Chapter One

1. Introduction

1.1 Betti bases

The study of the chemistry of the Betti bases was started when Betti reported a straight forward synthesis of 1- (α-aminobenzyl)-2-naphthol (the Betti base), starting from 2-naphthol, benzaldehyde and ammonia (Ghandi, *et al*. 2008; Metlushka, *et al*. 2008).

The Mannich reaction is one of the most frequently applied multicomponent reactions in organic chemistry (Paqett, 1995). One of its special variants is the modified three-component Mannich reaction, in which the electron-rich aromatic compounds are 1- or 2-naphthol. In this reaction, the nitrogen sources used (ammonia or amine) largely determines the reaction conditions and the method of isolation of the synthesized Mannich product (Szatmári and Fülöp. 2004).

The Betti procedure can be interpreted as an extension of the Mannich condensation, with formaldehyde replaced by aromatic aldehyde, secondary amine by ammonia and the C – H acid by an electron-rich aromatic compound, such as 2- naphthol (Töth, *et al*. 2006). The preparation of substituted Betti base derivatives by the modified Mannich reaction has subsequently become of considerable importance because a C – C bond is formed under mild experimental conditions (István and Ferenc. 2004). In later years, attention has been paid to the Betti's reaction, and a similar reaction can be performed by either using other naphthols (Pirrone, 1940) or quinolinols **(**Phillips and Barrall. 1956**)** or by replacing ammonia with alkylamines **(**Szatmari, *et al*. 2003**)**. In addition, a variety of racemic structures related to the Betti's bases have been prepared by addition of naphthols to the preformed imminium salts **(**Grumbach, *et al*. 1996**)**. In later years, the effort were done to synthesized the Betti's base derivatives in organic solvents such as EtOH, MeOH and Et_2O at room temperature or thermally under solventless condition (Saidi. and Azizi. 2003). In the past

decade, interest in the chemistry of the Betti base has intensified. Preparation of the enantiomers of the Betti base and its N-substituted derivatives is of significance since they can serve as chiral catalysts (Lu, *et al*. 2002). On the other hand, Betti base derivatives provide convenient access to many useful building blocks because the amino and the phenolic hydroxy groups can be converted into a wide variety of compounds (István and Ferenc. 2004). The Betti reaction is a convenient method with which to prepare α - aminobenzylnaphthol derivative (Betti, 1941).

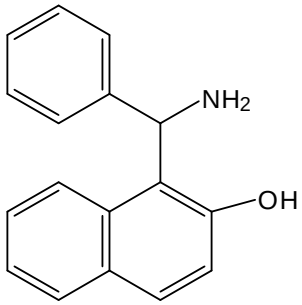


Fig. 1.1General structure of Betti base

Many unnatural homochiral amino-phenol compounds have been reported as excellent ligands in metal ion catalyzed asymmetric reactions in current asymmetric synthesis (Yuan, *et al*. 2002). The ligands, which have the structure of N,N- dialkyl Betti base are gaining increasing importance (Liu, *et al*. 2001). Among them, the derivatives of chiral N-methyl- N-alkyl Betti base have induced satisfactory reactivities and stereoselectivities in their catalyzed asymmetric reactions. The replacement of the N-methyl group in N-methyl-N-alkyl Betti base by a large-sized N-alkyl group did not bring any additional satisfactory results, but made the synthetic procedure more difficult (Yanmei, *et al*. 2004). Because the aliphatic amino moiety of Betti base has a relatively lower nucleophilic reactivity when compared to its phenoxyl group moiety, the N-alkylation of Betti base seriously lacks for regioselectivity by using routine methods (Vyskocil, *et al*. 1998). Therefore, no derivatives of chiral N,N-dialkyl Betti bases were prepared from nonracemic Betti base . The chiral N-methyl-N-alkyl Betti base was prepared mainly by the Mannich condensation of a chiral amine with benzaldehyde and 2-naphthol to yield a N-alkyl Betti base followed by a N-

methylation (Liu, *et al*. 2001). Since few of the N-alkyl Betti bases prepared by the Mannich condensation had satisfactory diastereopurity (Wang, *et al*. 2002), the diversity of the N-alkyl group in the N-methyl-N-alkyl Betti base is quite limited. On the other hand, the use of non-racemic amines has opened up a new area of application of these enantiopure aminonaphthols as chiral catalysts in enantioselective transformations (Boga, *et al*. 2001).

1.2.1 Synthesis of Betti base derivatives

Organic synthesis is a special branch of chemical synthesis and is concerned with the construction of organic compounds via organic reactions (March and Smith. 2001). Organic molecules can often contain a higher level of complexity compared to purely inorganic compounds, so the synthesis of organic compounds has developed into one of the most important aspects of organic chemistry (Corey and Cheng. 1995). There are two main areas of research fields within the general area of organic synthesis: total synthesis and methodology.

A total synthesis is the complete chemical synthesis of complex organic molecules from simple, commercially available or natural precursors (Nicolaou and Sorensen. 1996). In a linear synthesis there is a series of steps which are performed one after another until the molecule is made, this is often adequate for a simple structure (Wang, *et al*. 2002). The chemical compounds made in each step are usually referred to as synthetic intermediates. This is where several pieces (key intermediates) of the final product are synthesized separately, then coupled together, often near the end of the synthesis (Todd, 2005).

Each step of a synthesis involves a chemical reaction and reagents and conditions for each of these reactions need to be designed to give a good yield and pure product, with as little work as possible (March and Smith. 2001). However most intermediates are compounds that have never been made before and these will normally be made using general methods developed by methodology researchers. To be useful, these methods need to give high yields and to be reliable for a broad range of substrates (Corey and Cheng. 1995).

(Himani, *et a*l. 2010), reported the synthesis of different Betti bases via one pot Betti condensation reaction of 6-bromo-2- naphthol with different aromatic aldehydes in presence of ammonia as a coupling component.

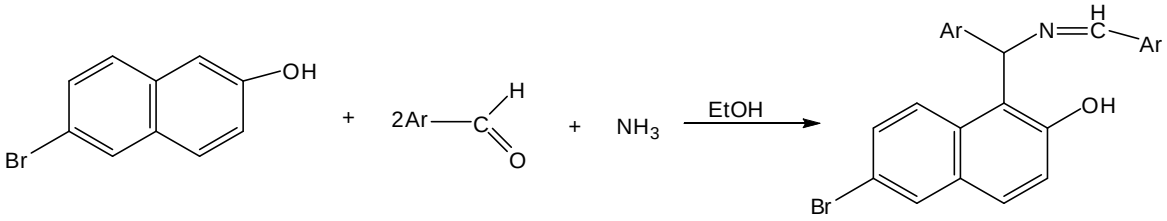


Fig. 1.2 Synthesis of Betti bases via one pot Betti condensation reaction

1.2.2 Synthesis of 1-(α- aminobenzyl)-2- naphthol derivatives

Aminonaphthols are easily prepared by the condensation of 2 – naphthol with ammonia and benzaldehyde (Betti, 1941). Though these derivatives were known since the beginning of the 20th century, their application in organic synthesis is of recent origin (Wang, *et al*. 2005). The original Betti base is thermally unstable and hence it is not suitable for preparation of the corresponding *N*, *N* – dialkyl derivatives under drastic conditions (Dong, *et al.* 2004). Generally, the derivatives of aminonaphthols were prepared by condensation of benzaldehyde, 2 – naphthol and amines in ethanol for 6 days (Boga, *et al*. 2001) in presence of acidic Al_2O_3 or $LiClO_4$ (Mojtahedi, *et al*. 2000). Condensation of β – naphthol and preformed imunium salts (Grumbach, *et al*. 1996) and photo addition of nucleophiles to 1 – alkenyl – 2 – naphthol also give the aminonaphthols (Yasuda, *et al*. 1995).

Accordingly, a simple method has been developed for preparing various derivatives of aminonaphthols following the original Betti procedure starting from benzaldehyde, 2 – naphthol and various amines at 78 ºC in ethanol solvent. In the preparation of aminonaphthols using primary amines, the yields were moderate to good, as the aminonaphthols could react further with benzaldehyde to give oxazine compounds. However, use of secondary amines gave the products in excellent yield (Mariappan, *et al*. 2009).

1.2.3 Syntheses of racemic compounds

The reaction was performed with 2-naphthol, benzaldehyde and ammonia (in a ratio of 1:2:1) to obtain 1,3-diphenyl-2,3-dihydro-1*H*-naphth [1,2- e][1,3] oxazine. The subsequent acidic hydrolysis and extraction with NH_4OH gave the desired aminonaphthol (Betti, 1941).

Racemic 1- (aminobenzyl)-2-naphthol (the Betti base) is available in bulk and was resolved into its enantiomers, (*S*)-**1** and (*R*)-**1**, early last century (Betti, 1941). However, they were never employed as chiral ligands in asymmetric catalysis until Cardellicchio's, *et al*. work in 1998, in which the asymmetric addition of diethylzinc to benzaldehyde was achieved. Similar to other reported amino-hydroxy ligands, tertiary amines gave better results than primary and secondary amines in most cases. No suitable method exists for regioselective *N*-alkylation of Betti base (Yanmei, *et al*. 2005). Its chiral *N*,*N*-dialkyl derivatives being prepared by resolving the corresponding racemic isomers or by condensation with chiral amines rather than directly from (*S*)-**1** or (*R*)-**1** (Cimarelli, *et al*. 2001).

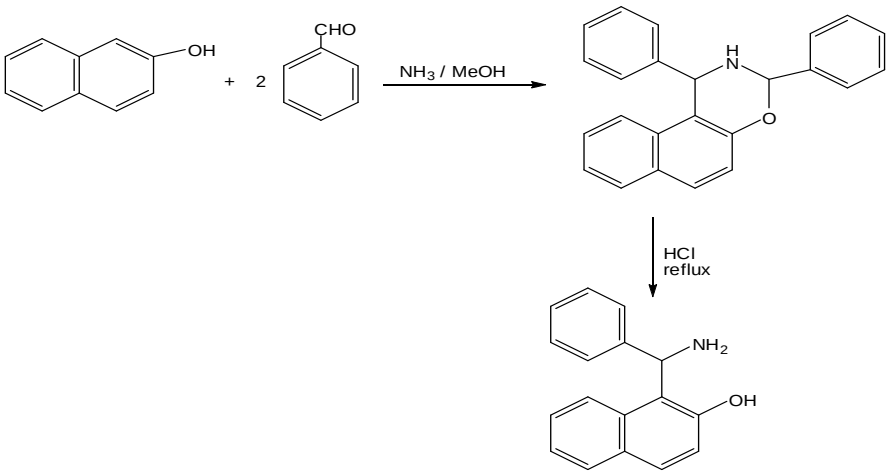


Fig. 1.3 Synthesis of Betti base via 1,3 oxazine

The reactions of 2 - naphthol with substituted benzylidene anilines in methanol led to the formation of *N*- monosubstituted Betti bases. The results can be interpreted as an extension of the Betti reaction because benzylidene anilines serve as aldehyde sources in the reaction, while primary amines were used instead of ammonia (Cordova, *et al*. 2002). In a study of the diazotization of 2-naphthol

with amines, by induction with microwave irradiation in the absence of solvent, replacement of the aromatic amine by benzylamine led to the formation of α-(2-hydroxy-1- naphthyl) dibenzylamine instead of the expected benzylazo-2-naphthol (Jin, *et al*. 2000). The Betti condensation was extended by using secondary amines (Brode and Littman. 1931), or cyclic amines (Seshadri, *et al*. 1969) resulting in *N,N*-disubstituted derivatives of the Betti base. In contrast with the conventional Mannich procedure, amino methylations using methylene iminium salts, which function as highly reactive Mannich reagents, furnish basic advantages, because they generally provide superior yields, while the reactions are faster and require milder conditions (Tramontini and Angiolini. 1990). This strategy was first applied by Risch, *et al.* 1996 and was extended by Saidi, *et al*. 2001. The iminium salts being prepared in 5 M ethereal lithium perchlorate.

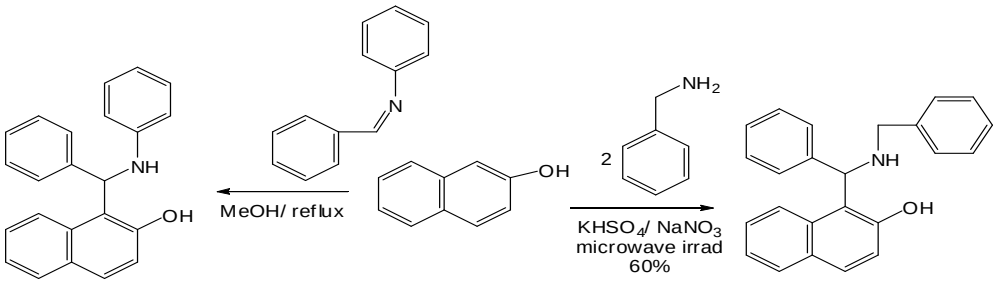


Fig. 1.4 Synthesis of *N*-monosubstituted Betti bases

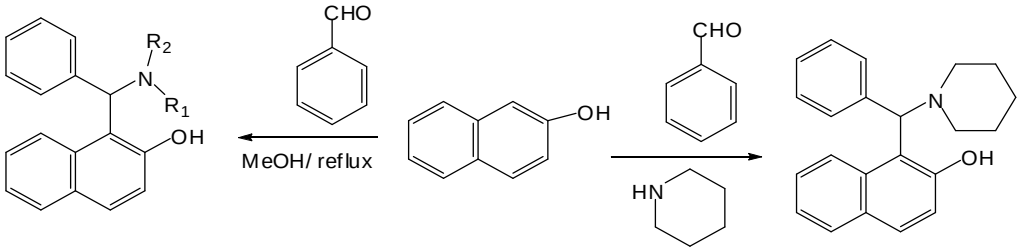
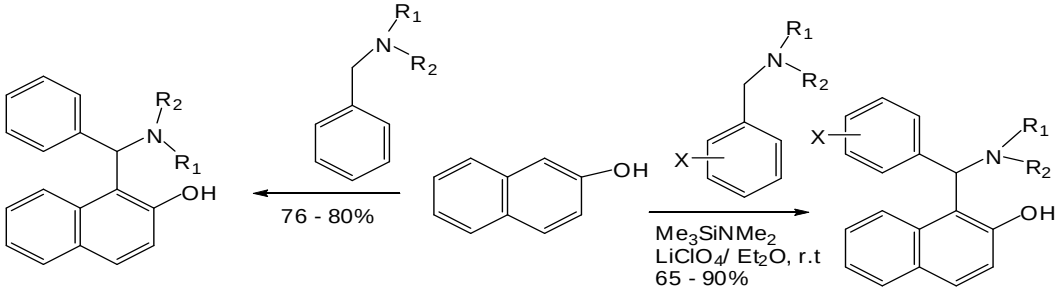


Fig. 1.5 Synthesis of *N,N*-disubstituted derivatives of Betti base



X = *m*-NO_2 ; 2,4-diCl ; H Fig. 1.6 Synthesis of *N,N*-dialkylated derivatives of the Betti base

Non-racemic amine derivatives of the Betti base showed very similar behavior to other reported amino-hydroxy ligands. Its tertiary amines gave better results than primary and secondary amines in most cases (Cardellicchio *et al*, 1999). However the non-racemic *N*,*N*-dialkylated derivatives of the Betti base that have been reported in the literature were usually prepared by resolution of the corresponding racemic isomers (Cardellicchio *et al*, 1998) or by condensation with chiral amines (Cimarelli *et al*,2001),rather than directly from *N*,*N*-dialkylation. This result strongly implies that there is no suitable method for the regioselective *N*,*N*-dialkylation of the Betti base so far and that the uses of the non-racemic Betti base, **(***S***)** or **(***R***)**, as a new chiral resource are seriously limited (Sztojkov, *et at*. 2005).

