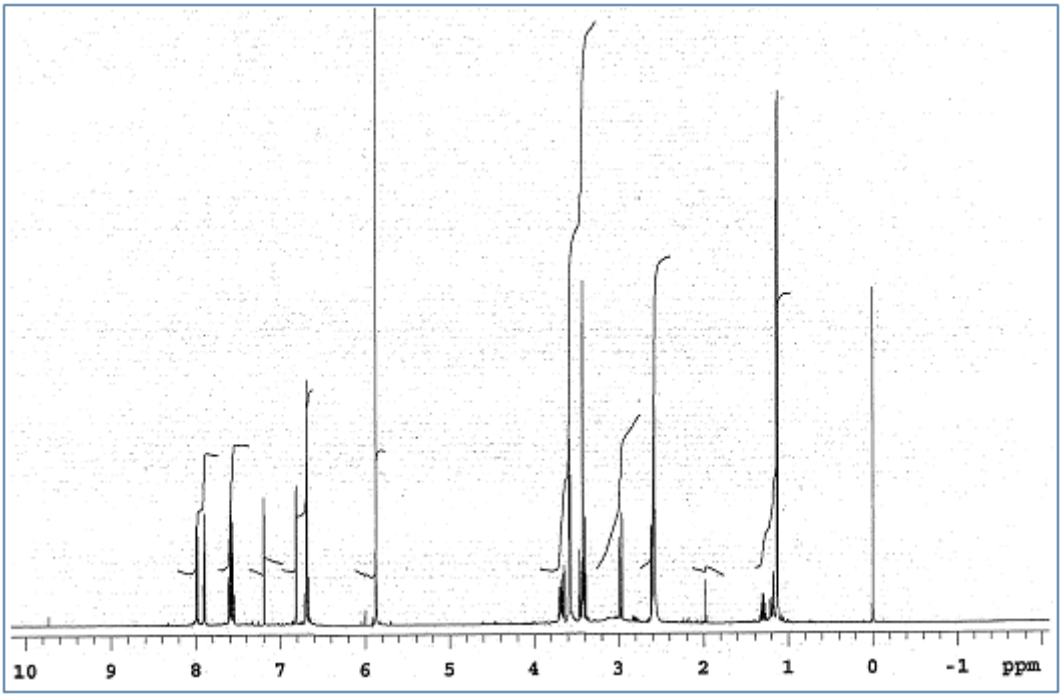


Figure 2.58: ^{1}H NMR ($CDCl_3$) spectrum of compound 18.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **18**; -CH_3 carbon was observed at δ = 20.88 ppm. S-CH_2 carbon at δ = 43.67 ppm. The piperazine carbons gave two signals at δ = 51.70, 52.57 ppm. N-**C**H_2-Ph was observed at δ = 61.65 ppm. CH_2-OH carbon at δ = 65.09 ppm. O-CH_2-O at δ = 99.94 ppm. Ar-C's were observed at δ = 106.93, 108.57, 121.42, 125.50, 125.66, 130.25, 131.04, 131.69, 131.90, 131.92, 132.84 ppm. =C-N were observed at δ = 145.81 ppm and =C-O at δ = 146.72 154.86 ppm. The carbonyl groups gave two signals at δ = 180.93, 181.18 ppm.

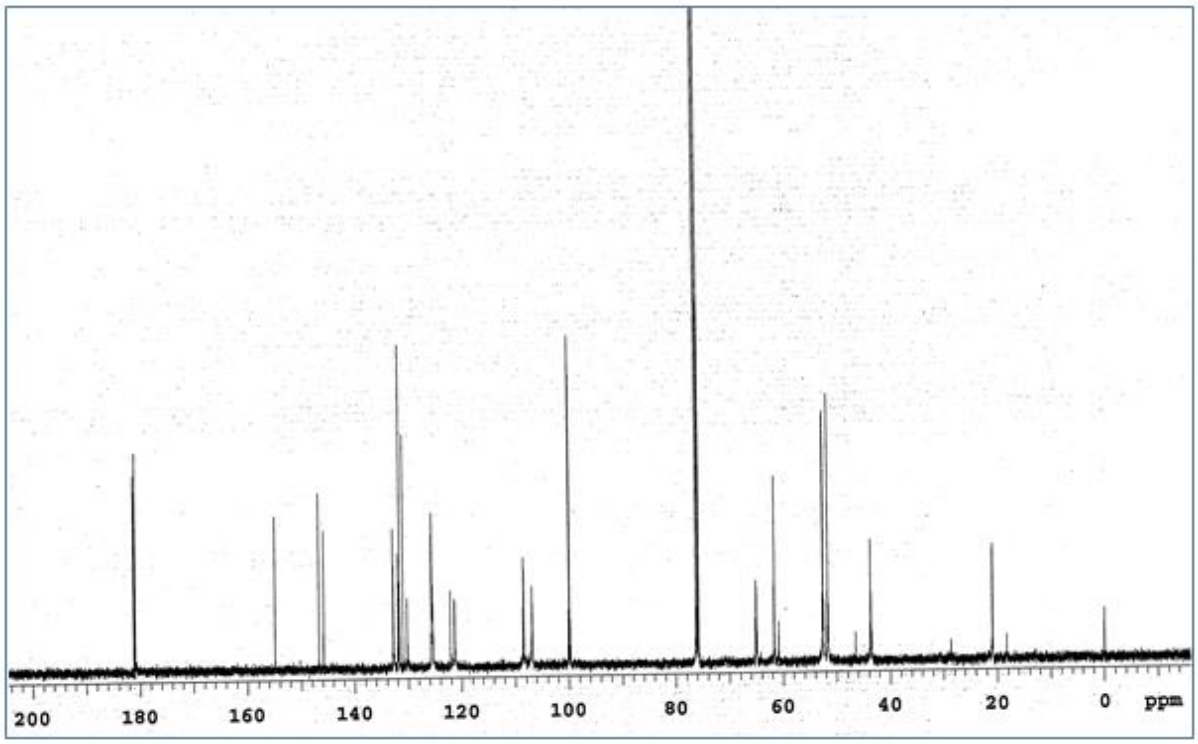


Figure 2.59: ^{13}C NMR ($CDCl_3$) spectrum of compound 18.

The mass spectrum of compound **18** which has the formula $C_{25}H_{26}N_2O_5S$ (M= 466.55 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **18** in the MS spectrum is *m/z*: (%) (100) 467 $[M+H]^+$. Figure 2.60.

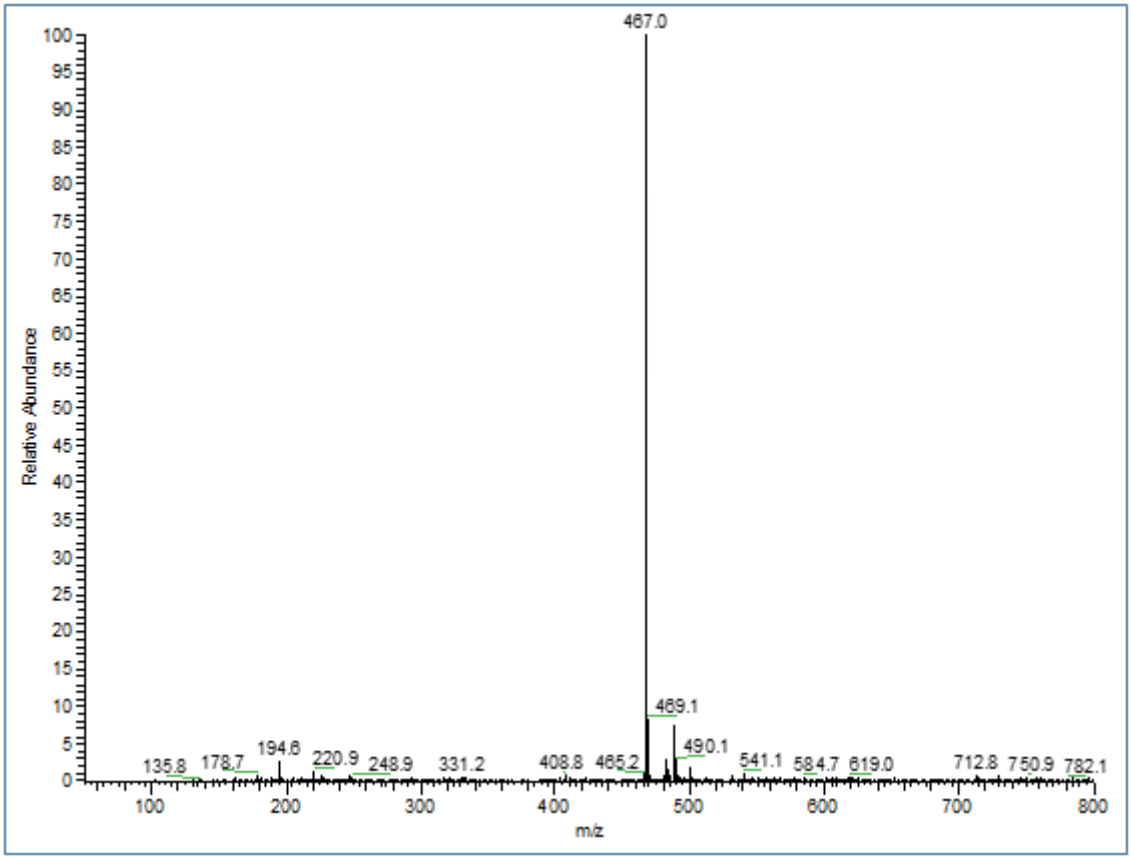
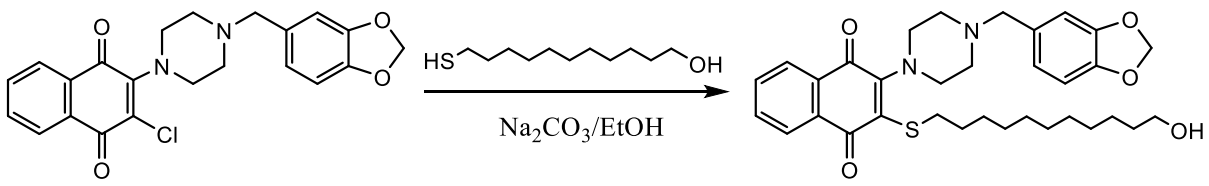


Figure 2.60: MS [+ESI] spectrum of compound 18.

2.1.18. Synthesis of new 2-(1-piperonylpiperazin-1-yl)-3-(11-hydroxyundecylthio)-1,4-NQ compound (19)

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** was reacted with 11-mercapto-1-undecanol, and new 2-(1-piperonylpiperazin-1-yl)-3-(11-hydroxyundecylthio)-1,4-NQ compound **(19)** was obtained. The product was separated by column chromatography.



14 19

In the IR spectrum of compound **19**; characteristic hydroxyl band (-OH) was seen at ν = 3397 cm^{-1}. Stretching bands for C-$H_{arom.}$, C-$H_{aliph.}$, carbonyl and carbon-carbon double bond were seen at ν = 3068 cm^{-1}, ν = 2920, 2850 cm^{-1}, ν = 1662 cm^{-1}, ν = 1590, 1526 cm^{-1}, respectively.

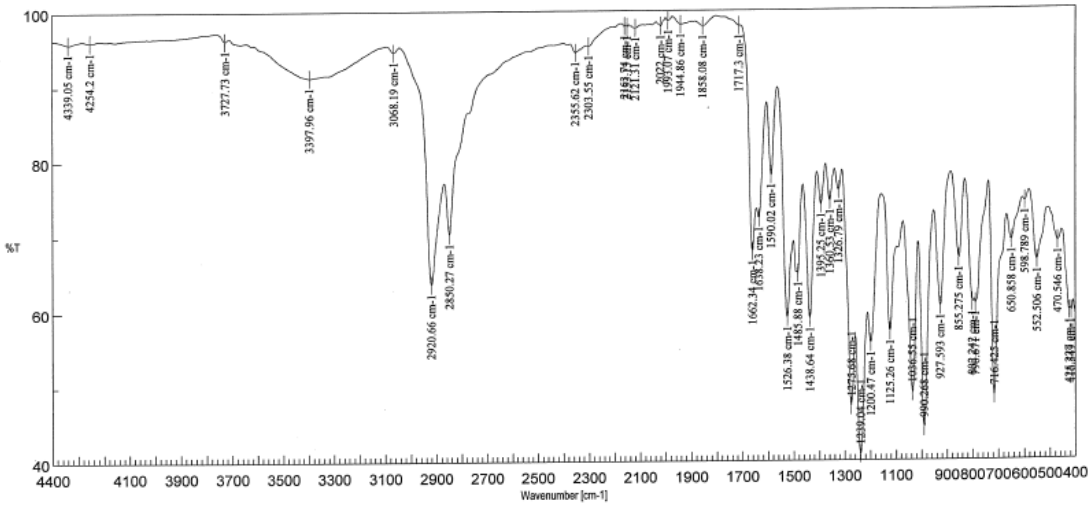


Figure 2.61: IR (film) spectrum of compound 19.

In the ^{1}H NMR ($CDCl_3$) spectrum of compound **19**; aliphatic CH_2 protons with -OH proton appeared as multiplet at δ = 1.16-1.29 ppm. $SCH_2C\mathbf{H_2}$ and $C\mathbf{H_2}CH_2OH$ protons appeared at δ = 1.42-1.50 ppm as multiplet. Protons of piperazine ring at δ = 2.57 ppm as singlet. -SCH_2 at δ = 2.77-2.80 ppm as triplet. N-CH_2-Ph protons at δ = 3.43 ppm as singlet. $C\mathbf{H_2}$-OH and the other protons of piperazine ring appeared at δ = 3.52-3.56 ppm as multiplet .O-CH_2-O protons at δ = 5.88 ppm as singlet. Protons of phenyl ring appeared at δ = 6.67-6.72 ppm as multiplet and at δ = 6.83 ppm as singlet. Protons of NQ group appeared at δ = 7.53-7.60, 7.89-7.91 and 7.96-7.98 ppm as multiplet.

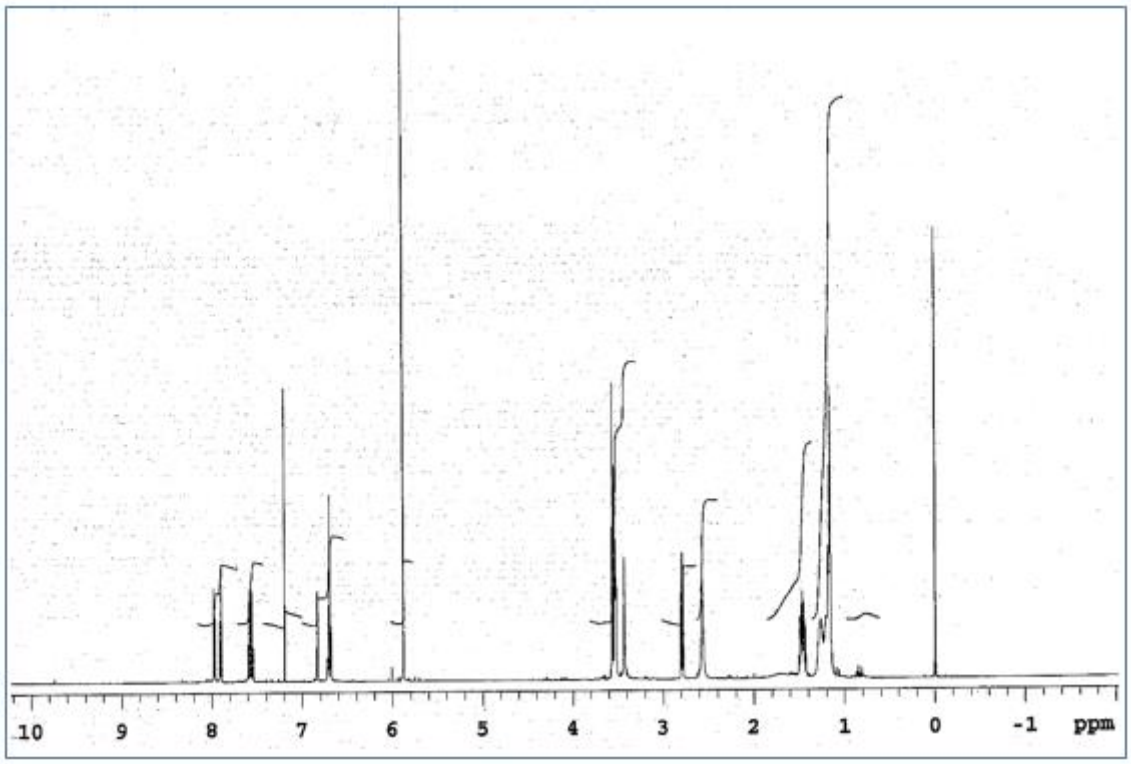


Figure 2.62: ^{1}H NMR ($CDCl_3$) spectrum of compound 19.

In the ^{13}C NMR ($CDCl_3$) spectrum of compound **19**; ***C***$H_2CH_2CH_2OH$ was observed at δ = 24.70 ppm. Aliphatic carbons were observed at δ = 27.65, 28.06, 28.34, 28.40, 28.49, 28.61 ppm. ***C***H_2CH_2OH at δ = 31.76 ppm. S-CH_2 carbon at δ = 33.72 ppm. The piperazine carbons gave two signals at δ = 51.00, 52.57 ppm. CH_2-OH carbon was observed at δ = 61.75 ppm. N-***C***H_2-Ph at δ = 62.00 ppm. O-CH_2-O at δ = 99.94 ppm. Ar-C's were observed at δ = 106.92, 108.51, 121.43, 125.22, 125.51, 131.15, 131.73, 131.92, 132.55 ppm. =C-N were observed at δ = 145.80 ppm and =C-O at δ = 146.71, 152.89 ppm. The carbonyl groups gave two signals at δ = 180.84, 181.07 ppm.

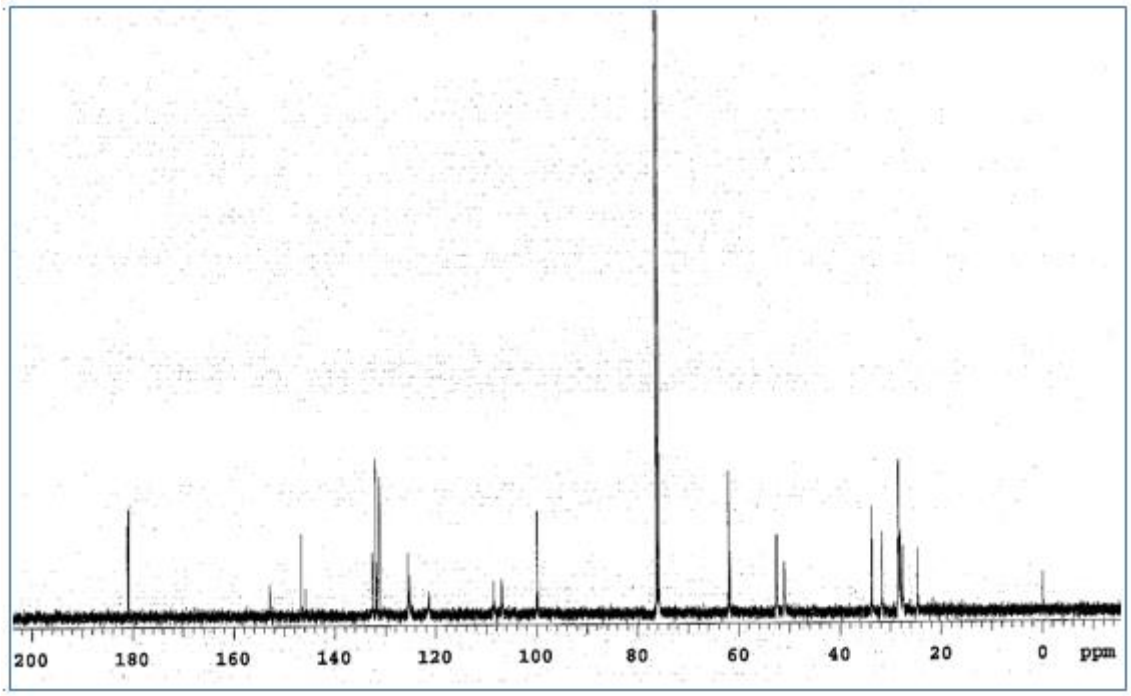


Figure 2.63: ^{13}C NMR ($CDCl_3$) spectrum of compound 19.

The mass spectrum of compound **19** which has the formula $C_{33}H_{42}N_2O_5S$ (M= 578.76 g/mole), was measured using the + ESI (Electrospray Ionization) technique. Accordingly, the molecular ion peak of compound **19** in the MS spectrum is *m/z*: (%) (100) 579 $[M+H]^+$. Figure 2.64.