1.3 Transformations reactions of Betti bases

In spite of the great reaction possibility resulting from the two functional groups in the Betti base, relatively few publications have appeared in this field Prasad and Joshi (1997), used the racemic Betti base for the transformation into 4-thiazolidinones. The first step was the preparation of the Schiff bases with substituted benzaldehydes, but the tautomeric capability of the condensation products was not discussed at all. Compounds were then treated with mercaptoacetic acid to obtain 2-aryl-3-[α-(2-hydroxy-1- naphthyl)-benzyl]-4-thiazolidinones, which exerted antibacterial activity (Naso, et al. *1999*). The authors utilized the high reactivity of the Betti base to study its reactions with 2-carboxybenzaldehyde, phosgene, phenyl isothiocyanate (followed by ring closure with methyl iodide) and salicylaldehyde (followed by ring closure with formaldehyde and acetaldehyde). The products and reaction conditions are showed bellow (Szatmári, *et al*. 2008).

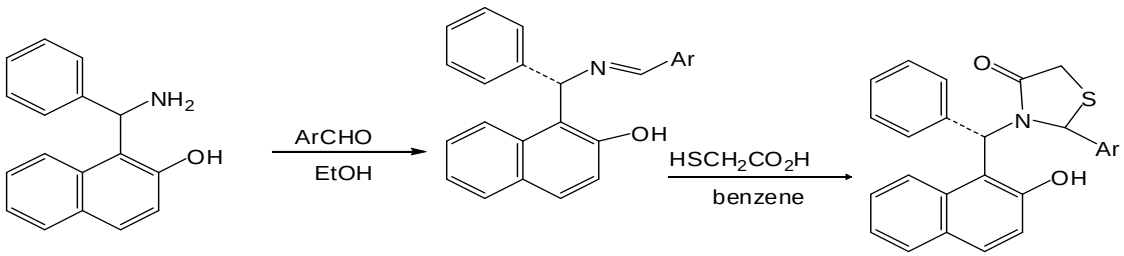
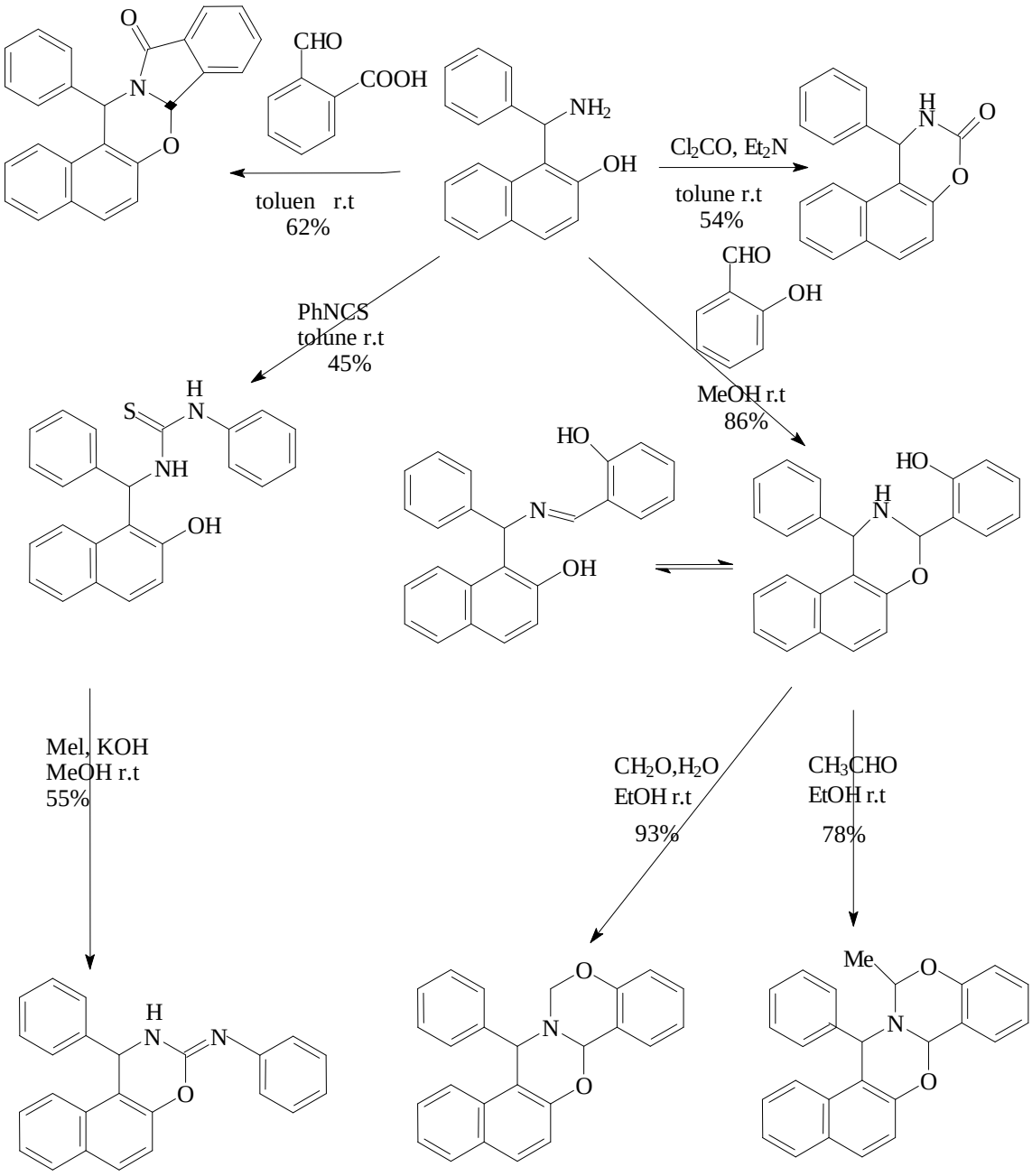


Fig. 1.7 Transformation of Betti base into 4-thiazolidinones



Scheme 1.1 Reaction of Betti base with different reagents followed by ring closure

Heydenreich, *et al*. (2006). achieved the synthesis of 1,2,3- triphenyl-2,3-dihydro-1H-naphth[1,2-e][1,3]oxazines by the reactions of 1-(α-phenylamino benzyl)-2-naphthol derivatives either with benzaldehyde or with substituted benzylidene-aniline in acetic acid, but the influence of the substituents on the diastereomeric ratios was not discussed (Istva, *et al*. 2009).

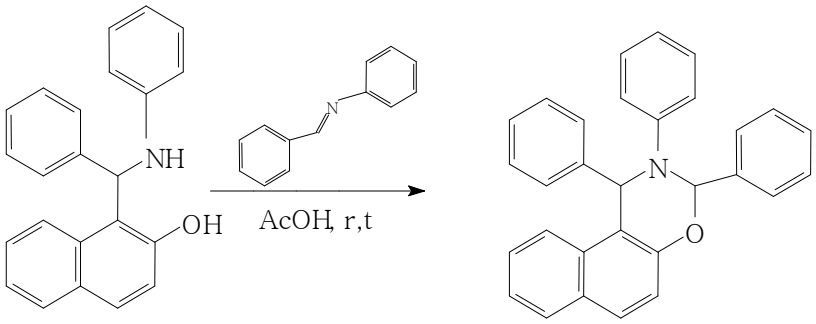


Fig 1.8 Synthesis of 1,2,3-triphenyl oxazines

Treatment of (S)-(+) with NaOH/MeI led to the trimethyl derivative (S) - (–) (Betti,1941). In order to prove the (S) configuration of the (+) produced, Palmieri, 2000 treated (S) - (+) with n-butanal, yielding the oxazine (–), which was reduced with $NaBH_4$ to (+) (Cardellicchio, *et al*. 2010).

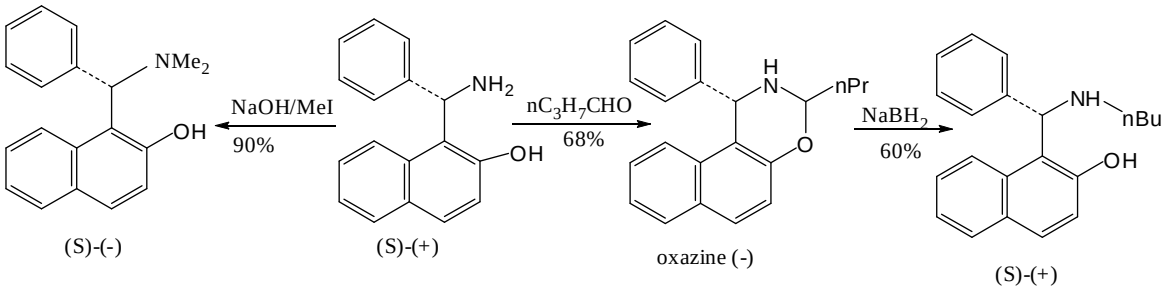
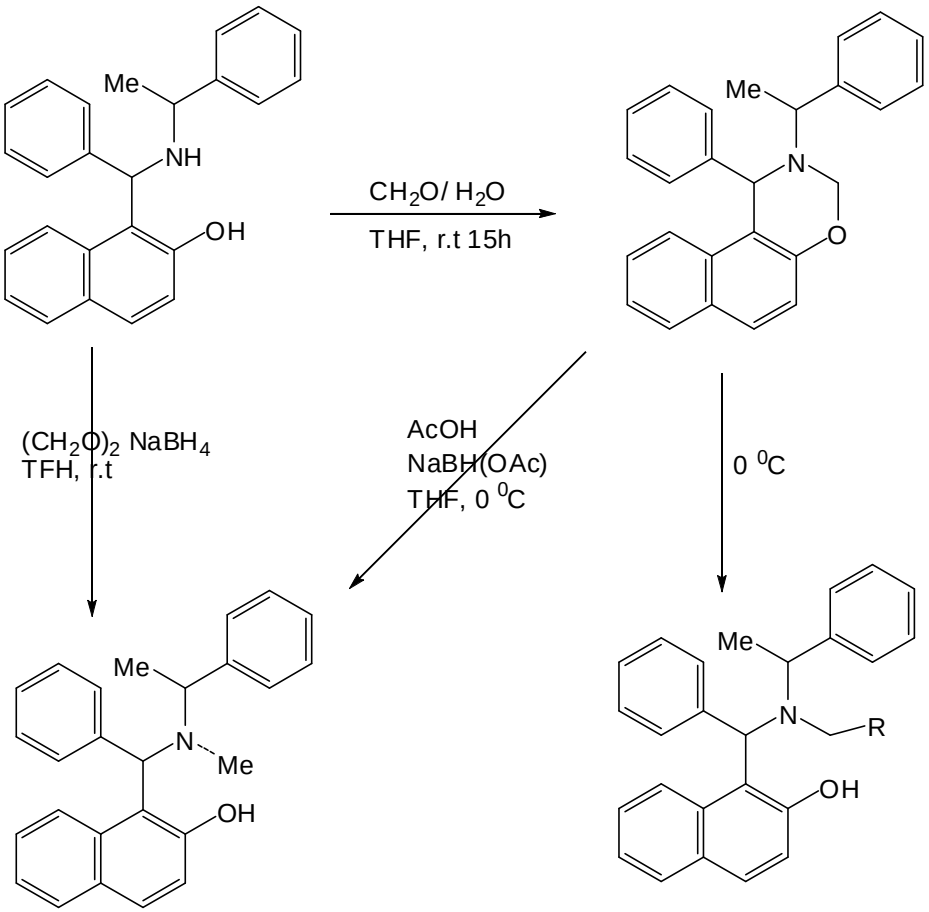


Fig 1.9 Treatment of (S)-(+)-Betti base to produce (S)-(+) and (S)-(-) Betti base derivatives

The enantiomers of the Betti base derivatives are not only good chiral ligands in asymmetric synthesis, but can also be applied as simple starting materials in the enantioselective syntheses of other chiral inductors (Ma, *et al*. 2007). A simple preparation of (1S,1'S) starting from (1 S ,1' S) is its direct N - methylation with paraformaldehyde, this was first carried out by Wang, *et al*. (2002). Palmieri, *et al*. (2000), reported the syntheses of (1R,1'R) and a wide group of tertiary aminonaphthols by reduction or alkylation with organometallic reagents (Cimarelli, *et al*. 2002).



Scheme 1.2 Synthesis of tertiaryaminonaphthols

The syntheses of (R)- and (S)-1-[α -(1- azacycloalkyl)benzyl]-2-naphthol were attained by Hu, *et al.* (2002), via selective N-cyclizations of (R)-(–) and (S)-(+) Betti bases in the presence of $NaBH_3CN$ to give 1- azacycloalka[2,1-b]oxazines, followed by selective cleavage of the C-O bonds with $LiAlH_4$.

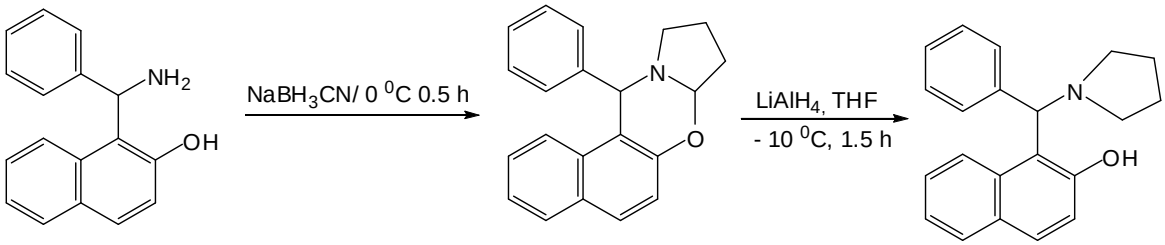
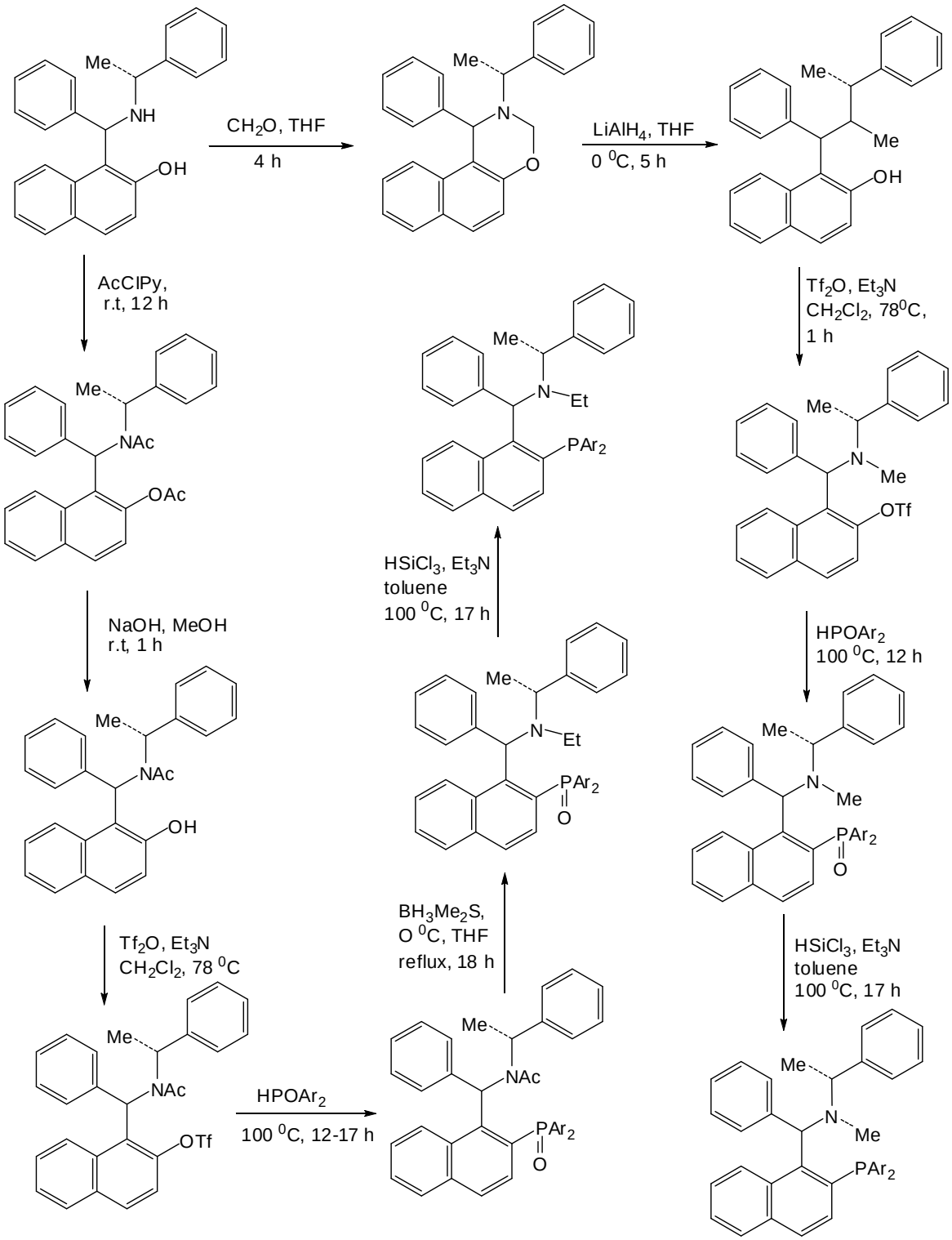


Fig 1.10 *N*-cyclization of Betti base to produce oxazine

Bojie and Jing. (2009), described the synthesis of a new type of chiral amino phosphine ligands from (1R,1'R) as starting material, formed by asymmetric 1-aminoalkylation of 2-naphthol with (R)-1-phenylethylamine and benzaldehyde.