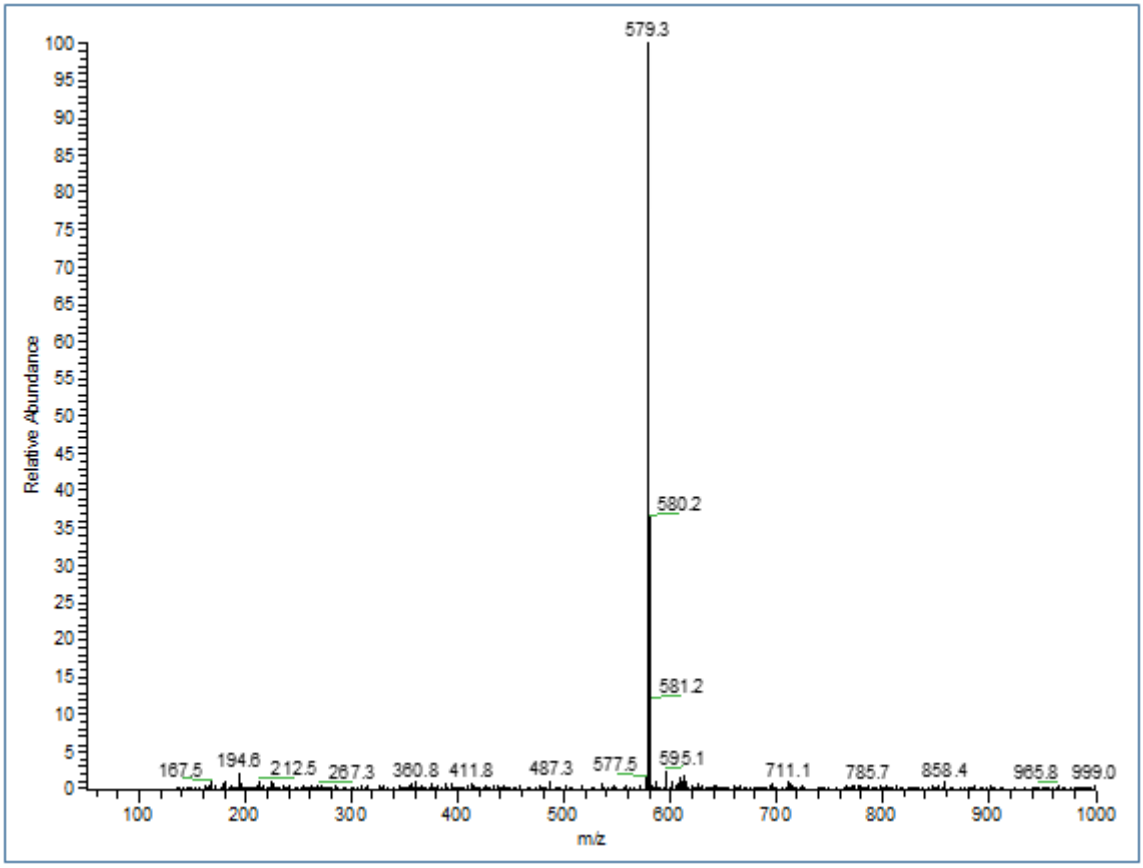


Figure 2.64: MS [+ESI] spectrum of compound 19.

3. RESULTS

3.1. INSTRUMENTS AND CHEMICALS USED IN THE EXPERIMENTS

Thin Layer Chromatography: DC-Alufolien Kieselgel 60 F_{254} (Merck).

UV lamb: CAMAC Muttenz-Schweiz 29200. Ultraviolet light (254 nm).

Desiccator: Chem-Dry-Laboratory Devices Inc., U.S.A

Melting point apparatus: Buchi SMP 20 B-540.

Elemental analyzer: Thermo Finnigan Flash EA 1112 Series.

IR Spectrometer: Perkin Elmer Precisely Spectrum One FT-IR (Perkin Elmer Analytical Instruments).

NMR Spectrometer: Varian UNITY INOVA (500 MHz).

MS spectrometer: Thermo Finnigan LCQ Advantage MAX LC/MS/MS.

Silica gel 60, particle size (63-200 μm) (Fluka), petroleum ether (technical), ethyl acetate (technical), chloroform (technical), ethanol (technical), Na_2CO_3 (Merck), $CaCl_2$ (Merck), 2,3-dichloro-1,4-NQ (Aldrich), 1-(2-cyanophenyl)piperazine (Aldrich), 2-mercaptoethanol (Merck), 4-mercapto-1-butanol (Aldrich), 6-mercapto-1-hexanol (Aldrich), 1-piperonyl piperazine (Aldrich), 1-mercapto-2-propanol (Aldrich), 6-amino-1-hexanol (Aldrich), 11-mercapto-1-undecanol (Aldrich), 2-chlorobenzylmercaptan (Aldrich), 2-phenyl-ethanethiol(Aldrich).

3.2. PROCEDURES FOR SYNTHESIS

Procedure 1

In this procedure, $CHCl_3$ was used as solvent (50 mL). Some nucleophiles were added to 2,3-dichloro-1,4-NQ solution, and the solution was stirred at rt. The reaction was checked by TLC. After completion of the reaction, the reaction mixture was extracted by chloroform (30 mL), washed with water 120 mL , and dried with $CaCl_2$. Then, $CHCl_3$ was evaporated and the mixture was purified on silica-gel 60 by column chromatography with solvent mixture (EtAc/PET 1:1 or 1:2 etc.)

Procedure 2

In this method, the NQ compound and the nucleophile were dissolved in ethanol, then sodium carbonate was added and the solution was stirred at rt. The reaction was checked by TLC. After completion of the reaction, the reaction mixture was extracted by chloroform (30 mL), washed with water 120 mL , and dried with $CaCl_2$. Then, $CHCl_3$ was evaporated and the mixture was purified on silica-gel 60 by column chromatography with solvent mixture (EtAc/PET 1:1 or 1:2 etc.)

3.3. EXPERIMENTS

3.3.1. Experiment 1: Reaction of 2,3-dichloro-1,4-NQ with 1-(2-cyanophenyl)piperazine

2,3-Dichloro-1,4-NQ **(1)** (1g, 4.4mmol) was reacted with 1-(2-cyanophenyl)piperazine (0.825g, 4.4mmol) according to procedure 1, and new 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ compound **(2)** was synthesized.

Compound 2: Red solid. Yield: 0.775 g (47%). R_f: 0.43 (EtAc:PET 1:2). M.p.: 166.9-167.5 ºC. ***FT-IR*** (KBr, cm^{-1}): ν = 2979 (C-$H_{arom.}$), 2903 (C-$H_{aliph.}$), 2220 (CN), 1652 (C=O), 1590, 1557 (C=C). ***^{1}H NMR (ppm)***: δ = 3.40-3.43 (t, 4H, 2$CH_{2\ piper.}$), 3.82-3.84 (t, 4H, 2$CH_{2\ piper.}$), 7.07-7.10 (m, 2H, 2CH_{Ph}), 7.52-7.56 (m, 1H, CH_{Ph}), 7.62-7.63 (m, 1H, CH_{Ph}), 7.69-7.75 (m, 2H, 2$CH_{naphth.}$), 8.05-8.07 (m, 1H, $CH_{naphth.}$), 8.15-8.17 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 51.44, 52.42 ($CH_{2\ piper.}$), 106.62 (CN), 118.23, 119.07, 126.69, 126.98, 131.46, 131.61, 133.25, 133.89, 133.93, 134.18, 134.38, 134.41 ($C_{arom.}$), 149.94, 155.42 (=C-N), 178.15, 181.85 (C=O). $C_{21}H_{16}ClN_3O_2$ (M = 377.83 g/mol). MS[+ESI]: *m/z* (%) (100) 378 $[M+H]^+$.

3.3.2. Experiment 2: Reaction of 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ with 2-mercaptoethanol

2-(1-(2-Cyanophenyl)piperazinyl)-3-chloro-1,4-NQ **(2)** (0.2g, 0.53mmol) was reacted with 2-mercaptoethanol (0.041g, 0.53mmol) according to procedure 2**,** and new 2-(1-(2-cyanophenyl)piperazinyl)-3-(2-hydroxyethylthio)-1,4-NQ compound **(3)** was synthesized.

Compound 3: Dark red oil. Yield: 0.185 g (84%). R_f: 0.2 (EtAc:PET 1:2). ***FT-IR*** (film, cm^{-1}): ν = 3390 (O-H), 3066, 2971 (C-$H_{arom.}$), 2908 (C-$H_{aliph.}$), 2216 (CN), 1662 (C=O), 1589, 1523 (C=C). ***^{1}H NMR (ppm)***: δ = 1.52 (s, 1H, OH), 2.99-3.01 (t, 2H, S-CH_2), 3.33-3.35 (t, 4H, 2$CH_{2\ piper.}$), 3.63-3.66 (t, 2H, C**H**$_2$-OH), 3.75-3.77 (t, 4H, 2$CH_{2\ piper.}$), 6.98-7.01 (m, 2H, 2CH_{Ph}), 7.43-7.47 (m, 1H, CH_{Ph}), 7.53-7.55 (m, 1H, CH_{Ph}), 7.58-7.65 (m, 2H, 2$CH_{naphth.}$), 7.93-7.95 (m, 1H, $CH_{naphth.}$), 8.01-8.02 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 38.67 (S-CH_2), 52.40, 52.69 ($CH_{2\ piper.}$), 60.88 (CH_2-OH), 106.52 (CN), 118.26, 118.98, 122,36, 124.28, 126.59, 126.77, 132.05, 132.71, 133.12, 133.89, 133.95, 134.43 ($C_{arom.}$), 155.40, 155.64 (=C-N), 181.81, 182.40 (C=O). $C_{23}H_{21}N_3O_3S$ (M = 419.50 g/mol). MS[+ESI]: *m/z* (%) (100) 420 $[M+H]^+$.

3.3.3. Experiment 3: Reaction of 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ with 4-mercapto-1-butanol

2-(1-(2-Cyanophenyl)piperazinyl)-3-chloro-1,4-NQ **(2)** (0.2g, 0.53mmol) was reacted with 4-mercapto-1-butanol (0.056g, 0.53mmol) according to procedure 2, and new 2-(1-(2-cyanophenyl)piperazinyl)-3-(4-hydroxybutylthio)-1,4-NQ compound **(4)** was synthesized.