Scheme 1.3 Synthesis of some types of chiral aminonaphtholphosphine ligands

The condensation products of 1-(α - aminobenzyl)-2-naphthol and benzaldehyde or substituted benzaldehydes are known in the literature and their structures have been showed as naphthoxazines or Schiff bases (Smith, *et al*. 1970).

Smith, *et al*. (1970) made the assumption that 1,3- diaryl groups prefer a pseudoequatorial position and therefore, a *cis* arrangement in the major ring-closed tautomer. In contrast with this assumption, from the NOESY spectrum of 1,3-oxazin (with X = pCl, Y = pNO_2), the authors proved that the major ring form in all tautomeric equilibria contains the 1,3-diaryl substituents in the *trans* position (Szatmári, *et al*. 2003). The common influence of aryl substituents at positions 1 and 3 was also studied. Multiple linear regression analysis of the log K values revealed that these are influenced in the trans-chain equilibria by a through-space inductive effect (σF) of substituent X besides the Hammett-Brown parameter of substituent Y. It was explained in terms of an anomeric effect quantitatively influenced by aryl substituents at position 1 (Szatmári, *et al*. 2000).

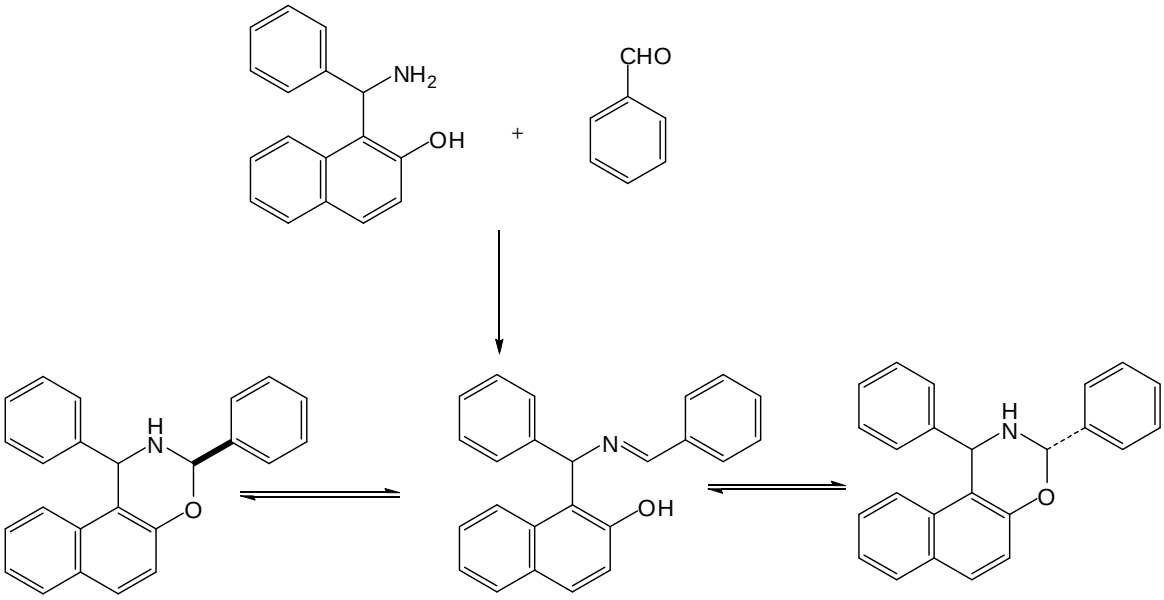


Fig 1.11 Condensation reaction between Betti base and benzaldehyde

To find evidence for the effects of alkyl substituents at position 3, and to prove the presence of an anomeric effect in this kind of naphthoxazines, 3-alkyl-1-aryl-2,3-dihydro-*1H*- naphth[1,2-e][1,3]oxazines were prepared by the condensation of substituted Betti bases with equivalent amounts of aliphatic aldehydes (Kang, *et al*. 1994). The ^{1}H NMR spectra of all compounds showed that, in $CDCl_3$ solution at 300 K, each of these components participated in two-component tautomeric mixtures containing C-3 epimeric naphthoxazines (B and C) (Szatmári, *et al*. 2000).

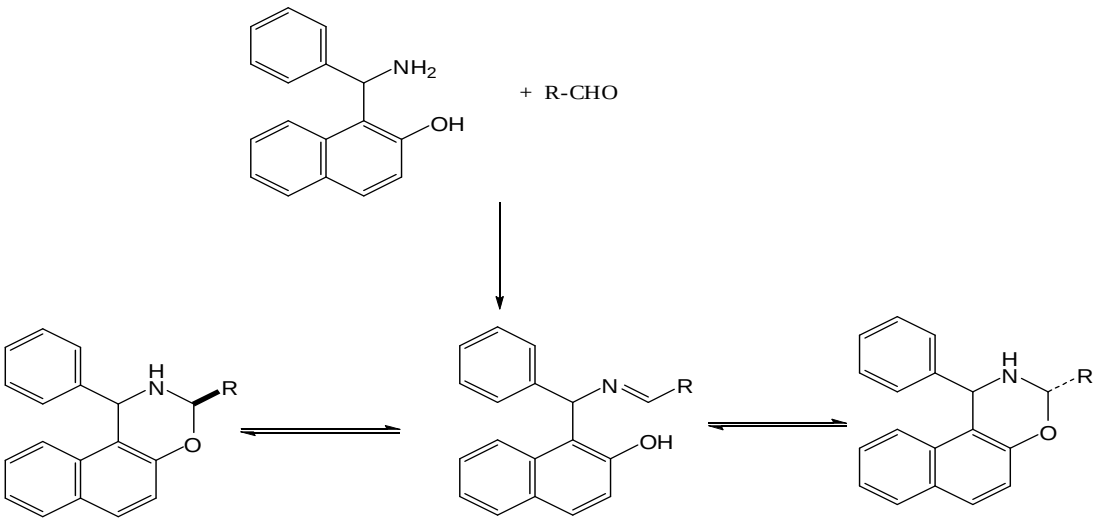


Fig 1.12 Condensation reactions between Betti base and aliphatic aldehydes

1.4 Alkylation of Betti bases

Many unnatural homochiral amino-phenol compounds have been reported as excellent ligands in metal ion catalyzed asymmetric reactions in current asymmetric synthesis (Yuan, *et al*. 2002). The ligands, which have the structure of *N,N* - dialkyl Betti base are gaining increasing importance (Ji, *et al*. 2003). Among them, the derivatives of chiral *N*-methyl - *N* - alkyl Betti base have induced satisfactory reactivities and stereoselectivities in their catalyzed asymmetric reactions.

Carbonyl compounds are alkylated enantioselectively by organometallic reagents in the presence of suitable chiral complexing agents (Noyori and Kitamura. 1991). The first reported enantioselective alkylation of aldehydes was performed by Betti, who reacted methylmagnesium iodide with benzaldehyde in the presence of *N,N*-dimethylbornylamine (Tarbell and Paulson. 1942). In recent times, enantioselective reactions of organolithium or organomagnesium compounds with aldehydes have been performed by an appropriate combination of carbonyl substrates, organometallic reagents and chiral modifiers (Noyori, 1994.). However, a significant improvement has been achieved by using organozinc compounds as alkylating agents (Soai and Niwa. 1992).

Summing up, the main distinctive features of these aminonaphthols are represented by an economical and simple synthesis, involving cheap starting materials which merge to give a more complex compound without side-products,

and by a subsequent expeditious procedure of resolution. Furthermore, the simplicity of the operations involved represents a good prerequisite for large scale applications.

1.5 Biological activity of Betti bases

Little attention has been paid to the Betti bases as far as their biological activity is concerned. Desai, *et al*. (1984) examined the *in vitro* antituberiostatic activity of 1-aryl-3-[α-(2-hydroxy-1- naphthyl)-benzyl] and 2-aryl-3-[α-(2-hydroxy-1- naphthyl)-benzyl]-4-thiazolidinones against the H37RV strain of Mycobacterium tuberculosis in Lowenstein-Jensen egg medium at 0.02 mg/mL. The retardation of the growth rate was studied for up to six weeks at 37 °C. The antibacterial activities of 1-aryl-3-[α-(2-hydroxy-1- naphthyl)-benzyl] and 2-aryl-3-[α-(2-hydroxy-1- naphthyl)-benzyl]-4-thiazolidinones were tested by means of an N-agar pour-plate method in DMF, and they proved to be active against *Escherichia coli* and *S. aureus*. It was found that 1-aryl-3-[α-(2-hydroxy-1-naphthyl)-benzyl] does not possess significant antimycobacterial activity; the presence of a thiazolidine nucleus is necessary for good antituberculotic activity, and the presence of halogen atoms enhances the antibacterial activity (István and Ferenc. 2004).

1.6 Ring – closure reactions

In the formation of rings from acyclic precursors, the key step is frequently the formation of a carbon-heteroatom linkage (Berkecz. 2007). The actual ring closure, or cyclization, however, may involve the formation of a carbon-carbon bond (Newkome and Pandler. 1982). In any case, ring formation reactions are divided into three general categories according to whether the cyclization reaction occurs primarily as a result of nucleophilic or electrophilic attack or by way of a cyclic transition state or by conversion of one heterocyclic ring into another (McNaught, 1976).

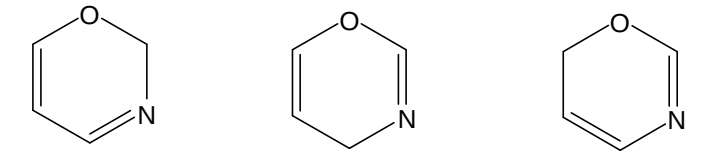
The first group of ring forming reactions comprises nothing more than intramolecular variants of reactions. In these processes, an n-member ring is formed by cyclisation of a chain of n atoms (Büchardt, 1076). The second group

of reactions is intermolecular, involving the simultaneous formation of two bonds between two different molecules. The third group consists of electrocyclic reactions, which are intramolecular and related mechanistically to cycloadditions (Andrews, 1980).

1.7 Chemistry of 1,3-oxazines

Oxazines are important group of organic dyes which are generally π – conjugated systems, with interesting photo – physical and lasting properties (Kolev, *etal*. 2008). Aromatic oxazines were first synthesized in 1944 by Holly and Cope through Mannich reactions from phenols, formaldehyde and amines (Holly and Cope. 1944).

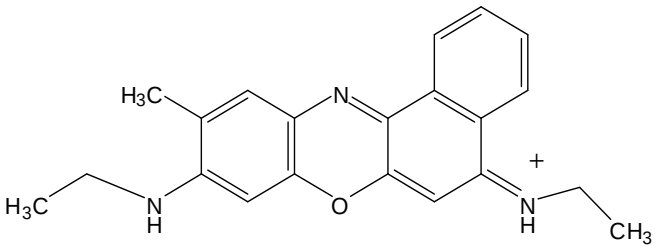
Six member heterocyclic rings containing oxygen and nitrogen are termed oxazine. The chemistry of 1,3-oxazine has been interested since the 1950s (Barton, *et al*. 1997). 1,3-oxazines belong to a class of compounds that have been largely studied due to their wide range of biological activities and easy synthetic accessibility (Zanatta, *et al*. 2005).



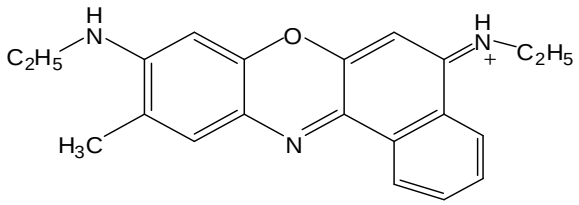
2H-1,3-oxazine 4H-1,3-oxazine 6H-1,3-oxazine

Fig 1.13General structures of oxazines

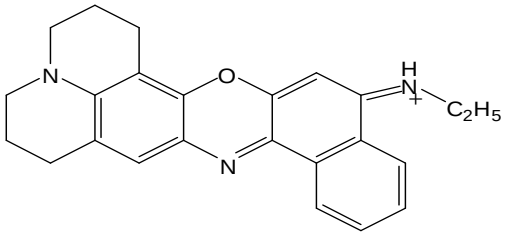
Nowadays oxazines are the subject of many literature and patent sources and are used as dye materials, anti-corrosion chemicals, and are often used in certain steps of synthesis of dye materials and drugs (Turgut and Oztürkcan. 2009). The following oxazines are the compounds for the most common used dye material (Milanchian, *etal*. 2009).



Oxazine a



Oxazine b



Oxazine c

Fig 1.14 Structures of most common oxazines used as dye materials

Zakerhamidi, *etal.* (2010) studies the aggregated properties of oxazine b and oxazine c dyes in polyacrylamide hydrogels with different compositional percentage of structural species were studied using optical spectroscopy. As the result, oxazine b and oxazine c aggregated form in all percentage of polyacrylamide are lower than these in aqueous medium (Turgut, *et al*. 2007). Several methods for the preparations of 1,3-oxazine derivatives have been previously reported (Khumtaveeporn and Alper. 1996).

The ring – chain tautomeric inter – conversion of *N*-unsubstituted 1,3-*N*-*O*-heterocycles and the corresponding hydroxyl alkyl imines can often be exploited advantageously in different areas of organic synthesis. Hence, the synthesis of these derivatives is of considerable interest (Lâzâr and Fülop. 2003).

Synthesis compounds of these classes may be easily obtained by the condensation of aldehydes and ketones with 3- aminopropan-1-ols in basic solution, thus the parent heterocycle, tetrahydro-1,3- oxazine, is synthesized by the condensation of 3- aminopropanol with formaldehyde (Coffey, 1978).

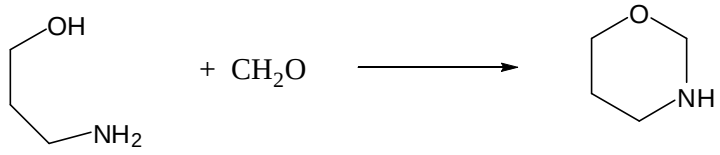


Fig 1.15 Synthesis of 1,3-oxazine

A broad range of synthetic applications demonstrates that 1,2- oxazine derivatives constitute a versatile class of nitrogen and oxygen heterocycles (Young, *et al*. 2003). Considerable attention has been paid to 6*H*-1,2- oxazines bearing a C-4,C-5-double bond (Zimmer, *et al*. 2002), which are useful intermediates in the synthesis of γ-lactams, γ-amino acids, amino alcohols, aziridines, pyrrolizidines, and pyrrolidine derivatives (Zimmer, *et al*. 2008).

1.8 Biological activity of oxazines

Nitrogen heterocycles are of special interest because they constitute an important class of natural and non-natural products, many of which exhibit useful biological activity (Sadig-ur-Rehman, *et al*. 2010). The synthesis of 1,3-oxazines has attracted attention in the past because of their potential as antibiotics, antitumor agent, analgesics and anticonvulsant and also generated great interest as antipsychotic and dopamine receptors (Damodiran, *et al*. 2009).

The biological activity of oxazines and their derivatives were represented early as 1937 (Novelli and Adams. 1937). Later several workers reported the fungistatic and bacteriostatic activity of these compounds. Chylinska, *et al*. 1971 examined dihydro-1,3-oxazine derivatives as antibacteria and oncostatic agents, the results of the experiments on the antibacterial activity of these compounds with aromatic rings condensed in position 5,6 *in vitro* and *in vivo* showed activity against various strains of *Escherchia coli*, *Colistridium pneumoniae* and *Salmonella typhi*. Both showed activity *in vivo* against tuberculosis produced in mice and guinea pigs (Jiu, *et al*. 2001).

Tetrahydro-1,3-oxazine derivatives have been used as analgesics, anticonvulsants and antipyretics (Poel, *et al*. 2002). Mono and dioxo-1,3-oxazine derivatives related to cyclic urethanes have been used as depressants of nervous system and sedatives (Jarrahpour, *et al*. 2004). 4-Oxo-2-thioxo-derivatives have been used as anticonvulsants and sleeping drugs. Dihydro-1,3-oxazines have been suggested as analgesics, sedatives, spasmolytics and fungicides (Ionescn and Mantsch. 1967). Both tetrahydro and dihydro-1,3-oxazine derivatives have been suggested as passive components of azodyes (Butenandt and Schafer. 1962).

Pyrimido[1,6]benzimidazol-1,3-oxazine derivatives have been screened for their antifungal activity and antibacterial activity, these compounds have been found to be highly active antimicrobial agents (Rattan, *et al*. 2009). Bis-benzoxazines exhibit various biological activities including antibacterial, antitumor, fungicidal and plant growth regulative properties (Alexander, *et al*. 1997). Benzo-1,3-oxazines are known to be biologically active as anti-malarial, anti-anginal, anti-hypertensive and potent anti-rheumatic agents (Damodiran, *et al*. 2009). Ramaiyan and Shanmugam. (2010), synthesized 6-alkylchloro-3-(4-(6-alkylchloro-2H-benzo[e][1,3]oxazine and tested for its *in vitro* antibacterial activity against some Gram positive (*Staphylococcus aureus* and *Bacillus subtilis*) and Gram negative (*Escherichia Coli, Klebsiella pneumonia* and *Pseudomonas aeruginosa*) bacteria. The compound showed significant activity *in vitro* against *E.coli* and do not show activity *in vitro* against the other tested organisms.

1.9Multicomponents reactions (MCRs)

Multicomponents reactions (MCRs) are those reactions in which three or more reactants come together in a single reaction vessel to form a new product which contains portions of all the components (Hulme and Gore. 2003). Multi-component reactions play an important role in combinatorial chemistry because of its ability to synthesize small drug-like molecules with several degrees of structural diversity. This reaction tool allows compounds to be synthesized in a few steps and usually in a one-pot operation (Xu, *et al*. 2004). Another typical benefit from these reactions is simplified purification, because all of the reagents are incorporated into the final product (Musonda, *et al*. 2004). Besides the usual multistep syntheses, an increasing number of organic chemical compounds are formed by multicomponent reactions, that convert more than two reactants directly into their products by one-pot reactions. In contrast to the multistep syntheses, the MCRs need minimal work, and they have often quantitative yields (Ivar, 2001).

The first multicomponent reactions were accomplished in 1838 when Laurent and Gerhardt formed the benzoylazotide from bitter almond oil and

ammonia via benzaldehyde, hydrogen cyanide (Laurent and Gerhardt. 1838). The chemistry of the MCRs officially began twelve years later, when Strecker introduced the general formation of α -aminocyanides from ammonia, carbonyl compounds, and hydrogen cyanide. The preparation of heterocyclic compounds by MCRs was introduced in the early 1880s (Böttinger, 1981). Since then, many named reactions of MCRs were developed. This ended in 1960, when Hellmann and Opitz 1960 demonstrated that all of these classical named reactions are α -aminoalkylations of nucleophiles, including the preparations of heterocyclic products by MCRs that are α -aminoalkylations and subsequent ring-forming reactions of further bifunctional reactants (Passerini, 1921).

Three types of multicomponent reactions are known. Type I MCRs are equilibrium between the reactants, intermediates, and final products, whereas Type II MCRs consist of equilibria between reactants and intermediates whose final product is in practice irreversibly formed. Type III MCRs are sequences of practically irreversible subreactions that proceed from the reactants to the products (Ivar, 1997).

Multicomponent reactions have recently emerged as valuable tools in the preparation of structurally diverse chemical libraries of drug-like heterocyclic compounds (Ugi, *et al*. 2000). The multicomponent reaction story began as far back as 1850 by the publication of the Strecker reaction. In view of the increasing interest for the preparation of large heterocyclic compound libraries, the development of new and synthetically valuable multicomponent reactions remains a challenge for both academic and industrial research teams (Bienaymé, *et al.* 2000). Although functionalized indole ring systems have been found frequently in biologically active molecules, indole derivatives as MCRs partners are rather under represented.

Aim and objectives

Study of the chemistry of the Betti bases started when Mario Betti reported that, synthesis of 1,3-diphenyl-2,3-dihydro-*1H*-naphth-[1,2-e][1,3]oxazine from condensation of 2-naphthol, benzaldehyde and methanolic ammonia. Acidic hydrolysis of the ring compound led to 1-(α-aminobenzyle)-2-naphthol (Betti base). This aminonaphthol became known in literature as the Betti base, and the protocol as the Betti reaction. The preparation of substituted Betti base derivatives by the modified Mannich reaction has subsequently become of considerable importance because a C – C bond is formed under mild experimental conditions. On the other hand, Betti base derivatives provide convenient access to many useful building blocks because the amino and the phenolic hydroxyl groups can be converted into a wide variety of derivatives.

The present study aims to synthesize some Betti base derivatives directly or via 1,3-naphthoxazines. The synthetic design of the required compounds could be established through the retrosynthetic analysis and the use of disconnection approach in these molecules.

The main aims of this study can be summarized shortly as:

a- Synthesis of certain designed Betti base derivatives directly or through 1,3-naphthoxazines approach.

b- Derivatization and functionalization of the resultant Betti bases with special emphasis upon the preparation of heterocyclic compounds.

c- Diazotization of the Betti base derivatives with specific reagents to prepare azo dyes.

d- Examination of the synthetic applicability of these compounds through simple ring – closure reactions.

e- Synthetic designing of the target molecules and their preparation based upon retrosynthetic analysis and disconnection approach and examination of the different synthetic pathway.

f- Analysis of the synthesized compounds using spectroscopic techniques.

g- Testing some of the synthesized compounds for possible biological activities as racemic and non-racemic structures if possible.

Chapter two

2. Materials and methods

2.1 Materials

2.1.1 Chemicals

Diethylamine, ethylamine, hydrochloric, methylamine, N,N-dimethylamino benzaldehyde, propylamine, pyrrolidine, sodium nitrite, sulfonilamide, 4,4-dinitrobenzaldehyde and β-naphthol and *o*-nitrobenzaldehyde were all obtained from CDH Laboratories reagent, India. Ammonia solution, anisaldehyde, benzaldehyde, butylamine, cinmalaldehyde, salycialdehyde and sodium sulphate were all obtained from LOBA cheme Pvt. Ltd, India. Aniline was obtained from Riedel – deHaën Germany. *p* - aminoacetophenone, assay reagent was obtained from Blulux Laboratories (P), Ltd, India. Sodium hydroxide analytical grade was obtained from Nice Laboratory reagent India.

2.1.2 Solvents

Acetone, chloroform, ethanol (absolute) and methanol (absolute), all analytical grade, were obtained from LOBA Cheme Pvt. Ltd, India. Ethyl acetate analytical grade was obtained from Romil LTD, UK.

2.1.3 Thin Layer Chromatography (TLC)

Thin layer chromatography was carried out using precoated plate with silica gel GF_{254} for TLC LR, s.d-fine Cheme Limited India (stationary phase) and different types of mobile phase with different solvents, in different ratios, were used (table 2.6).

2.1.4 Ultra Violet Spectroscopy (UV)

UV spectra were recorded on a UV – VIS 1800 spectrophotometer, double beam wavelength 190 – 1100 nm. Shimadzu, Japan,

2.1.5 Infrared Spectroscopy (IR)

Infrared spectra were recorded on FT-IR spectrophotometer, 1000 (USA) Perkin Elmer (USA) as KBr disc (table 2.3).

2.1.6 Nuclear Magnetic Resonance (NMR) spectrophotometry

^{1}H-NMR spectra was recorded on Ultrashield-500 plus instrument (BRUKER, Germany – 500MHz) spectrometers using DMSO as a solvent (table 2.4).

2.2.7 Mass spectroscopy (MS)

The mass spectral instrument used in this work is ISQ Single Quadrupole MS, Germany (table 2.5).

2.2.8 Gas chromatography – mass spectroscopy (GC-MS)

Gas chromatography – mass spectroscopy (GC-MS) was recorded on QP 2010 GC instrument (Shimadzu, Japan).

2.1.9 Melting Point

Melting points were determined using melting point apparatus from bibby sterilin, UK.

2.1.10 General equipment

* All glass ware of Pyrex type.
* Electronic balance A & D – GR – 120, Japan
* Fume cupboard FCI 80 from technological laboratory furniture manufacturer (LABTIC). Ltd, USA.
* Magnetic hotplate stirrer R000100726 from bibby sterilin LTD, UK.
* Water bath R000102811 from bibby sterilin LTD, UK.

2. 2 Methods

2.2.1 General procedure for the synthesis of 1,3oxazines (I – XIV)

In a 25 ml round bottom flask equipped with air condenser were placed the following: A solution of β- naphthol (1 mmol) in absolute methanol (0.5ml), 2mmol of the aryl- or heteroaryl aldehyde and 25 % methanolic ammonia solution (0.5 ml). The mixture was left to stand at ambient temperature for 2 days, during which the crystalline products were separated out. The crude crystals were filtered off, washed with cold methanol (2 x 2mL) and purified by recrystallization (scheme 2.1).

1,3-Diphenyl-nitroaniline -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine I

White colour; yield 64% (0.267g); m.p 157 – 159° C; recrystallized ethyl acetate; IR (cm^{-1}) 3050, 2830, 1600, 1375, 1200; ^{1}H-NMR (DMSO): δ (ppm) = 6.86-6.89 (m,12H, Ar-H), 6.94-7.17 (m,15H, Ar-H), 2.83 (s, 1H, CH), 4.00 (s, 1H, CH); MS: 413: (m/z): 77, 91, 231, 315, 393, 413.

1,3-Di-4,4-dimethoxy phenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine II

Brown colour; yield 77% (0.133 g); m.p 121 – 123° C ; recrystallized ethyl acetate; UV, ethanol λ_{max} (nm) 242: IR (cm^{-1}) 3300, 3050, 2860, 1554, 1450, 1250, 1170; ^{1}H-NMR (DMSO): δ (ppm) = 7.18-7.65 (m,6H, Ar-H), 7.71-8.19 (m,8H, Ar-H), 1.97 (s,1H, NH), 3.85 (d, 6H, OCH_3), 3.97 (s,1H, CH), 4,34 (s, 1H, CH); MS: 397: (m/z): 77, 91, 150, 231, 315, 397.

1,3-Di-2-nitrophenyl-3-nitrophenyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3] oxazine III

Yellow colour; yield 58% (0.25 g); m.p 158 – 162° C ; recrystallized ethyl acetate; IR (cm^{-1}) 3050, 2900, 1500, 1430, 1210, 1550, 1350; MS: 548: (m/z): 102, 135, 262, 429, 540.

1,3-Di-4-methoxyphenyl-3-nitrophenyl-2,3-dihydro-1*H*-naphtho[1,2-e] [1,3]oxazine IV

Yellow colour; yield 54% (0.30 g); m.p 121 – 123° C ; recrystallized ethyl acetate; IR (cm^{-1}) 3050, 3000, 1480, 1375, 1170, 1120; ^{1}H-NMR (DMSO): δ (ppm) = 7.34 – 7.53 (m, 6H, Ar-H), 7.79-7.91 (m,10H, Ar-H), 3.71 (s, 6H, OCH_3), 2.61 (s, 1H, CH), 4.45 (s, 1H, CH).

1,3-Dihydroxyphenyl-3-nitrophenyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3] oxazine V

Yellow colour; yield 61% (0.32 g); m.p 134 – 136° C ; recrystallized ethyl acetate; IR (cm^{-1}) 3200, 3050, 2860, 1600, 1440, 1200, 1350.

1,3-Diphenyl-2-propyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine VI

White colour; yield 78% (0.324 g); m.p 135 – 137° C; recrystallized ethyl acetate; IR (cm^{-1}) 2940, 3050, 1450, 1220; ^{1}H-NMR (DMSO): δ (ppm) = 2.53 (s,

7H, C_3H_7), 5.71 (s, H, CH), 2.51 (s, 1H, CH), 7.26 – 7.61 (m, 16H, Ar – H); MS: 397: (m/z): 94, 121, 232, 248, 315, 395.

1,3-Di-*o*-hydroxyphenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine VII

Bright yellow colour; yield 54% (0.219g); m.p 147 – 149° C (lit 160 – 161 °C); recrystallized ethyl acetate; IR (cm^{-1}) 3300, 3050, 2820, 1554, 1380, 3250, 850; ^{1}H-NMR (DMSO): δ (ppm) = 6.64 – 6.91 (m, 6H, Ar-H), 7.06 – 7.78 (m, 8H, Ar-H), 2.01 (s, 1H, NH), 2.56 (s,1H, CH), 4.06 (s, 1H, CH), 8.80 (s, 2H, OH); MS; 369: m/z: 94, 121, 221, 279, 370.

1,3-Di-*o*-nitrophenyl-2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine VIII

Light brown colour; yield 79% (0.138 g); m.p 123 – 125° C (lit 200 – 201 °C); recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 273; IR (cm^{-1}) 3300, 3050, 2920, 1554, 1370, 1171, 1550, 1340; ^{1}H-NMR (DMSO): δ (ppm) = 2.51 (s, 1H, NH), 2.60 (s, 1H, CH), 4.86 (s, 1H, CH), 7.34 – 8.51 (m, 14, Ar – H); MS:427: (m/z): 78, 151, 178, 244, 322, 422.