Compound 4: Dark red oil. Yield: 0.206 g (87%). R_f: 0.86 (EtAc). ***FT-IR*** (film, cm^{-1}): ν = 3415 (O-H), 3066, 2970 (C-$H_{arom.}$), 2905 (C-$H_{aliph.}$), 2216 (CN), 1661 (C=O), 1589, 1524 (C=C). ***^{1}H NMR (ppm)***: δ = 1.58-1.65 (m, 5H, $SCH_2C\mathbf{H_2}$, $C\mathbf{H_2}CH_2OH$, OH), 2.89- 2.92 (t, 2H, S-CH_2), 3.31-3.33 (t, 4H, $2CH_{2\ piper.}$), 3.56-3.59 (t, 2H, CH_2-OH), 3.68-3.70 (t, 4H, $2CH_{2\ piper.}$), 6.97-7.01 (m, 2H, $2CH_{Ph}$), 7.43-7.46 (m, 1H, CH_{Ph}), 7.52-7.54 (m, 1H, CH_{Ph}), 7.57-7.62 (m, 2H, $2CH_{naphth.}$), 7.92-7.94 (m, 1H, $CH_{naphth.}$), 7.97-7.99 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 26.09 ($SCH_2\mathbf{C}H_2$), 31.65 ($SCH_2CH_2\mathbf{C}H_2$), 34.49 (S-CH_2), 52.12, 52.40 ($CH_{2\ piper.}$), 62.20 (CH_2-OH), 106.42 (CN), 118.31, 119.05, 122,28, 126.34, 126.64, 127.04, 132.12, 132.86, 132.98, 133.70, 133.94, 134.42 ($C_{arom.}$), 155.80, 155.47 (=C-N), 181.64, 182.20 (C=O). $C_{25}H_{25}N_3O_3S$ (M = 447.55 g/mol). MS[+ESI]: *m/z* (%) (100) 486 $[M+K]^+$.

3.3.4. Experiment 4: Reaction of 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ with 1-mercapto-2-propanol

2-(1-(2-Cyanophenyl)piperazinyl)-3-chloro-1,4-NQ **(2)** (0.2g, 0.53mmol) was reacted with1-mercapto-2-propanol (0.049g, 0.53mmol) according to procedure 2**,** and new 2-(1-(2-cyanophenyl)piperazinyl)-3-(2-hydroxy-1-propylthio)-1,4-NQ compound **(5)** was synthesized.

Compound 5 : Dark red oil. Yield: 0.099 g (43%). R_f: 0.4 (EtAc:PET 1:1). ***FT-IR*** (film, cm^{-1}): ν = 3387 (O-H), 3069, 2967 (C-$H_{arom.}$), 2905, 2841 (C-$H_{aliph.}$), 2217 (CN), 1663 (C=O), 1590, 1524 (C=C). ***^{1}H NMR (ppm)***: δ = 1.15-1.18 (m, 4H, CH_3, OH), 2.65-2.70 (m, 2H, S-CH_2), 3.33-3.35 (t, 4H, $2CH_{2\ piper.}$), 3.74-3.76 (m, 5H, $2CH_{2\ piper.}$, C**H**-OH), 6.98-7.01 (m, 2H, $2CH_{Ph}$), 7.43-7.47 (m, 1H, CH_{Ph}), 7.52-7.54 (m, 1H, CH_{Ph}), 7.58-7.64 (m, 2H, $2CH_{naphth.}$), 7.93-7.95 (m, 1H, $CH_{naphth.}$), 8.01-8.03 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 20.96 (CH_3), 43.55 (S-CH_2), 51.39, 51.71 ($CH_{2\ piper.}$), 65.12 (CH-OH), 105.49 (CN), 117.25, 117.93, 121.44, 123.94, 125.75, 131.03, 131.68, 132.12, 132.94, 132.92, 133.36, 133.42 ($C_{arom.}$), 154.37, 154.51 (=C-N), 180.79, 181.29 (C=O). $C_{24}H_{23}N_3O_3S$ (M = 433.52 g/mol). MS[+ESI]: *m/z* (%) (100) 434 $[M+H]^+$.

3.3.5. Experiment 5: Reaction of 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ with 6-mercaptohexanol

2-(1-(2-Cyanophenyl)piperazinyl)-3-chloro-1,4-NQ **(2)** (0.12g, 0.32 mmol) was reacted with 6-mercaptohexanol (0.043g, 0.32mmol) according to procedure 2**,** and new 2-(1-(2-cyanophenyl)piperazinyl)-3-(6-hydroxyhexylthio)-1,4-NQ compound **(6)** was synthesized.

Compound 6: Dark red oil. Yield: 0.065 g (43%). R_f: 0.44 (EtAc:PET 1:1). ***FT-IR*** (film, cm^{-1}): ν = 3402 (O-H), 2978 (C-$H_{arom.}$), 2906 (C-$H_{aliph.}$), 2216 (CN), 1662 (C=O), 1589, 1524 (C=C). ***^{1}H NMR (ppm)***: δ = 1.28-1.32 (m, 2H, C**H**$_2$CH_2OH), 1.34-1.40 (m, 2H, SCH_2C**H**$_2$), 1.45-1.55 (m, 4H, CH_2-CH_2), 1.61 (s, 1H, OH), 2.84-2.87 (t, 2H, S-CH_2), 3.32-3.34 (t, 4H, 2$CH_{2\ piper.}$), 3.53-3.55 (t, 2H, C**H**$_2$-OH), 3.69-3.71 (t, 4H, 2$CH_{2\ piper.}$), 6.98-7.03 (m, 2H, 2CH_{Ph}), 7.44-7.47 (m, 1H, CH_{Ph}), 7.52-7.55 (m, 1H, CH_{Ph}), 7.57-7.63 (m, 2H, 2$CH_{naphth.}$), 7.93-7.95 (m, 1H, $CH_{naphth.}$), 7.98-8.00 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 25.24 (SCH_2CH_2CH_2***C***H_2), 28.39 (SCH_2***C***H_2), 29.56 (SCH_2CH_2***C***H_2), 32.58 (***C***H_2CH_2OH), 34.67 (S-CH_2), 52.08, 52.44 ($CH_{2\ piper.}$), 62.73 (CH_2-OH), 106.44 (CN), 118.29, 119.07, 119.15, 122.41, 126.34, 126.63, 127.27, 132.13, 132.89, 133.68, 133.96, 134.44 ($C_{arom.}$), 153.79, 155.47 (=C-N), 181.71, 182.18 (C=O). $C_{27}H_{29}N_3O_3S$ (M = 475.6 g/mol). MS[+ESI]: *m/z* (%) (83) 476 $[M+H]^+$, MS[-ESI]: *m/z* (%) (100) 474 $[M-H]^+$.

3.3.6. Experiment 6: Reaction of 2,3-dichloro-1,4-NQ with 6-amino-1-hexanol

2,3-Dichloro-1,4-NQ **(1)** (3.88g, 17mmol) was reacted with 6-amino-1-hexanol (2g, 17mmol) according to procedure 2**,** and known 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ compound **(7)** was synthesized.

Compound 7: Red solid. 1.88 g (36%). R_f: 0.33 (EtAc:PET 1:1). M.p.: 95-97 ºC. $C_{16}H_{28}O_3NCl$ (M = 307.1 g/mol). This compound was previously synthesized.

3.3.7. Experiment 7: Reaction of 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ with 2-mercaptoethanol

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** (0.2g, 0.65mmol) was reacted with 2-mercaptoethanol (0.051g, 0.65mmol) according to procedure 2**,** and new 2-(6-aminohexyl-1-ol)-3-(2-hydroxyethylthio)-1,4-NQ compound **(8)** was synthesized.

Compound 8: Orange solid. Yield: 0.113 g (49%). R_f: 0.39 (EtAc). M.p.: 74.9-75.2ºC. ***FT-IR*** (KBr, cm^{-1}): ν = 3341, 3227 (N-H, O-H), 2980 (C-$H_{arom.}$), 2919, 2852 (C-$H_{aliph.}$), 1686 (C=O),

1590, 1536 (C=C). ***^{1}H NMR (ppm)***: δ = 1.26 (s, 2H, 2OH), 1.46-1.50 (m, 4H, $NHCH_2CH_2C\mathbf{H_2}C\mathbf{H_2}$), 1.61-1.63 (q, 2H, $NH(CH_2)_4C\mathbf{H_2}CH_2OH$), 1.72-1.77 (q, 2H, $NHCH_2C\mathbf{H_2}$), 2.84-2.86 (t, 2H, NH-C$\mathbf{H_2}$), 3.64-3.69 (m, 4H, $NH(CH_2)_5C\mathbf{H_2}OH$, $S\text{-}CH_2$), 3.98-4.01 (t, 2H, $SCH_2C\mathbf{H_2}OH$), 7.62-7.65 (m, 1H, $CH_{naphth.}$), 7.73-7.76 (m, 1H, $CH_{naphth.}$), 8.03-8.05 (m, 1H, $CH_{naphth.}$), 8.17-8.19 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 25.44, 26.54, 30.49, 32.49 ($CH_{2\ aliph.}$), 45.91 ($S\text{-}CH_2$), 47.50 ($NH\text{-}CH_2$), 59.91 ($SCH_2\boldsymbol{C}H_2OH$), 62.73 ($NH(CH_2)_5\boldsymbol{C}H_2OH$), 126.66, 127.08, 132.29, 133.65, 134.97 ($C_{arom.}$), 181.36 (C=O). $C_{18}H_{23}NO_4S$ (M = 349.44 g/mol). MS[+ESI]: *m/z* (%) (100) 350 $[M+H]^+$.

3.3.8. Experiment 8: Reaction of 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ with 4-mercapto-1-butanol

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** (0.2g, 0.65mmol) was reacted with 4-mercapto-1-butanol (0.069g, 0.65mmol) according to procedure 2**,** and new 2-(6-aminohexyl-1-ol)-3-(4-hydroxybutylthio)-1,4-NQ compound **(9)** was synthesized.