1,3-Di-phenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine IX

Light orange crystals; yield 81% (0.46 g); m.p 135 – 137°C (lit 134 – 137 °C); recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 228; IR (cm^{-1}) 3319, 3050, 2850, 1598, 1440, 1210,1236; ^{1}H-NMR (DMSO): δ (ppm) = 7.26 – 7.52 (m, 6H, Ar-H), 7.50 – 7.87 (m, 10H, Ar-H), 2.51 (s, 1H, NH), 4.51 (s, H, CH), 5.56 (s, 1H, CH); MS: 337: m\z 148, 203, 263, 291, 320.

1,3-N,N-dimethylaniline -2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine X

Yellow colour; yield 79% (0.35 g); m.p 123 – 127° C ; recrystallized ethyl acetate; IR (cm^{-1}) 3340, 3050, 2900, 1600, 1375, 1195, 1216.

1,3-Di-*o*-hydroxyphenyl-2-benzenesulfonamide -1*H*-naphtho[1,2-e][1,3] oxazine XI

Yellow colour; yield 81% (0.46 g); m.p 161 – 163° C ; recrystallized ethyl acetate; IR (cm^{-1}) 3300, 3050, 2810, 1550, 1450, 1150, 1250, 3400, 1350, 1150.

1,3-distyryl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine XII

Grey colour; yield 77% (0.34 g); m.p 190 – 192° C; recrystallized ethyl acetate; IR (cm^{-1}) 3310, 3050, 2860, 1460, 1440, 1200; ^{1}H-NMR (DMSO): δ (ppm) =7.03

– 7.48 (m, 6H, Ar-H), 7.63 – 7.82 (m, 12H, Ar-H), 2.49 (s, 2H, NH_2), 4.10 (s, 1H, CH), 2.84 (s, 1H, CH); MS: 389: m/z: 270, 297, 370, 391.

1,3-Di-4-methoxyphenyl-2-benzenesulfonamide -1*H*-naphtho[1,2-e][1,3] oxazine XIII

Brown colour; yield 91% (0.54 g); m.p 147 – 150° C ; recrystallized ethyl acetate; IR (cm^{-1}) 3300, 3050, 2900, 1550, 1375, 1195,1150, 1173; ^{1}H-NMR (DMSO): δ (ppm) = 6.18 – 6.95 (m, 6H, Ar-H), 7.19 - 7.52 (m, 8H, Ar-H), 2.49 (s, 2H, NH_2), 4.68 (s, 2H, CH), 2.86 (s, 1H, CH), 3.88 (s, 6H, OCH_3).

1,3-Di-*o*-nitrophenyl-2-benzenesulfonamide-1*H*-naphtho[1,2-e][1,3]oxazine XIV

Yellow colour; yield 70% (0.33 g); m.p 118 – 120°C ; recrystallized ethyl acetate; IR (cm^{-1}) 3310, 3050, 2840, 1600, 1370, 1178,1350, 1150, 1550, 1340; ^{1}H-NMR (DMSO): δ (ppm) = 7.00 – 7.47 (m, 6H, Ar-H), 7.61 – 7.90 (m, 12H, Ar-H), 2.85 (s, 2H, NH_2), 4.49(s, 2H, CH), 4.34 (s, 1H, CH).

2.2.2 General procedure for the synthesis of 1-[α-aminosubstituted benzyl]-2-naphthols (method 1) (XV – XXVII)

In a 25 ml round bottom flask equipped with a reflux condenser and mounted over a hot plate magnetic stirrer were placed the following. 1 m mol of compounds (I - XIV) were suspended in 20 % HCl (20 ml) and the mixture was stirred under reflux for 6 hours, whereby the crystalline hydrochloride salt of compounds **(**I – XIV) separated out and was filtered off and washed with ethyl acetate. The hydrochloride salt was suspended in water and the mixture was treated with concentrated ammonia solution (3 ml) and extracted with ethyl acetate (3 x 5mL). After drying by sodium sulphate and evaporation of the ethyl acetate phase, crude crystalline compounds (XV – XXVII) were obtained, purified by recrystallization (scheme 2.2).

1-(α-phenyl-phenylamino)-2-naphthol XV

Brown colour; yield 90% (0.32 g); m.p 123 – 127°C (lit 124 – 125); recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 229; IR (cm^{-1}) 3310, 3400, 3050, 2800, 1550, 1440, 1050; ^{1}H-NMR (DMSO): δ (ppm) = 7.19 – 7.51 (m, 6H,

Ar-H), 7.69 – 7.95 (m, 5H, Ar-H), 7.69 – 7.95 (m, 5H, Ar-H), 2.51 (s, 1H, NH), 4.01 (s, 1H, CH), 9.75 (s,1H, OH); MS 325: (m/z): 98, 120, 142, 156, 233, 328.

1-[α-amino-4-methoxybenzyl]-2-naphthol XVI

Dark yellow colour; yield 65% (0.18 g); m.p 123 – 125°C; recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 230; IR (cm^{-1}) 3300, 3400, 3050, 2840, 1460, 1370, 1100; ^{1}H-NMR (DMSO): δ (ppm) = 6.92 – 7.40 (m, 6H, Ar-H), 7.72 – 7.78 (m, 4H, Ar-H), 2.08 (s, 2H, NH_2), 3.69 (s, 6H, OCH_3), 3.31 (s, 1H, CH), 9.75 (d, 1H, OH) J = 2.3 Hz.

1-(α-amino-*m*-nitrophenyl-4-nitrobenzyl)-2-naphthol XVII

Brown colour; yield 66% (0.35 g); m.p 192 – 195° C; recrystallized ethyl acetate; IR (cm^{-1}) 3300, 3250, 3050, 2900, 1600, 1375, 1350, 1550.

1-(α-amino-4-methoxyphenyl-4-nitrobenzyl)-2-naphthol XVIII

Dark yellow colour; yield 43% (0.22 g); m.p 173 – 176°C; recrystallized ethyl acetate; IR (cm^{-1}) 3340, 3400, 3050, 2870. 1500, 1450, 1150, 1350; MS: 400: m/z: 98, 129, 232, 286, 401.

1-(α-amino-2-hydroxyphenyl-4-nitrobenzyl)-2-naphthol XIX

Brown colour; yield 63% (0.34 g); m.p 210 – 215°C; recrystallized ethyl acetate; IR (cm^{-1}) 3290 , 3400 , 3050, 2860, 1597, 1430, 1550; MS:386: m/z: 74, 102, 121,136, 233, 257, 318, 381.

1-[α-*N*-propylaminobenzyl]-2-naphthol XX

White colour; yield 67% (0.253 g); m.p 163 – 165°C (lit 165 – 166, 164 – 166); recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 241, IR (cm^{-1}) 3300, 3200, 3050, 2780, 1460, 1375, 1240; ^{1}H-NMR (DMSO): δ (ppm) = 7.81 – 8.00 (m, 6H, Ar-H), 7.30 – 7.50 (m, 5H, Ar-H, 2.20 (s, 7H C_3H_7), 2.54 (s, 1H, NH), 5.05 (s, 1H, CH) 2.85 (s,1H,CH); MS: 29: m/z: 107, 136, 155, 172, 262, 290.

1-[α-amino-*o*-hydroxybenzyl)]-2-naphthol XXI

Yellow colour; yield 70% (0.185 g); m.p 152 – 154°C (lit 147–148 °C); recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 231, 174; IR (cm^{-1}) 3314, 3270, 3050, 2880, 1517, 1375; ^{1}H-NMR (DMSO): δ (ppm) = 6.72 – 6.88 (m, 6H,

Ar-H), 7.19 – 7.87 (m, 4H, Ar-H), 2.51 (s,2H, NH_2), 4.04 (s, 1H, CH), 8.81 (s, 2H, OH); MS: 265: m/z: 108, 135, 230, 244, 263.

1-[α-amino-*o*-nitrobenzyl)]-2-naphthol XXII

Brown colour; yield 63% (0.27 g); m.p 207 – 209°C (lit 200 – 202 °C); recrystallized ethyl acetate; IR (cm^{-1}) 3320, 3400, 3050, 2900, 1600, 1440, 1550, 1350; ^{1}H-NMR (DMSO): δ (ppm) = 7.36 – 7.65 (m, 6H, Ar-H), 7.81 – 7.96 (m, 4H, Ar-H), 2.08 (s, 2H, NH_2), 4.74 (s, 1H, CH), 8.05 (s, 1H, OH).

1-[α-aminobenzyl]-2-naphthol XXIII

White colour; yield 88% (0.31 g); m.p 118 – 120 °C (lit 124 – 125 °C); recrystallized ethyl; UV, ethanol, λ_{max} (nm) 230, 274; IR (cm^{-1}) 3300, 3260, 3050, 2870, 1514, 1460; H^1-NMR (DMSO): δ (ppm) = 7.72 – 7.75 (m, 6H, Ar-H), 6.81 – 7.40 (m, 5H, Ar-H), 2.10 (s,2H, NH_2), 4.31 (s, 1H, CH), 9.70 (s, 1H, OH).

1-(α-amino-4-dimethylaminobenzylyl)-2-naphthol XXIV

Yellow colour; yield 54% (0.23 g); m.p 113 – 115°C; recrystallized ethyl acetate; IR (cm^{-1}) 3305, 3200, 3050, 2830, 1550, 1372; MS: 292: m/z: 73, 107, 172, 263, 290.

3-(α-amino-2-hydroxybenzyl-benzenesulfonamide)-2-naphthol XXV

Yellow colour; yield 76% (0.32 g); m.p 193 – 197°C; recrystallized ethyl acetate; IR (cm^{-1}) 3300, 3250, 3050, 2890, 1550, 1375, 1350, 1155; H^1-NMR (DMSO): δ (ppm) = 7.42 – 7.70 (m, 6H, Ar-H), 6.81 – 7.00 (m, 5H, Ar-H), 2.10 (s,2H, NH_2), 3.87 (s, 1H, CH), 8.60 (s, 1H, OH).

3-(α-amino-4-methoxybenzyl-benzenesulfonamide)-2-naphthol XXVI

Brown colour; yield 63% (0.27 g); m.p 183– 187°C; recrystallized ethyl acetate; IR (cm^{-1}) 3300, 3250, 3050, 2800, 1600, 1375, 1350, 1150; MS: 434: m/z: 91, 107, 155, 182, 260, 288, 330, 358, 432.

3-(α-amino-2-nitrobenzyl-benzenesulfonamide)-2-naphthol XXVII

Black colour; yield 61% (0.28 g); m.p 172 – 174°C; recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 239; IR (cm^{-1}) 3350, 3200 , 3050, 2850, 1460, 1375, 1350, 1150, 1110; MS: 449: m/z: 98, 170, 241, 276, 366, 452.

2.2.3 General procedure for the synthesis of 1-(α aminosubstituted benzyl)-2-naphthol (method 2) (XV, XX, XXIII and XXVIII – XXXI)

In a 25 ml round bottom flask equipped with air condenser were placed the following.1.44 g (10 mmol) of β-naphthol in 15 ml water, 10 mmol of aromatic aldehyde and 10 mmol of the required amine were added. The reaction mixture was stirred at ambient temperature for one hour. Water was then decanted, and the precipitated product was separated upon addition of 10 ml of ethanol to the mixture with stirring, while cooling at 0-5^{o}C. The precipitate was filtered, washed with cold ethanol, dried, and purified by recrystallization from ethanol (scheme 2.3).

1-(α-phenyl-phenylamino)-2-naphthol XV

Brown colour; yield 90% (0.32 g); m.p 123 – 127°C (lit 124 – 125); recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 229; IR (cm^{-1}) 3310, 3400, 3050, 2800, 1550, 1440, 1050; ^{1}H-NMR (DMSO): δ (ppm) = 7.19 – 7.51 (m, 6H, Ar-H), 7.69 – 7.95 (m, 5H, Ar-H), 7.69 – 7.95 (m, 5H, Ar-H), 2.51 (s, 1H, NH), 4.01 (s, 1H, CH), 9.75 (s,1H, OH); MS 325: (m/z): 98, 120, 142, 156, 233, 328.

1-(α-propylaminobenzyl)-2-naphthol XX

White colour; yield 67% (0.253 g); m.p 163 – 165°C (lit 165 – 166, 164 – 166); recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 241, IR (cm^{-1}) 3300, 3200, 3050, 2780, 1460, 1375, 1240; ^{1}H-NMR (DMSO): δ (ppm) = 7.81 – 8.00 (m, 6H, Ar-H), 7.30 – 7.50 (m, 5H, Ar-H, 2.20 (s, 7H, C_3H_7), 2.54 (s, 1H, NH), 5.05 (s, 1H, CH) 2.85 (s,1H,CH); MS: 29: m/z: 107, 136, 155, 172, 262, 290.

1-[α-aminobenzyl]-2-naphthol XXIII

White colour; yield 88% (0.31 g); m.p 118 – 120 °C (lit 124 – 125 °C); recrystallized ethyl; UV, ethanol, λ_{max} (nm) 230, 274; IR (cm^{-1}) 3300, 3260, 3050, 2870, 1514, 1460; ^{1}H-NMR (DMSO): δ (ppm) = 7.72 – 7.75 (m, 6H, Ar-H), 6.81 – 7.40 (m, 5H, Ar-H), 2.10 (s,2H, NH_2), 4.53 (s, 1H, CH), 9.70 (s, 1H, OH).

1-(α-methylaminophenyl)-2-naphthol XXVIII

Orange; yield 77% (0.30 g); m.p 113 – 115°C; recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 227, 274; IR (cm^{-1}) 3300, 3265, 3050, 1629, 2900, 1583,

1350; ^{1}H-NMR (DMSO) δ (ppm) = 6.14 – 7.02 (m, 6H, Ar-H), 7.14 – 7.40 (m, 5H, Ar-H), 2.08 (s, 3H, CH_3), 2.51 (s, 1H, NH), 5.72 (s, 1H, CH), 9.67 (s, 1H, OH).

1-(α-diethylaminophenyl)-2-naphthol XXIX

Brown; yield 43% (0.19 g); m.p 118 – 120°C (lit 123 – 124); recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 230, 274; IR (cm^{-1}) 3264, 3050, 2870, 1584, 1380, 1270; ^{1}H-NMR (DMSO): δ (ppm) = 7.67 – 7.77 (m, 6H, Ar-H), 7.09 – 7.40 (m, 5H, Ar-H), 3.42 (s, 10H, diethyl), 2.71 (s, 1H, CH), 9.78 (s, 1H, OH); MS: 305: m/z: 96, 120, 156, 191, 205, 233, 306.

1-(α-phenylpyrrolidine)-2-naphthol XXX

brown; yield 19% (0.37 g); m.p 97 – 99°C; recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 239; IR (cm^{-1}) 3200 – 3385, 3050, 2860, 1600, 1440, 1237; MS: 303: m/z: 94, 126, 191, 215, 233, 303.

1-(α-butylaminophenyl)-2-naphthol XXXI

Light pink, yield 92% (0.39 g); m.p 131 – 133°C; recrystallized ethyl acetate; UV, ethanol, λ_{max} (nm) 244; IR (cm^{-1}) 3314, 3200, 3050, 2861, 1622, 1375; ^{1}H-NMR (DMSO): δ (ppm) = 7.67 – 7.92 (m, 6H, Ar-H), 7.06 – 7.54 (m, 11H, Ar-H), 5.93 (s, 1H, CH), 2.5 (d, 1H, NH) J = 3.83 Hz, 2.08 (s, 9H, C_4H_9), 9.80 (s, 1H, OH); MS: 305: (m/z) 91, 144, 215, 233, 300.