Compound 9: Dark red solid. Yield: 0.104 g (42%). R_f: 0.43 (EtAc). M.p.: 78.1-80ºC. ***FT-IR*** (KBr, cm^{-1}): ν = 3285 (N-H, O-H), 3013 ($C\text{-}H_{arom.}$), 2929, 2853 ($C\text{-}H_{aliph.}$), 1668 (C=O), 1588, 1549 (C=C). ***^{1}H NMR (ppm)***: δ = 1.26 (s, 2H, 2OH), 1.45-1.74 (m, 12H, $6CH_2$-), 2.83-2.86 (t, 2H, NH-C$\mathbf{H_2}$), 3.65-3.69 (m, 4H, $NH(CH_2)_5C\mathbf{H_2}OH$, $S\text{-}CH_2$), 3.91-3.94 (t, 2H, $S(CH_2)_3C\mathbf{H_2}OH$), 7.60-7.63 (m, 1H, $CH_{naphth.}$), 7.70-7.74 (m, 1H, $CH_{naphth.}$), 8.02-8.04 (m, 1H, $CH_{naphth.}$), 8.13-8.15 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 25.43, 26.53, 30.56, 31.84, 32.52, 34.92 ($CH_{2\ aliph.}$), 45.96 ($S\text{-}CH_2$), 47.51 ($NH\text{-}CH_2$), 62.28 ($S(CH_2)_3\boldsymbol{C}H_2OH$), 62.72 ($NH(CH_2)_5\boldsymbol{C}H_2OH$), 126.47, 126.59, 126.68, 130.61, 132.06, 133.86, 134.67 ($C_{arom.}$), 180.23, 181.45 (C=O). $C_{20}H_{27}NO_4S$ (M = 377.50 g/mol). MS[+ESI]: *m/z* (%) (100) 378 $[M+H]^+$.

3.3.9. Experiment 9: Reaction of 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ with 6-mercaptohexanol

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** (0.2g, 0.65mmol) was reacted with 6-mercaptohexanol (0.088g, 0.65mmol) according to procedure 2**,** and new 2-(6-aminohexyl-1-ol)-3-(6-hydroxyhexylthio)-1,4-NQ compound **(10)** was synthesized.

Compound 10: Dark red solid. Yield: 0.144 g (55%). R_f: 0.45 (EtAc). M.p.: 81.1-82.8ºC. ***FT-IR*** (KBr, cm^{-1}): ν = 3276 (N-H, O-H), 3070, 3012 ($C\text{-}H_{arom.}$), 2925, 2852 ($C\text{-}H_{aliph.}$), 1669 (C=O), 1588, 1549 (C=C). ***^{1}H NMR (ppm)***: δ = 1.26 (s, 2H, 2OH), 1.35-1.74 (m, 16H, $8CH_2$-), 2.80-2.84 (t, 2H, $S\text{-}CH_2$), 3.62-3.68 (m, 4H, NH-C$\mathbf{H_2}$, $NH(CH_2)_5C\mathbf{H_2}OH$), 3.90-3.93 (t, 2H,

S(CH_2)$_5$C**H$_2$**OH), 6.49 (s, 1H, NH), 7.60-7.63 (m, 1H, $CH_{naphth.}$), 7.70-7.73 (m, 1H, $CH_{naphth.}$), 8.02-8.04 (m, 1H, $CH_{naphth.}$), 8.13-8.15 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 25.31, 25.49, 26.59, 28.55, 29.79, 30.62, 32.57, 34.97 ($CH_{2\ aliph.}$), 46.00 (S-CH_2), 47.51 (NH-CH_2), 62.78 (S(CH_2)$_5$***C***H_2OH), 62.85 (NH(CH_2)$_5$***C***H_2OH), 126.45, 126.65, 130.64, 132.03, 133.86, 134.63 ($C_{arom.}$), 180.11, 181.48 (C=O). $C_{22}H_{31}NO_4S$ (M = 405.55 g/mol). MS[+ESI]: *m/z* (%) (100) 406 $[M+H]^+$.

3.3.10. Experiment 10: Reaction of 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ with 11-mercapto-1-undecanol

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** (0.2g, 0.65mmol) was reacted with 11-mercapto-1-undecanol (0.132g, 0.65 mmol) according to procedure 2**,** and new 2-(6-aminohexyl-1-ol)-3-(11-hydroxyundecylthio)-1,4-NQ compound **(11)** was synthesized.

Compound 11: Red solid. Yield: 0.154 g (51%). R_f: 0.22 (EtAc:PET 1:1). M.p.: 81.5-82.6ºC. ***FT-IR*** (KBr, cm^{-1}): ν = 3427, 3372, 3294 (N-H, O-H), 3069 (C-$H_{arom.}$), 2923, 2850 (C-$H_{aliph.}$), 1668 (C=O), 1589, 1549 (C=C). ***^{1}H NMR (ppm)***: δ = 1.16-1.67 (m, 28H, 13CH_2-, 2OH), 2.71-2.74 (t, 2H, S-CH_2), 3.54-3.60 (m, 4H, NH-C**H$_2$**, S(CH_2)$_{10}$C**H$_2$**OH), 3.81-3.85 (t, 2H, NH(CH_2)$_5$C**H$_2$**OH), 7.51-7.54 (m, 1H, $CH_{naphth.}$), 7.61-7.65 (m, 1H, $CH_{naphth.}$), 7.93-7.95 (m, 1H, $CH_{naphth.}$), 8.05-8.07 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 24.49, 24.68, 25.60, 27.85, 28.34, 28.43, 28.45, 28.50, 28.84, 29.62, 31.58, 31.74, 34.06 ($CH_{2\ aliph.}$), 44.99 (S-CH_2), 46.49 (NH-CH_2), 61.75 (S(CH_2)$_{10}$***C***H_2OH), 62.03 (NH(CH_2)$_5$***C***H_2OH), 125.39, 125.50, 129.64, 130.95, 132.86, 133.58 ($C_{arom.}$), 179.05, 180.49 (C=O). $C_{27}H_{41}NO_4S$ (M = 475.68 g/mol). MS[-ESI]: *m/z* (%) (100) 474 $[M-H]^+$.

3.3.11. Experiment 11: Reaction of 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ with 2-chlorobenzyl mercaptan

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** (0.2g, 0.65mmol) was reacted with 2-chlorobenzyl mercaptan (0.103g, 0.65 mmol) according to procedure 2**,** and new 2-(6-aminohexyl-1-ol)-3-(2-chlorobenzenemethylthio)-1,4-NQ compound **(12)** was synthesized.

Compound 12: Dark red oil. Yield: 0.138 g (49%). R_f: 0.35 (EtAc:PET 1:1). ***FT-IR*** (film, cm^{-1}): ν = 3423, 3321 (N-H, O-H), 3063 (C-$H_{arom.}$), 2927, 2856 (C-$H_{aliph.}$), 1672 (C=O), 1590, 1548 (C=C). ***^{1}H NMR (ppm)***: δ = 1.18 (s, 1H, OH), 1.23-1.33 (m, 4H, 2CH_2), 1.36-1.42 (q, 2H, NHCH_2C**H$_2$**), 1.47-1.53 (q, 2H, C**H$_2$**CH_2OH), 3.41- 3.44 (t, 2H, NH-C**H$_2$**), 3.57-3.59 (t, 2H, C**H$_2$**-OH), 4.03 (s, 2H, S-CH_2), 6.94-6.98 (m, 2H, 2CH_{Ph}), 7.04-7.07 (m, 1H, CH_{Ph}), 7.24-7.26

(d, 1H, CH_{Ph}), 7.52-7.55 (m, 1H, $CH_{naphth.}$), 7.65-7.68 (m, 1H, $CH_{naphth.}$), 7.91-7.92 (m, 1H, $CH_{naphth.}$), 8.11-8.13 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 25.41 (***C***$H_2CH_2CH_2OH$), 26.47 ($NHCH_2CH_2$***C***H_2), 30.05 ($NHCH_2$***C***H_2), 32.56 (***C***H_2CH_2OH), 36.84 (S-CH_2), 45.82 (NH-CH_2), 62.81 (CH_2-OH), 126.54, 126.63, 126.67, 128.39, 128.55, 129.47, 129.59, 130.85, 131.00, 132.01, 132.05, 133.81, 134.82, 136.08 ($C_{arom.}$), 180.18, 181.31 (C=O). $C_{23}H_{24}ClNO_3S$ (M = 429.96 g/mol). MS[+ESI]: *m/z* (%) (100) 452 $[M+Na]^+$.

3.3.12. Experiment 12: Reaction of 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ with 2-phenylethanethiol

2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)** (0.2g, 0.65mmol) was reacted with 2-phenylethanethiol (0.09g, 0.65mmol) according to procedure 2**,** and new 2-(6-aminohexyl-1-ol)-3-(2-phenylethylthio)-1,4-NQ compound **(13)** was synthesized.

Compound 13: Dark red oil. Yield: 0.191 g (71%). R_f: 0.3 (EtAc:PET 1:1). ***FT-IR*** (film, cm^{-1}): ν = 3423, 3325 (N-H, O-H), 3061, 3022 (C-$H_{arom.}$), 2926, 2855 (C-$H_{aliph.}$), 1671 (C=O), 1590, 1548 (C=C). ***^{1}H NMR (ppm)***: δ = 1.18 (s, 1H, OH), 1.30-1.37 (m, 4H, $2CH_2$), 1.49-1.57 (m, 4H, $NHCH_2C$**H$_2$**, C**H$_2$**CH_2OH), 2.80-2.83 (t, 2H, S-CH_2), 3.03-3.06 (t, 2H, NH-C**H$_2$**), 3.56-3.59 (t, 2H, CH_2-Ph), 3.67-3.70 (t, 2H, C**H$_2$**-OH), 7.03-7.09 (m, 3H, $3CH_{Ph}$), 7.12-7.15 (m, 2H, $2CH_{Ph}$), 7.50-7.54 (m, 1H, $CH_{naphth.}$), 7.61-7.64 (m, 1H, $CH_{naphth.}$), 7.91-7.93 (m, 1H, $CH_{naphth.}$), 8.05-8.07 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 25.48 (***C***$H_2CH_2CH_2OH$), 26.55 ($NHCH_2CH_2$***C***H_2), 30.49 ($NHCH_2$***C***H_2), 32.57 (***C***H_2CH_2OH), 35.69 (S-CH_2), 36.08 (CH_2-Ph), 46.00 (NH-CH_2), 62.78 (CH_2-OH), 126.42, 126.53, 128.25, 128.30, 128.39, 128.43, 128.60, 130.61, 131.99, 131.97, 132.02, 133.86, 134.61, 140.19 ($C_{arom.}$), 180.06, 181.33(C=O). $C_{24}H_{27}NO_3S$ (M = 409.54 g/mol). MS[-ESI]: *m/z* (%) (100) 408 $[M-H]^+$.

3.3.13. Experiment 13: Reaction of compound (1) with 1-piperonylpiperazine

2,3-Dichloro-1,4-NQ **(1)** (2g, 8.8mmol) was reacted 1-piperonylpiperazine (1.94g, 8.8mmol) according to procedure 1**,** and known 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ compound **(14)** was synthesized.

Compound 14: Dark red solid. Yield: 1.56 g (43%). R_f: 0.39 (EtAc:PET 1:2). M.p.: 167-169 ºC. $C_{22}H_{19}ClN_2O_4$ (M = 410.86 g/mol). This compound was previously synthesized.

3.3.14. Experiment 14: Reaction of 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ with 2-mercaptoethanol

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** (0.263g, 0.64mmol) was reacted with 2-mercaptoethanol (0.05g, 0.64mmol) according to procedure 2**,** and new 2-(1-piperonylpiperazin-1-yl)-3-(2-hydroxyethylthio)-1,4-NQ compound **(15)** was synthesized.

Compound 15: Dark red oil. Yield: 0.079 g (27%). R_f: 0.34 (EtAc). ***FT-IR*** (film, cm^{-1}): ν = 3300 (O-H), 3100 (C-$H_{arom.}$), 2899, 2809 (C-$H_{aliph.}$), 1650 (C=O), 1587, 1548 (C=C). ***^{1}H NMR (ppm)***: δ = 1.18 (s, 1H, OH), 2.41 (s, 4H, 2$CH_{2\ piper.}$), 2.80-2.94 (m, 4H, 2$CH_{2\ piper.}$), 3.08-3.10 (m, 2H, S-CH_2), 3.33-3.40 (m, 2H, N-CH_2-Ph), 4.47-4.49 (m, 2H, C**H$_2$**-OH), 5.86-5.88 (m, 2H, O-CH_2-O), 6.63-6.69 (m, 2H, 2CH_{Ph}), 6.76 (s, 1H, CH_{Ph}), 7.60-7.63 (m, 2H, 2$CH_{naphth.}$), 7.98-8.04 (m, 2H, 2$CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 38.82 (S-CH_2), 52.30, 52.88 ($CH_{2\ piper.}$), 62.88 (CH_2-OH), 65.92 (N-CH_2-Ph), 100.92 (O-CH_2-O), 107.88, 109.35, 122.24, 124.50, 126.34, 126.88, 130.80, 131.48, 132.73, 133.71, 133.83 ($C_{arom.}$), 146.73 (=C-N), 147.69, 151.61 (=C-O), 176.48, 181.65 (C=O). $C_{24}H_{24}N_2O_5S$ (M = 452.52 g/mol). MS[+ESI]: *m/z* (%) (100) 453 $[M+H]^+$.

3.3.15. Experiment 15: Reaction of 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ with 4-mercapto-1-butanol

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** (0.3g, 0.73mmol) was reacted with 4-mercapto-1-butanol (0.078g, 0.73 mmol) according to procedure 2, and new 2-(1-piperonylpiperazin-1-yl)-3-(4-hydroxybutylthio)-1,4-NQ compound **(16)** was synthesized.

Compound 16: Dark red oil. Yield: 0.157 g (45%). R_f: 0.54 (EtAc). ***FT-IR*** (film, cm^{-1}): ν = 3364 (O-H), 2961 (C-$H_{arom.}$), 2907 (C-$H_{aliph.}$), 1662 (C=O), 1589, 1525 (C=C). ***^{1}H NMR (ppm)***: δ = 1.18 (s, 1H, OH), 1.56-1.61 (m, 4H, CH_2 –CH_2), 2.56-2.58 (m, 4H, 2$CH_{2\ piper.}$), 2.82-2.85 (t, 2H, S-CH_2), 3.44 (s, 2H, N-CH_2-Ph), 3.52-3.57 (m, 6H, C**H$_2$**-OH, 2$CH_{2\ piper.}$), 5,88 (s, 2H, O-CH_2-O), 6.68-6.72 (m, 2H, 2CH_{Ph}), 6.83 (s, 1H, CH_{Ph}), 7.54-7.60 (m, 2H, 2$CH_{naphth.}$), 7.89-7.97 (m, 2H, 2$CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 25.96 (SCH$_2$***C***H$_2$), 31.64 (SCH$_2$CH$_2$***C***H$_2$), 34.46 (S-CH_2), 52.06, 53.53 ($CH_{2piper.}$), 62.20 (CH_2-OH), 62.72 (N-CH_2-Ph), 100.96 (O-CH_2-O), 107.96, 109.55, 122.54, 125.31, 126.27, 126.57, 132.13, 132.82, 132.88, 133.64 ($C_{arom.}$), 146.85 (=C-N), 147.74, 154.16 (=C-O), 181.83, 182.11 (C=O). $C_{26}H_{28}N_2O_5S$ (M = 480.58 g/mol). MS[+ESI]: *m/z* (%) (100) 481 $[M+H]^+$.

3.3.16. Experiment 16: Reaction of 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ with 6-mercaptohexanol

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** (0.3g, 0.73mmol) was reacted with 6-mercaptohexanol (0.098g, 0.73 mmol) according to procedure 2, and new 2-(1-piperonylpiperazin-1-yl)-3-(6-hydroxyhexylthio)-1,4-NQ compound **(17)** was synthesized.

Compound 17: Dark red oil. Yield: 0.157 g (42%). R_f: 0.3 (EtAc:PET 1:1). ***FT-IR*** (film, cm^{-1}): ν = 3397 (O-H), 3067 (C-$H_{arom.}$), 2923, 2857 (C-$H_{aliph.}$), 1663 (C=O), 1589, 1526 (C=C). ***^{1}H NMR (ppm)***: δ = 1.18-1.48 (m, 7H, 3$CH_{2\ aliph.}$, OH), 2.57-2.59 (t, 4H, 2$CH_{2\ piper.}$), 2.77-2.80 (m, 2H, $SCH_2C\mathbf{H_2}$), 3.44 (s, 2H, S-CH_2), 3.53-3.55 (m, 8H, $C\mathbf{H_2}$-OH, 2$CH_{2\ piper.}$, N-CH_2-Ph), 5.87 (s, 2H, O-CH_2-O), 6.67-6.70 (m, 2H, 2CH_{Ph}), 6.83 (s, 1H, CH_{Ph}), 7.55-7.59 (m, 2H, 2$CH_{naphth.}$), 7.89-7.97 (m, 2H, 2$CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 25.20 ($SCH_2CH_2CH_2\boldsymbol{C}H_2$), 28.34 ($SCH_2\boldsymbol{C}H_2$), 29.47 ($SCH_2CH_2\boldsymbol{C}H_2$), 32.53 ($\boldsymbol{C}H_2CH_2OH$), 34.62 (S-$CH_2$), 51.96, 53.52 ($CH_{2\ piper.}$), 62.65 (N-$CH_2$-Ph), 62.72 ($CH_2$-OH), 100.96 (O-$CH_2$-O), 107.96, 109.96, 122.52, 125.68, 126.25, 126.55, 132.14, 132.77, 132.79, 132.89, 133.60 ($C_{arom.}$), 146.86 (=C-N), 147.73, 154.03 (=C-O), 181.84, 182.09 (C=O). $C_{28}H_{32}N_2O_5S$ (M = 508.63 g/mol). MS[+ESI]: *m/z* (%) (100) 509 $[M+H]^+$.

3.3.17. Experiment 17: Reaction of 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ with 1-mercapto-2-propanol

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** (0.3g, 0.73mmol) was reacted with 1-mercapto-2-propanol (0.067g, 0.73 mmol) according to procedure 2**,** and new 2-(1-piperonylpiperazin-1-yl)-3-(2-hydroxy-1-propylthio)-1,4-NQ compound **(18)** was synthesized.

Compound 18: Dark red oil. Yield: 0.096 g (29%). R_f: 029 (EtAc:PET 1:1). ***FT-IR*** (film, cm^{-1}): ν = 3358 (O-H), 3068, 2961 (C-$H_{arom.}$), 2915, 2854 (C-$H_{aliph.}$), 1663 (C=O), 1589, 1525 (C=C). ***^{1}H NMR (ppm)***: δ = 1.12-1.13 (d, 3H, CH_3), 1.17 (s, 1H, OH), 2.57-2.62 (m, 4H, 2$CH_{2\ piper.}$), 2.96-2.99 (m, 2H, S-CH_2), 3.39-3.46 (m, 4H, 2$CH_{2\ piper.}$), 3.57-3.59 (m, 2H, N-CH_2-Ph), 3.64-3.70 (m, 1H, C**H**-OH), 5.87 (s, 2H, O-CH_2-O), 6.67-6.72 (m, 2H, 2CH_{Ph}), 6.83 (s, 1H, CH_{Ph}), 7.54-7.60 (m, 2H, 2$CH_{naphth.}$), 7.89-7.91 (m, 1H, $CH_{naphth.}$), 7.96-7.98 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 20.88 (CH_3), 43.67 (S-CH_2), 51.70, 52.57 ($CH_{2\ piper.}$), 61.65 (N-CH_2-Ph), 65.09 (CH-OH), 99.94 (O-CH_2-O), 106.93, 108.57, 121.42, 125.50, 125.66, 130.25, 131.04, 131.69, 131.90, 131.92, 132.84 ($C_{arom.}$), 145.81 (=C-N), 146.72, 154.86 (=C-O), 180.93, 181.18 (C=O). $C_{25}H_{26}N_2O_5S$ (M = 466.55 g/mol). MS[+ESI]: *m/z* (%) (100) 467 $[M+H]^+$.

3.3.18. Experiment 18: Reaction of 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ with 11-mercapto-1-undecanol

2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ **(14)** (0.2g, 0.48mmol) was reacted with 11-mercapto-1-undecanol (0.099g, 0.48 mmol) according to procedure 2**,** and new 2-(1-piperonylpiperazin-1-yl)-3-(11-hydroxyundecylthio)-1,4-NQ compound **(19)** was synthesized.

Compound 19: Dark red oil. Yield: 0.16 g (57%). R_f: 038 (EtAc:PET 1:1). ***FT-IR*** (film, cm^{-1}): ν = 3397 (O-H), 3068 (C-$H_{arom.}$), 2920, 2850 (C-$H_{aliph.}$), 1662 (C=O), 1590, 1526 (C=C). ***^{1}H NMR (ppm)***: δ = 1.16-1.29 (m, 15H, 7$CH_{2\ aliph.}$, OH), 1.42-1.50 (m, 4H, SCH_2C**H_2**, C**H_2**CH_2OH), 2.57 (s, 4H, 2$CH_{2\ piper.}$), 2.77-2.80 (t, 2H, S-CH_2), 3.43 (s, 2H, N-CH_2-Ph), 3.52-3.56 (m, 6H, C**H_2**-OH, 2$CH_{2\ piper.}$), 5.88 (s, 2H, O-CH_2-O), 6.67-6.72 (m, 2H, 2CH_{Ph}), 6.83 (s, 1H, CH_{Ph}), 7.53-7.60 (m, 2H, 2$CH_{naphth.}$), 7.89-7.91 (m, 1H, $CH_{naphth.}$), 7.96-7.98 (m, 1H, $CH_{naphth.}$). ***^{13}C NMR (ppm):*** δ = 24.70 (***C***$H_2CH_2CH_2OH$), 27.65, 28.06, 28.34, 28.40, 28.49, 28.61 ($CH_{2\ aliph.}$), 31.76 (***C***H_2CH_2OH), 33.72 (S-CH_2), 51.00, 52.57 ($CH_{2\ piper.}$), 61.75 (CH_2-OH), 62.00 (N-CH_2-Ph), 99.94 (O-CH_2-O), 106.92, 108.51, 121.43, 125.22, 125.51, 131.15, 131.73, 131.92, 132.55 ($C_{arom.}$), 145.80 (=C-N), 146.71, 152.89 (=C-O), 180.84, 181.07 (C=O). $C_{33}H_{42}N_2O_5S$ (M = 578.76 g/mol). MS[+ESI]: *m/z* (%) (100) 579 $[M+H]^+$.