2.2.4 General procedure for synthesis of azo dyes (XXXII – XXXX)

In 100 ml conical flask 0.01 mol of Betti base derivatives (II**,** VII**,** XX**,** XXVIII**,** XXIX and XXXI) dissolved in 30 ml sodium hydroxide solution (10%). The mixture was stirred until complete dissolution. The solution was cooled with an ice-water bath.

The benzenediazonium salt was prepared by dissolved 0.01 mol (0.7 g) of sodium nitrite in 5 ml water. 0.011 mol (1.89 g) of sulfanilamide or (0.14 g) of *p*-aminoacetophenone in 45 ml water, 12 ml of concentrated hydrochloric acid was added slowly and the mixture was stirred until sulfanilamide *p*-aminoaceto phenone dissolved completely. The solution cooled in an ice-water bath to 0°C, and then sodium nitrite solution was added slowly by a dropper. The mixture

well-stirred during the addition, when the addition was complete the mixture was stirred for another 2 – 3 minutes. The benzenediazonium salt was added slowly to the Betti base solution during which the mixture was stirred efficiently and cooled in an ice-water bath, the addition takes about 5 minutes (colour forms). When the addition was completed, the mixture was stirred at 0°C for 5 – 10 minutes to ensure the reaction goes to completion. The mixture was filtered by suction filtration, the solid product on the Büchner funnel was washed with a small amount of water. The product dried for 2 days and weighted (scheme 2.4).

1-(4-((4-(amino(2-hydroxyphenyl)methyl)-3-hydroxynaphthalen-2-ol) diazenyl)phenyl) ethanone XXXII

Red break colour yield 80% (0.38 g), m.p 143 – 146°C; recrystallized ethanol; IR, (cm^{-1}) 3381, 3250, 3050, 1580, 1440, 2850, 1689; ^{1}H-NMR (DMSO): δ (ppm) = 7.57 – 7.98 (m, 5H, Ar-H), 6.63–7.01(m, 5H, Ar-H), 7.34– 8.17(m, 4H, Ar-H), 2.48 (s, 2H, NH_2), 8.45 (s, 1H, OH), 5.32 (s,1H, CH), 3.63 (s, 3H, CH_3).

1-(4-((4-(amino(4-methoxyphenyl)methyl)-3-hydroxynaphthalen-2-ol) diazenyl)phenyl) ethanone XXXIII

Orange colour yield 61% (0.26 g), m.p 173 – 176°C; recrystallized ethanol; IR (cm^{-1}) 3300, 3200, 3050, 1550, 1380, 2900, 1661; MS: 411: m/z: 94, 126, 209, 287, 342, 411.

1-(4-((4-((butylamino)(phenyl)methyl)-3-hydroxynaphthalen-2-ol) diazenyl) phenyl)ethanone XXXIV

Red colour yield 92% (0.38 g), m.p 210 – 215°C; recrystallized ethanol; IR (cm^{-1}) 3410, 3270, 3050, 1550, 1440, 2850, 1675; ^{1}H-NMR (DMSO): δ (ppm) = 7.04 –7.36(m, 5H, Ar-H), 6.62–7.00 (m, 5H, Ar-H), 7.73–8.05 (m, 4H, Ar-H), 2.49 (s, 1H, NH), 3.68 (s, 9H C_4H_9), 5.52 (s, 1H, CH), 8.89 (s, 1H OH), 3.84 (t, 3H, CH_3); MS: 451: m/z: 76, 123, 198, 286, 348, 447.

4-((3-hydroxy-4-(phenyl(propylamino)methyl)naphthalen-2-ol)diazenyl) benzenesulfonamide XXXV

Yellow colour yield 78% (0.37 g), m.p 145 – 147°C; recrystallized ethanol; IR (cm^{-1}) 3320, 3210, 3050, 1550, 1440, 2830, 1550, 1350.

4-((4-(amino(4-methoxyphenyl)methyl)-3-hydroxynaphthalen-2-ol) diazenyl) benzene sulfonamide XXXVI

Light orange colour yield 72% (0.33 g), m.p 154 – 157°C; recrystallized ethanol; IR (cm^{-1}) 3300, 3200, 3050, 1600, 1375, 2920, 1550, 1350, 1100; ^{1}H-NMR (DMSO): δ (ppm) = 7.53 – 7.61 (m, 5H, Ar-H), 7.38–7.45 (m, 4H, Ar-H), 7.83–7.94 (m, 4H, Ar-H), 2.36 (s, 2H, NH_2), 4.53 (s, 1H, CH), 3.86 (s, 3H, OCH_3), 9.73 (s, 1H, OH); MS: 462: m/z: 94, 121, 221, 249, 370,432, 452.

4-((4-((butylamino)(phenyl)methyl)-3-hydroxynaphthalen-2-ol)diazenyl) benzenesulfonamide XXXVII

Orange colour yield 86% (0.42 g), m.p 189 – 191°C; recrystallized ethanol; IR (cm^{-1}) 3397, 3200, 3050, 1460, 1440, 1150, 1350; ^{1}H-NMR (DMSO): δ (ppm) = 7.21 – 7.67 (m, 5H, Ar-H), 7.03 – 7.10 (m, 5H, Ar-H), 7.83 – 8.13 (m, 4H, Ar-H), 2.43 (s, 1H NH), 3.27 (s, 2H, NH_2), 4.30 (s, 9H, C_4H_9), 5.21 (s, 1H, CH), 8.61 (s, 1H, OH); MS: 446: m/z: 102, 242, 287, 396, 437.

4-((3-hydroxy-4-((methylamino)(phenyl)methyl)naphthalen-2-ol)diazenyl) benzene sulfonamide XXXVIII

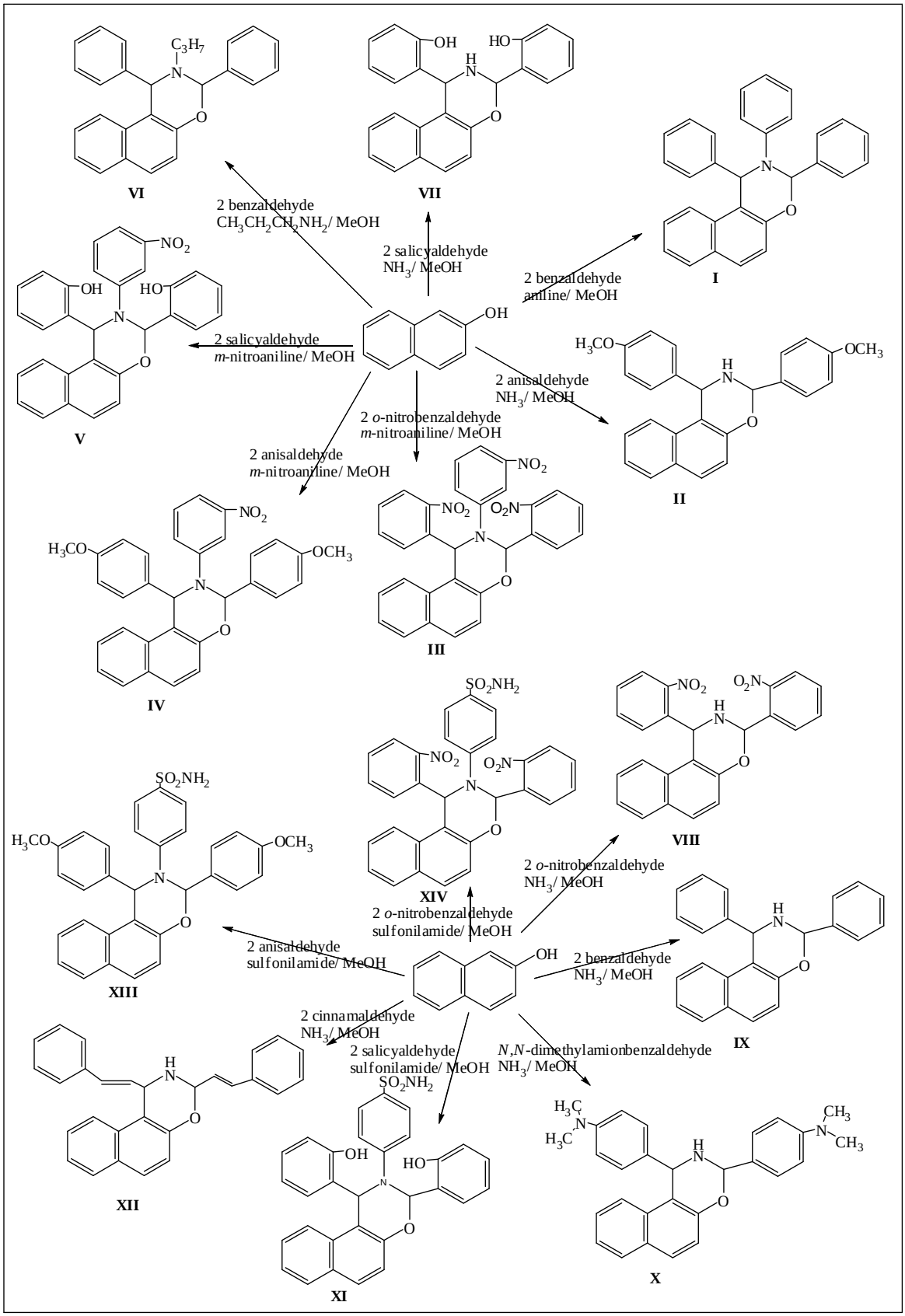
Orange colour yield 82% (0.37 g), m.p 202 – 205°C; recrystallized ethanol; IR (cm^{-1}) 3306, 3285, 3050, 1550, 1450, 2925, 1550, 1150; ^{1}H-NMR (DMSO): δ (ppm) = 6.45 – 7.12 (m, 5H, Ar-H), 7.23 – 7.49 (m, 5H, Ar-H), 7.63 – 8.00 (m, 4H, Ar-H), 2.51 (s, 1H, NH), 4.13 (s, 2H, NH_2), 3.78 (s, 3H, CH_3), 4.24 (s, 1H, CH), 8.01 (s, 1H OH).

4-((4-((diethylamino)(phenyl)methyl)-3-hydroxynaphthalen-2-ol)diazenyl) benzene sulfonamide XXXIX

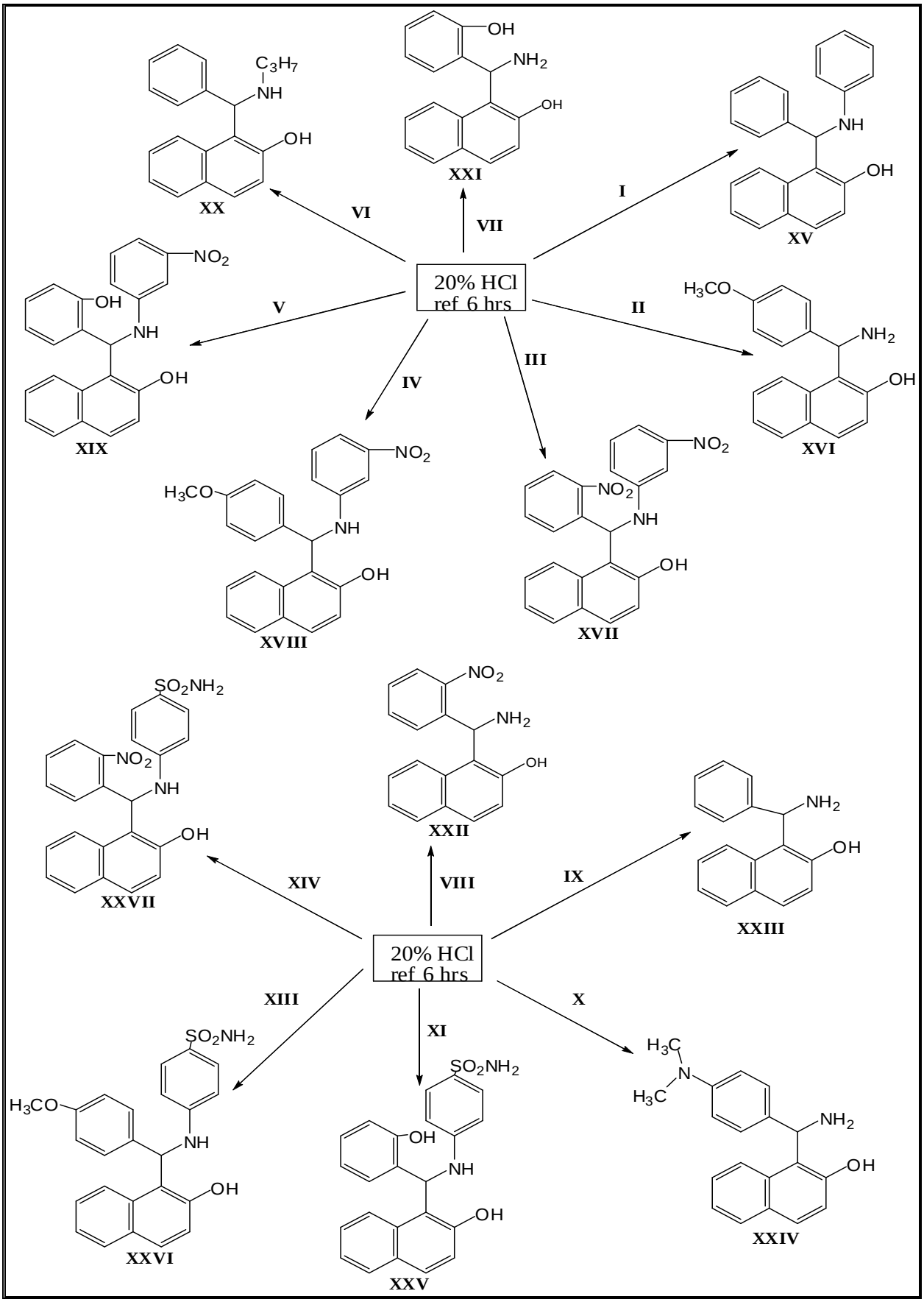
Brown colour yield 64% (0.36 g), m.p 210 – 212°C; recrystallized ethanol; IR (cm^{-1}) 3300, 3207, 3050, 1550, 1360, 2850, 1150, 1350.