4. DISCUSSION

The new compounds (**2, 3, 4, 5, 6, 8, 9, 10, 11, 12, 13, 15, 16, 17, 18** and **19**) which were synthesized in this study, were obtained by nucleophilic substitution reactions using one N-nucleophile and different S-nucleophiles.

Four naphthoquinone compounds were used as starting material, They are:

- 2,3-Dichloro-1,4-NQ **(1)**.
- 2-(1-(2-Cyanophenyl)piperazinyl)-3-chloro-1,4-NQ **(2)**. It is a new compound and was prepared in this study.
- 2-(6-Aminohexyl-1-ol)-3-chloro-1,4-NQ **(7)**. This compound is not new.
- 2-(1-Piperonylpiperazin-1-yl)-3-chloro-1,4-NQ (**14**). This compound is not new.

Firstly, 2,3-dichloro-1,4-(NQ) (**1**) was reacted with 1-(2-cyanophenyl)piperazine to give new 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ compound **(2)**. As was shown in ^{1}H NMR for this compound; protons of piperazine ring appeared at δ = 3.40-3.42 and 3.82-3.84 ppm as triplet. In ^{13}C NMR; the piperazine carbons gave two signals at δ = 51.44, 52.42 ppm. Carbon of the cyano group was observed at δ = 106.62 ppm, while the carbonyl groups gave two signals at δ = 178.15, 181.85 ppm.

Secondly, the new compound **(2)** was reacted with different thiols and new compounds **(3, 4, 5** and **6)** were obtained.

The new 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ compound **(2)** was reacted with 2-mercaptoethanol and new compound **(3)** was obtained. As was shown in IR spectrum for compound **(3)**; broad hydroxyl band (-OH) was seen at ν = 3390 cm^{-1}. In ^{1}H NMR; protons of piperazine ring appeared at δ = 3.33-3.35 and 3.75-3.77 ppm as triplet. In ^{13}C NMR; the piperazine carbons gave two signals at δ = 52.40, 52.69 ppm. Carbon of the cyano group was observed at δ = 106.52 ppm, while the carbonyl groups gave two signals at δ = 181.81, 182.40 ppm.

The new 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ compound **(2)** was reacted with 4-mercapto-1-butanol and new compound **(4)** was obtained. As was shown in IR spectrum for compound **(4)**; broad hydroxyl band (-OH) was seen at ν = 3415 cm^{-1}. In ^{1}H NMR; protons of piperazine ring appeared at δ = 3.31-3.33 and 3.68-3.70 ppm as triplet. In ^{13}C NMR; the piperazine carbons gave two signals at δ = 52.12, 52.40 ppm. Carbon of the cyano group was

observed at δ = 106.42 ppm, while the carbonyl groups gave two signals at δ = 181.64 and 182.20 ppm.

The new 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ compound **(2)** was reacted with 1-mercapto-2-propanol and new compound **(5)** was obtained. As was shown in IR spectrum for compound **(5)**; broad hydroxyl band (-OH) was seen at ν = 3387 cm^{-1}. In ^{1}H NMR; protons of piperazine ring appeared at δ = 3.33-3.35 ppm as triplet and at 3.74-3.76 ppm as multiplet. In ^{13}C NMR; the piperazine carbons gave two signals at δ = 51.39, 51.71 ppm. Carbon of the cyano group was observed at δ = 105.49 ppm, while the carbonyl groups gave two signals at δ = 180.79, 181.29 ppm.

The new 2-(1-(2-cyanophenyl)piperazinyl)-3-chloro-1,4-NQ compound **(2)** was reacted with 6-mercapto-1-hexanol and new compound **(6)** was obtained. As was shown in IR spectrum for compound **(6)**; broad hydroxyl band (-OH) was seen at ν = 3402 cm^{-1}. In ^{1}H NMR; protons of piperazine ring appeared at δ = 3.32-3.34 and 3.69-3.71 ppm as triplet. In ^{13}C NMR; the piperazine carbons gave two signals at δ = 52.08, 52.44 ppm. Carbon of the cyano group was observed at δ = 106.44ppm, while the carbonyl groups gave two signals at δ = 181.71, 182.18 ppm.

Thirdly, 2,3-dichloro-1,4-NQ **(1)** was reacted with 6-amino-1-hexanol and known 2-(6-aminohexyl-1-ol)-3-chloro-1,4-NQ compound **(7)** was obtained. This known compound was then used as starting material and reacted with different thiols to synthesize the new compounds **(8, 9, 10, 11, 12** and **13)**.

The known compound **(7)** was reacted with 2-mercaptoethanol and new compound **(8)** was obtained. As was shown in IR spectrum for compound **(8)**; characteristic stretching bands for (-NH and -OH) were seen at ν = 3341, 3227 cm^{-1}. In ^{1}H NMR; -OH protons appeared at δ = 1.26 ppm as singlet, while NH-C**H₂** protons at δ = 2.84-2.86 ppm as triplet. In ^{13}C NMR; NH-CH_2 carbon was observed at δ = 47.50 ppm, and the carbonyl groups gave a signal at δ = 181.36 ppm.

The known compound **(7)** was reacted with 4-mercapto-1-butanol and new compound **(9)** was obtained. As was shown in IR spectrum for compound **(9)**; characteristic stretching bands for (-NH and -OH) were seen at ν = 3285 cm^{-1}. In ^{1}H NMR; -OH protons appeared at δ = 1.26 ppm as singlet, while NH-C**H₂** protons at δ = 2.83-2.86 ppm as triplet. In ^{13}C NMR; NH-CH_2 carbon was observed at δ = 47.51 ppm, and the carbonyl groups gave two signals at δ = 180.23 and 181.45 ppm.

The known compound **(7)** was reacted with 6-mercapto-1-hexanol and new compound **(10)** was obtained. As was shown in IR spectrum for compound **(10)**; characteristic stretching bands for (-NH and -OH) were seen at ν = 3276 cm^{-1}. In ^{1}H NMR; -OH protons appeared at δ = 1.26 ppm as singlet, while NH-C**H₂** protons together with $NH(CH_2)_5C\mathbf{H_2}OH$ protons appeared at δ = 3.62-3.68 ppm as multiplet. –NH proton appeared at δ = 6.49 ppm as singlet. In ^{13}C NMR; NH-CH_2 carbon was observed at δ = 47.51 ppm, and the carbonyl groups gave two signals at δ = 180.11, 181.48 ppm.

The known compound **(7)** was reacted with 11-mercapto-1-undecanol and new compound **(11)** was obtained. As was shown in IR spectrum for compound **(11)**; characteristic stretching bands for (-NH and -OH) were seen at ν = 3427, 3372, 3294 cm^{-1}. In ^{1}H NMR; -OH protons with aliphatic CH_2 protons appeared at δ = 1.16-1.67 ppm as multiplet, while NH-C**H₂** protons together with $S(CH_2)_{10}C\mathbf{H_2}OH$ protons appeared at δ = 3.54-3.60 ppm as multiplet. In ^{13}C NMR; NH-CH_2 carbon was observed at δ = 46.49 ppm, and the carbonyl groups gave two signals at δ = 179.05, 180.49 ppm.

The known compound **(7)** was reacted with 2-chlorobenzylmercaptan and new compound **(12)** was obtained. As was shown in IR spectrum for compound **(12)**; characteristic stretching bands for (-NH and -OH) were seen at ν = 3423, 3321 cm^{-1}. In ^{1}H NMR; -OH protons appeared at δ=1.18 ppm as singlet, while -SCH_2 protons appeared at δ= 4.03 ppm as singlet. In ^{13}C NMR; S-CH_2 carbon was observed at δ= 36.84 ppm, and the carbonyl groups gave two signals at δ= 180.18, 181.31 ppm.

The known compound **(7)** was reacted with 2-phenylethanethiol and new compound **(13)** was obtained. As was shown in IR spectrum for compound **(13)**; characteristic stretching bands for (-NH and -OH) were seen at ν = 3423, 3325 cm^{-1}. In ^{1}H NMR; -OH protons appeared at δ = 1.18 ppm as singlet. -SCH_2 protons appeared at δ = 2.80-2.83 ppm as triplet, while CH_2-Ph protons at δ = 3.56-3.59 ppm as triplet. In ^{13}C NMR; S-CH_2 carbon was observed at δ = 35.69 ppm, CH_2-Ph carbon at δ = 36.08 ppm, and the carbonyl groups gave two signals at δ = 180.06, 181.33 ppm.

Fourthly, 2,3-dichloro-1,4-NQ **(1)** was reacted with 1-piperonylpiperazine and known 2-(1-piperonylpiperazin-1-yl)-3-chloro-1,4-NQ compound **(14)** was obtained. This known compound was then used as starting material and reacted with different thiols to synthesize the new compounds **(15**, **16**, **17**, **18** and **19)**.

The known compound **(14)** was reacted with 2-mercaptoethanol and new compound **(15)** was obtained. As was shown in IR spectrum for compound **(15)**; broad hydroxyl band (-OH) was seen at ν = 3300 cm^{-1}. In ^{1}H NMR; -OH proton appeared at δ = 1.18 ppm as singlet. Protons of piperazine ring at δ = 2.41 ppm as singlet and at 2.80-2.94 ppm as multiplet. N-CH_2-Ph protons appeared at δ = 3.33-3.40 ppm as multiplet, while O-CH_2-O protons appeared at δ = 5.86-5.88 ppm as multiplet. In ^{13}C NMR; the piperazine carbons gave two signals at δ = 52.30, 52.88 ppm, N-***C***H_2-Ph was observed at δ = 65.92 ppm, O-CH_2-O at δ = 100.92 ppm, and the carbonyl groups gave two signals at δ = 176.48, 181.65 ppm.