4-((4-(amino(2-hydroxyphenyl)methyl)-3-hydroxynaphthalen-2-ol)diazenyl) benzene sulfonamide XXXX

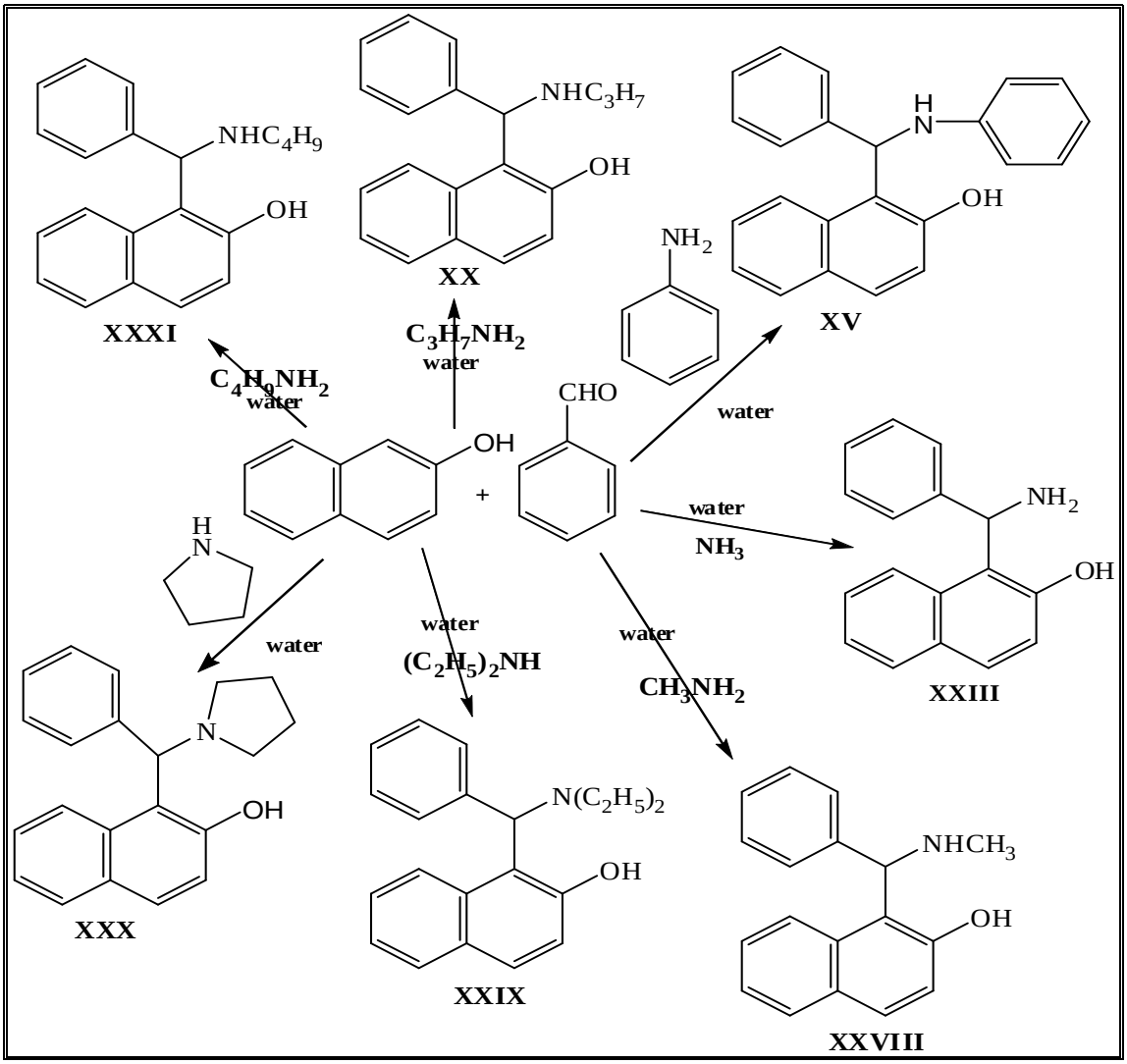
Orange colour yield 54% (0.27 g), m.p 162 – 164°C; recrystallized ethanol; IR (cm^{-1}) 3308, 3200, 3050, 1600, 1375, 2890, 1140, 1350.



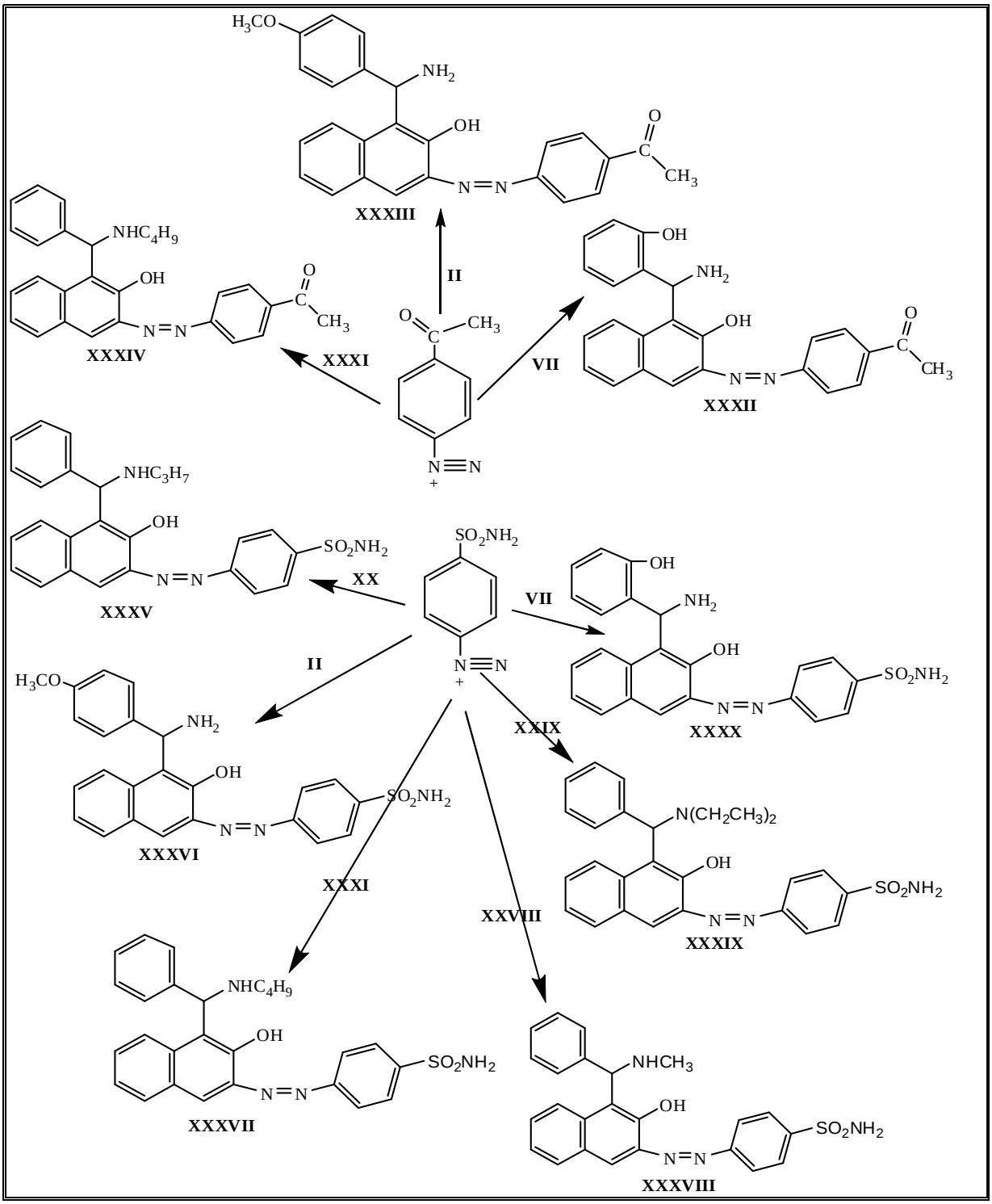
Scheme (2.1): Synthesis of 1,3-naphthoxazines derivatives



Scheme (2.2): Synthesis of derivatives of Betti bases via 1,3-naphthoxazine



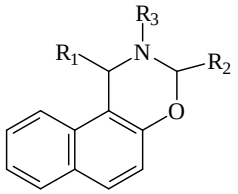
Scheme (2.3): Synthesis of Betti bases (method two)

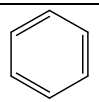
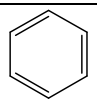
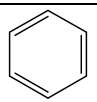
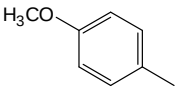
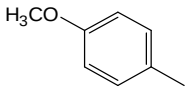
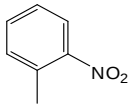
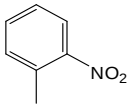
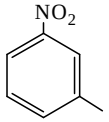
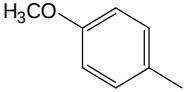
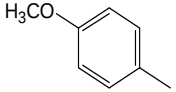
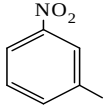
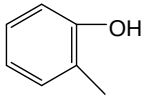
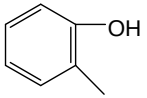
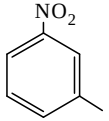


Scheme (2.4): Synthesis of azo dyes from Betti base derivatives

Table. 2.1. Chemical names of some synthesized compounds

Table. 2.1.1. Chemical names of 1,3-oxazines derivatives



Compd No	R_1	R_2	R_3	Name
I				1,3-Diphenyl-nitroaniline -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine
II			H	1,3-Di-4,4-dimethoxy phenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine
III				1,3-Di-2-nitrophenyl-3-nitrophenyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3] oxazine
IV				1,3-Di-4-methoxyphenyl-3-nitrophenyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine
V				1,3-Dihydroxyphenyl-3-nitrophenyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine

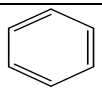
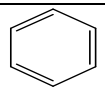
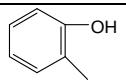
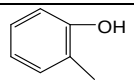
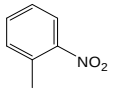
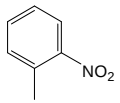
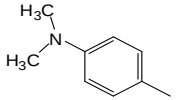
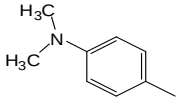
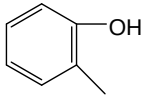
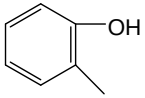
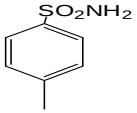
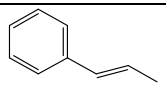
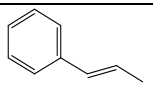
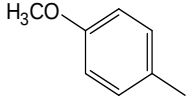
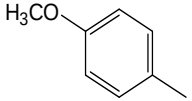
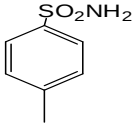
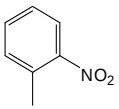
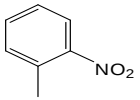
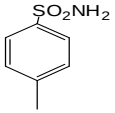
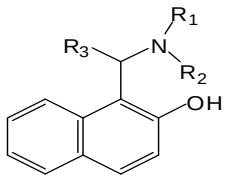
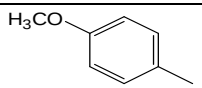
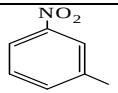
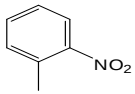
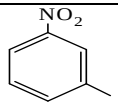
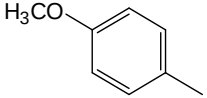
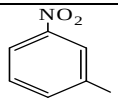
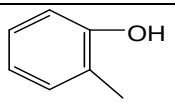
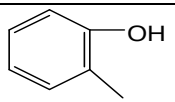
VI			C_3H_7	1,3-diphenyl-2-propyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine
VII			H	1,3-Di-*o*-hydroxyphenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine
VIII			H	1,3-Di-*o*-nitrophenyl-2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine
IX			H	1,3-diphenyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine
X			H	1,3-N,N-dimethylaniline- 2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine
XI				1,3-Di-*o*-hydroxyphenyl-2-benzenesulfonamide -1*H*-naphtho[1,2-e][1, 3]oxazine
XII			H	1,3-distyryl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine
XIII				1,3-Di-4-methoxyphenyl-2-benzenesulfonamide -1*H*-naphtho[1,2-e][1, 3]oxazine
XIV				1,3-Di-*o*-nitrophenyl-2-benzenesulfonamide-1*H*-naphtho[1,2-e][1,3] oxazine

Table. 2.1.2. Chemical names of the Betti base derivatives



Compd No	R_1	R_2	R_3	Name
XV		H		1-(α-phenyl-aminobenzyl)-2-naphthol
XVI	H	H		1-[α-amino-4-methoxybenzyl]-2-naphthol
XVII		H		1-(α-amin-*m*-onitrophenyl-4-nitrobenzyl)-2-naphthol
XVIII		H		1-(α-amino-4-methoxyphenyl-4-nitrobenzyl)-2-naphthol
XIX		H		1-(α-amino-2-hydroxyphenyl-4-nitrobenzyl)-2-naphthol
XX	C_3H_7	H		1-[α-*N*-propylaminobenzyl]-2-naphthol
XXI	H	H		1-[α-amino-*o*-hydroxybenzyl)]-2-naphthol

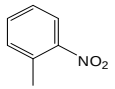
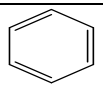
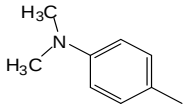
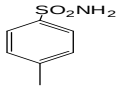
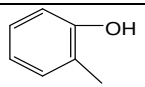
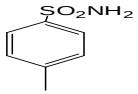
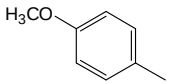
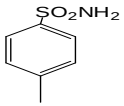
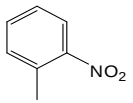
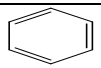
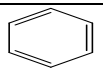
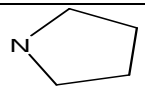
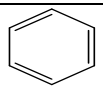
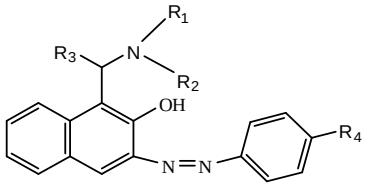
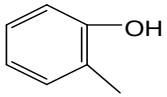
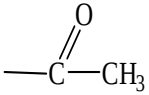
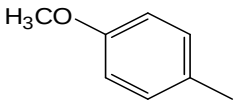
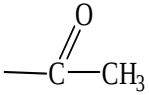
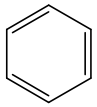
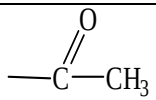
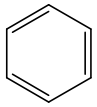
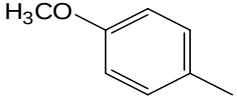
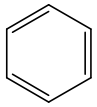
XXII	H	H		1-[α-amino-o-nitrobenzyl)]-2-naphthol
XXIII	H	H		1-[α-aminobenzyl]-2-naphthol
XXIV	H	H		1-(α-amino-4-dimethylaminobenzylyl)-2-naphthol
XXV		H		3-(α-amino-2-hydroxybenzyl-benzenesulfonamide)-2-naphthol
XXVI		H		3-(α-amino-4-methoxybenzyl-benzenesulfonamide)-2-naphthol
XXVII		H		3-(α-amino-2-nitrobenzyl-benzenesulfonamide)-2-naphthol
XXVIII	CH_3	H		1-(α-methylaminobenzyl)-2-naphthol
XXIX	C_2H_5	C_2H_5		1-(α-diethylaminobenzylyl)-2-naphthol
XXX		-		1-(α-benzylpyrrolidine)-2-naphthol
XXXI	C_4H_9	H		1-(α-butylaminobenzyl)-2-naphthol

Table. 2.1.3. Chemical names of azo dyes



Compd No	R_1	R_2	R_3	R_4	Name
XXXII	H	H			1-(4-((4-(amino(2-hydroxyphenyl)methyl)-3-hydroxynaphthalen-2-ol) diazenyl)phenyl)ethanone
XXXIII	H	H			1-(4-((4-(amino(4-methoxyphenyl)methyl)-3-hydroxynaphthalen-2-ol) diazenyl)phenyl)ethanone
XXXIV	H	C_4H_9			1-(4-((4-((butylamino)(phenyl)methyl)-3-hydroxynaphthalen-2-ol)diazenyl) phenyl)ethanone
XXXV	H	C_3H_7		SO_2NH_2	4-((3-hydroxy-4-(phenyl(propylamino)methyl)naphthalen-2-ol)diazenyl) benzenesulfonamide
XXXVI	H	H		SO_2NH_2	4-((4-(amino(4-methoxyphenyl)methyl)-3-hydroxynaphthalen-2-ol)diazenyl) benzenesulfonamide
XXXVII	H	C_4H_9		SO_2NH_2	4-((4-((butylamino)(phenyl)methyl)-3-hydroxynaphthalen-2-ol)diazenyl) benzenesulfonamide