The known compound **(14)** was reacted with 4-mercapto-1-butanol and new compound **(16)** was obtained. As was shown in IR spectrum for compound **(16)**; broad hydroxyl band (-OH) was seen at ν = 3364 cm^{-1}. In ^{1}H NMR; -OH proton appeared at δ = 1.18 ppm as singlet. Protons of piperazine ring at δ = 2.56-2.58 ppm as multiplet, and the other protons of piperazine ring appeared togother with -C**H₂**OH protons at δ = 3.52-3.57 ppm as multiplet. N-CH_2-Ph protons appeared at δ = 3.44 ppm as singlet, while O-CH_2-O protons at δ = 5.88 ppm as singlet. In ^{13}C NMR; the piperazine carbons gave two signals at δ = 52.06, 53.53 ppm. N-***C***H_2-Ph was observed at δ = 62.72 ppm, O-CH_2-O at δ = 100.96 ppm, and the carbonyl groups gave two signals at δ = 181.83, 182.11 ppm.

The known compound **(14)** was reacted with 6-mercapto-1-hexanol and new compound **(17)** was obtained. As was shown in IR spectrum for compound **(17)**; broad hydroxyl band (-OH) was seen at ν = 3397 cm^{-1}. In ^{1}H NMR; -OH proton with aliphatic CH_2 protons appeared at δ = 1.18-1.48 ppm as singlet. Protons of piperazine ring at δ = 2.57-2.59 ppm as triplet. The other protons of piperazine ring appeared togother with N-CH_2-Ph and with C**H₂**OH protons at δ = 3.53-3.55 ppm as multiplet. O-CH_2-O protons appeared at δ = 5.87 ppm as singlet. In ^{13}C NMR; the piperazine carbons gave two signals at δ = 51.96, 53.52 ppm. N-***C***H_2-Ph was observed at δ = 62.65 ppm, O-CH_2-O at δ = 100.96 ppm and the carbonyl groups gave two signals at δ = 181.84, 182.09 ppm.

The known compound **(14)** was reacted with 1-mercapto-2-propanol and new compound **(18)** was obtained. As was shown in IR spectrum for compound **(18)**; broad hydroxyl band (-OH) was seen at ν = 3358 cm^{-1}. In ^{1}H NMR; -OH proton appeared at δ = 1.17 ppm as singlet. Protons of piperazine ring at δ = 2.57-2.62 and 3.39-3.46 ppm as multiplet. N-CH_2-Ph protons at δ = 3.57-3.59 ppm as multiplet. O-CH_2-O protons at δ = 5.87 ppm as singlet. . In ^{13}C NMR; the piperazine carbons gave two signals at δ = 51.70, 52.57 ppm. N-***C***H_2-Ph was observed at δ =

61.65 ppm. O-CH_2-O at δ = 99.94 ppm and the carbonyl groups gave two signals at δ = 180.93, 181.18 ppm.

The known compound **(14)** was reacted with 11-mercapto-1-undecanol and new compound **(19)** was obtained. As was shown in IR spectrum for compound **(19)**; broad hydroxyl band (-OH) was seen at ν = 3397 cm^{-1}. In ^{1}H NMR; -OH proton with aliphatic CH_2 protons appeared at δ = 1.16-1.29 ppm as singlet. Protons of piperazine ring at δ = 2.57 ppm as singlet. The other protons of piperazine ring appeared togother with C**H**$_2$-OH protons at δ = 3.52-3.56 ppm as multiplet. N-CH_2-Ph protons at δ =3.43 ppm as singlet. O-CH_2-O protons at δ = 5.88 ppm as singlet. In ^{13}C NMR; the piperazine carbons gave two signals at δ = 51.00, 52.57 ppm. N-***C***H_2-Ph was observed at δ = 62.00 ppm. O-CH_2-O at δ = 99.94 ppm and the carbonyl groups gave two signals at δ = 180.84, 181.07 ppm.

5. CONCLUSION AND RECOMMENDATIONS

In this study, sixteen novel naphthoquinone compounds were synthesized in good yields; one N-substituted naphthoquinone compound and various S-substituted naphthoquinone compounds.

Recommendations:

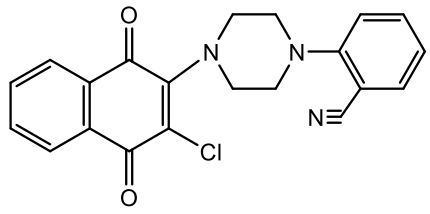
- Furthering research in these new naphthoquinone compounds due to their significance in organic chemistry.

- Researching the biological activities of these compounds concerning the antitumor, antibacterial and antifungal.

- Exploiting these compounds in medical industry.

- Using these compounds in different fields (textile, polymer, drug, etc.).

5.1 COLLECTIVE STRUCTURES OF NEW SYNTHESIZED COMPOUNDS



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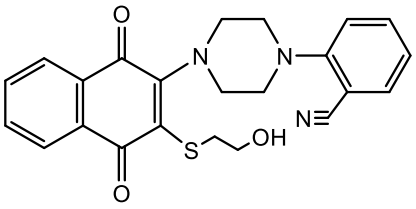

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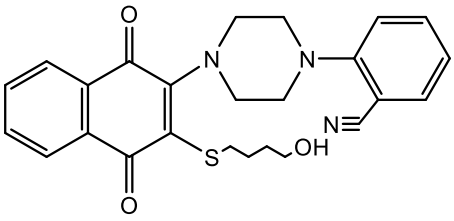

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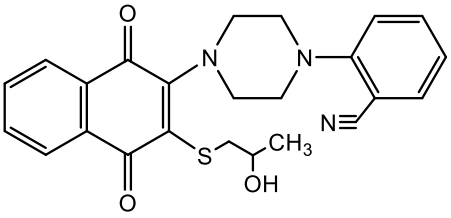

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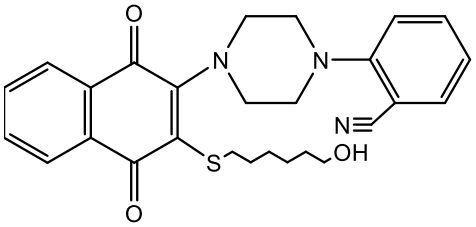

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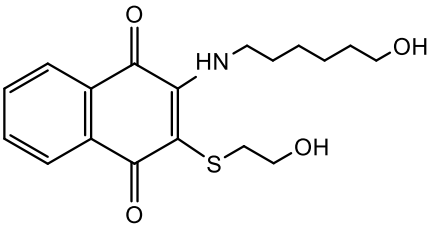

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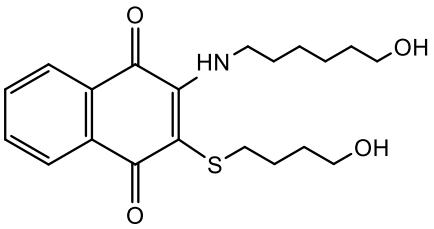

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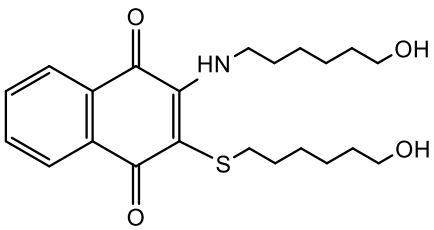

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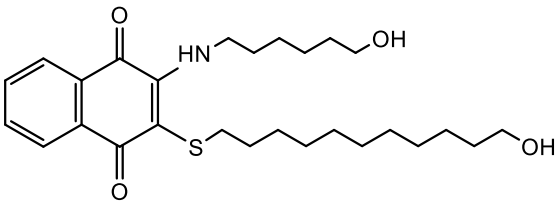

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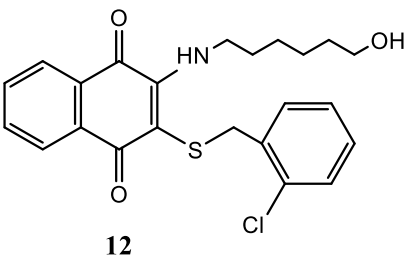

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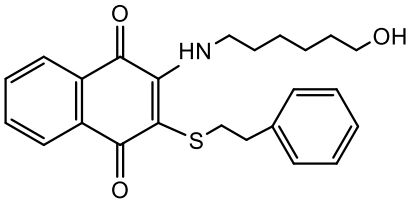

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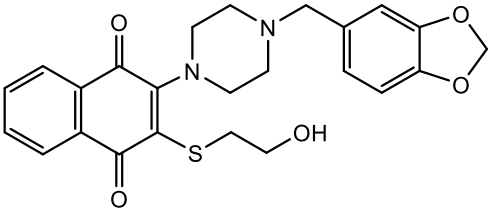

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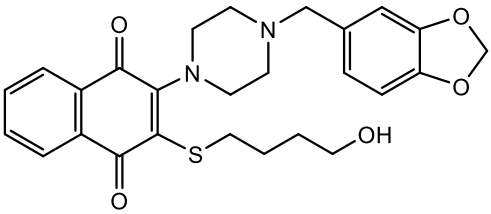

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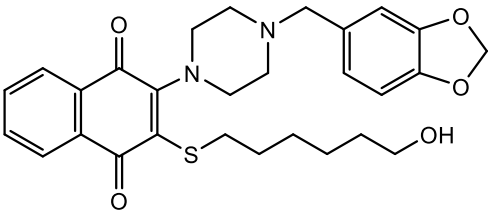

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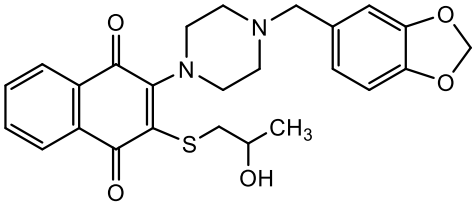

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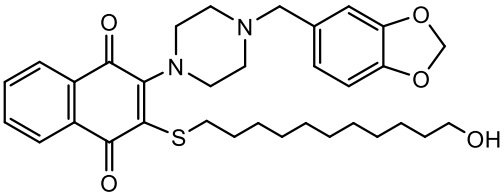

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Gokmen Z., **Alahmad H.,** Synthesis of Biologically Active Naphthoquinone Derivatives, 1st International Symposium on Graduate Research in Science Focus on Entrepreneurship and Innovation, Istanbul University, Beyazit-İstanbul, 4-6 October 2018, p. 98
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