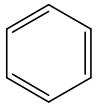
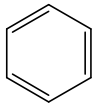
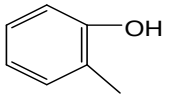
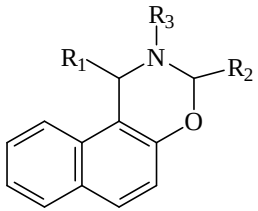
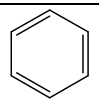
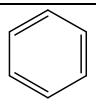
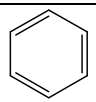
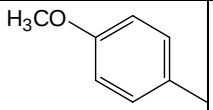
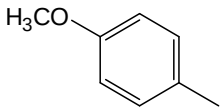
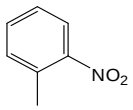
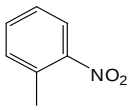
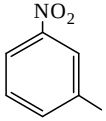
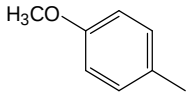
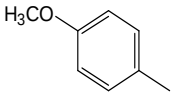
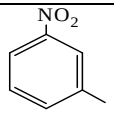
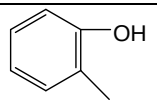
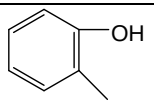
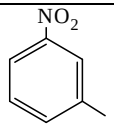
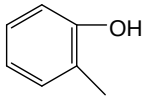
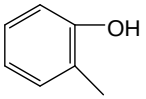
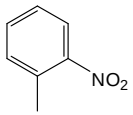
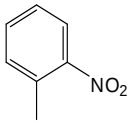
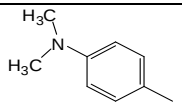
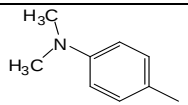
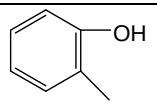
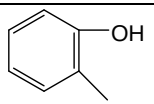
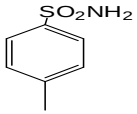
XXXVIII	H	CH_3		SO_2NH_2	4-((3-hydroxy-4-((methylamino)(phenyl)methyl)naphthalen-2-ol)diazenyl) benzenesulfonamide
XXXIX	C_2H_5	C_2H_5		SO_2NH_2	4-((4-((diethylamino)(phenyl)methyl)-3-hydroxynaphthalen-2-ol)diazenyl) benzenesulfonamide
XXXX	H	H		SO_2NH_2	4-((4-(amino(2-hydroxyphenyl)methyl)-3-hydroxynaphthalen-2-ol)diazenyl) benzenesulfonamide

Table. 2.2. Reaction conditions of some synthesized compounds

Table. 2.2.1. Reaction conditions of the 1,3 – naphthoxazine derivative



Cpd No	R_1	R_2	R_3	Temp/ °C	Time/ h	Solvent	Y in g	Y%	Rec solvent	m.p/°C
I				r.t	48	methanol	0.26	64	ethyl acetate	157–159
II			H	r.t	72	methanol	0.13	77	ethyl acetate	121–123
III				r.t	48	methanol	0.25	58	ethyl acetate	158–162
IV				r.t	48	methanol	0.30	54	ethyl acetate	121–123

V				r.t	48	methanol	0.32	61	ethyl acetate	134–136
VI			C_3H_7	r.t	48	methanol	0.33	78	ethyl acetate	135–137
VII			H	r.t	48	methanol	0.22	54	ethyl acetate	147–149 (Lit 160 – 161)
VIII			H	r.t	48	methanol	0.14	79	ethyl acetate	123–125 (Lit 200 – 201)
IX			H	r.t	48	methanol	0.46	81	ethyl acetate	135–137 (Lit 134 – 137)
X			H	r.t	48	methanol	0.35	79	ethyl acetate	123–127
XI				r.t	48	methanol	0.46	81	ethyl acetate	161–163

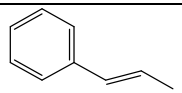
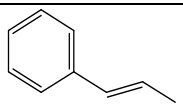
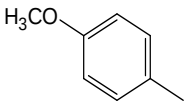
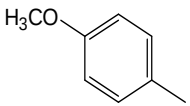
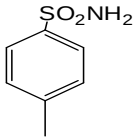
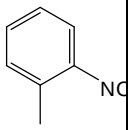
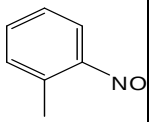
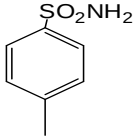
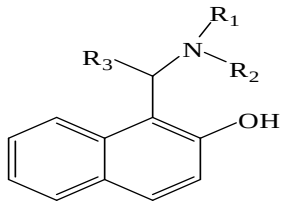
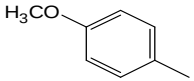
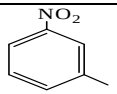
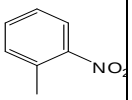
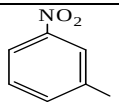
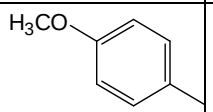
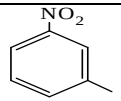
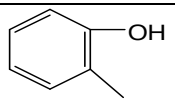
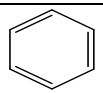
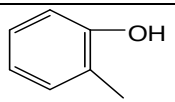
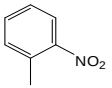
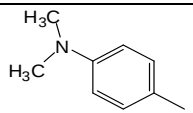
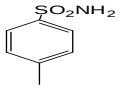
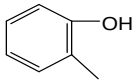
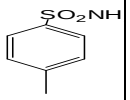
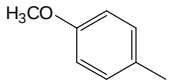
XII			H	r.t	48	methanol	0.34	77	ethyl acetate	190–192
XIII				r.t	48	methanol	0.54	91	ethyl acetate	147–150
XIV				r.t	48	methanol	0.33	70	ethyl acetate	118–120

Table. 2.2.2. Reaction conditions of the Betti base derivatives



Cpd No	R_1	R_2	R_3	Temp/ °C	Time/ h	Solvent	Y in g	Y%	Rec solvent	m.p/ °C
XV		H		150°	Reflux 6	20% HCl	0.21	48	ethyl acetate	123 – 127 (lit 124 – 125)
XVI	H	H		150°	Reflux 6	20% HCl	0.18	65	ethyl acetate	123 – 125
XVII		H		150	Reflux 6	20% HC	0.35	66	ethyl acetate	192 – 195
XVIII		H		150	Reflux 6	20% HC	0.22	43	ethyl acetate	173 – 176

XIX		H		150	Reflux 6	20% HC	0.34	63	ethyl acetate	210 – 215
XX	C_3H_7	H		150°	Reflux 6	20% HCl	0.25	67	ethyl acetate	163 – 165 (lit 165 – 166, 164 – 166)
XXI	H	H		150°	Reflux 6	20% HCl	0.19	70	ethyl acetate	152 – 154 (Lit 147 – 148)
XXII	H	H		150°	Reflux 6	20% HCl	0.27	63	ethyl acetate	200 – 203 (Lit 180 – 181)
XXIII	H	H		150°	Reflux 6	20% HCl	0.15	46	ethyl acetate	118 – 120 (Lit 124 – 125)
XXIV	H	H		150	Reflux 6	20% HCl	0.23	54	ethyl acetate	113 – 115
XXV		H		150	Reflux 6	20% HCl	0.32	76	ethyl acetate	193 – 197
XXVI		H		150	Reflux 6	20% HCl	0.27	63	ethyl acetate	183 – 187

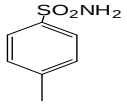
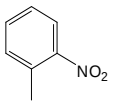
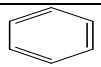
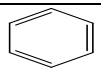
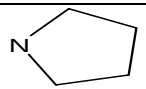
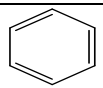
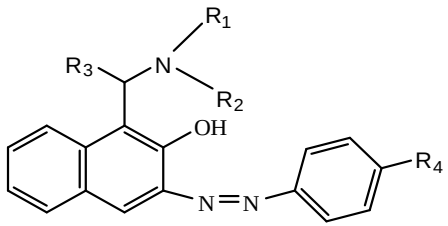
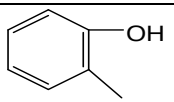
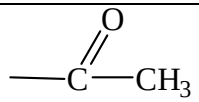
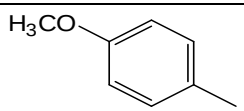
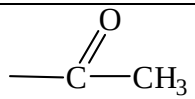
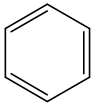
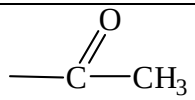
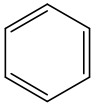
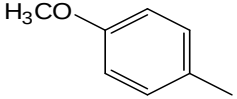
XXVII		H		150	Reflux 6	20% HCl	0.31	71	ethyl acetate	172 – 174
XXVIII	CH_3	H		r. t	48	methanol	0.30	78	ethyl acetate	113 – 115
XXIX	C_2H_5	C_2H_5		r. t	48	methanol	0.19	43	ethyl acetate	118 – 120 (Lit 123 - 124)
XXX		-		r. t	7 days	methanol	0.37	19	ethyl acetate	97 – 99
XXXI	C_4H_9	H		r. t	48	methanol	0.39	92	ethyl acetate	131 – 133

Table 2.2.3. Reaction conditions of the azo dyes



Cpd No	R_1	R_2	R_3	R_4	Temp/ °C	Time/	Y in g	Y%	Rec solvent	m.p/ °C
XXXII	H	H			0	20 min	0.38	80	Ethanol	143 – 146
XXXIII	H	H			0	20 min	0.26	61	Ethanol	173 – 176
XXXIV	H	C_4H_9			0	20 min	0.38	92	Ethanol	210 – 215
XXXV	H	C_3H_7		SO_2NH_2	0	20 min	0.37	78	Ethanol	145 – 147
XXXVI	H	H		SO_2NH_2	0	20 min	0.33	72	Ethanol	154 – 157

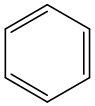
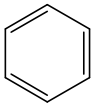
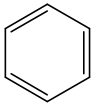
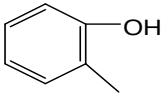
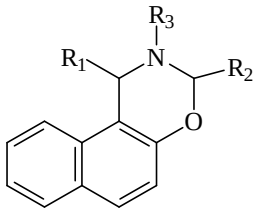
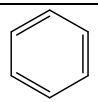
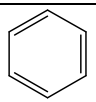
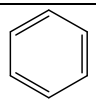
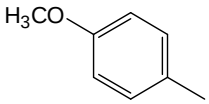
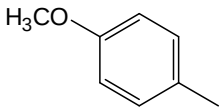
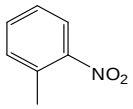
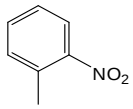
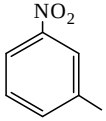
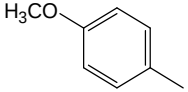
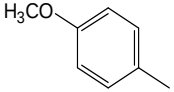
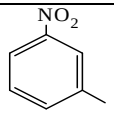
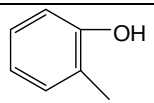
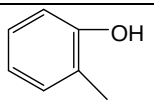
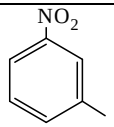
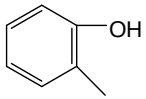
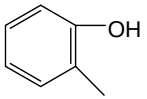
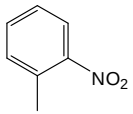
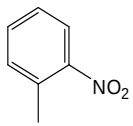
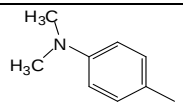
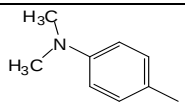
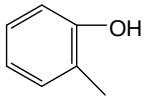
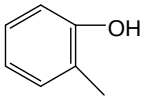
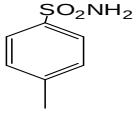
XXXVII	H	C_4H_9		SO_2NH_2	0	20 min	0.42	86	Ethanol	189 – 191
XXXVIII	H	CH_3		SO_2NH_2	0	20 min	0.37	82	Ethanol	202 – 205
XXXIX	C_2H_5	C_2H_5		SO_2NH_2	0	20 min	0.36	64	Ethanol	210 – 212
XXXX	H	H		SO_2NH_2	0	20 min	0.27	54	Ethanol	162 – 164

Table. 2.3. IR data (cm^{-1}) of some synthesized compounds

Table. 2.3.1. IR data (cm^{-1}) of the 1,3 – naphthoxazine derivative



Cpd No	R_1	R_2	R_3	NH st.vib	C–H st.vib aliphatic	C≡C—H st.vib	C–H st.vib	C–O st.vib	others
I				-	2830	1600 3050	1375	1200	-
II			H	3300	2860	1554 3050	1445	1250	1170 (OCH_3)
III				-	2860	1500 3050	1430	1210	1350 (NO_2) sym, 1557 (NO_2) asym
IV				-	3000	1480 3050	1375	1170	1120 (OCH_3) 1350 (NO_2) sym, 1550 (NO_2) asym

V				-	2800	1600 3050	1440	1200	1350 (NO_2) sym, 1550 asym 3200 (OH)
VI			C_3H_7	-	2940	1600 3050	1460	1220	-
VII			H	3310	2820	1554 3050	1375	1190	3250 (OH)
VIII			H	3300	2920	1554 3050	1373	1171	1550 (NO_2) asym, 1340 (NO_2) sym
IX			H	3319	2850	1598 3050	1440	1210	1236 (C – N)
X			H	3340	2900	1600 3050	1375	1195	1216 (C-N)
XI				-	2810	1550 3050	1450	1157	3400 (OH), 1350 (SO_2) asym, 1150 (SO_2) sym, 3300 (NH_2)

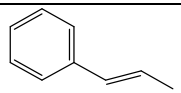
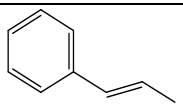
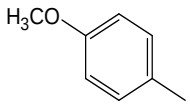
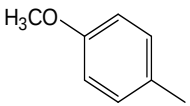
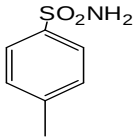
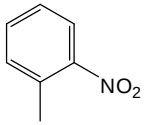
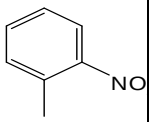
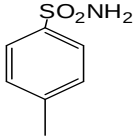
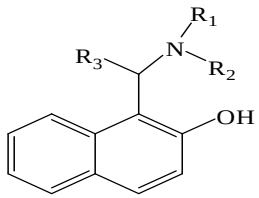
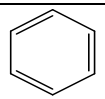
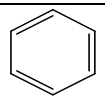
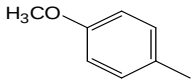
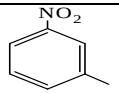
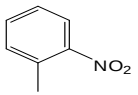
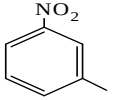
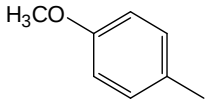
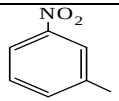
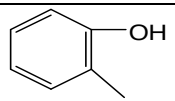
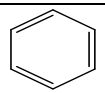
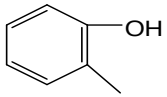
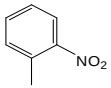
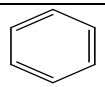
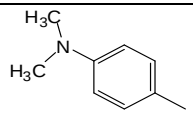
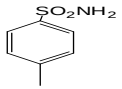
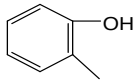
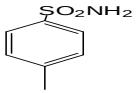
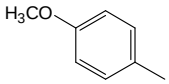
XII			H	3320	2840	1554 3050	1440	1200	-
XIII				-	2900	1550 3050	1375	1190	1150 (SO_2) sym, 1340 (SO_2) asym, 1173 (OCH_3), 3400 (NH_2)
XIV				-	2850	1600 3050	1370	1178	1170 (SO_2) sym, 1350 (SO_2) asym, 1150 (NO_2) sym, 3310 (NH_2)

Table. 2.3.2. IR data (cm^{-1}) of the Betti base derivatives



Cpd No	R_1	R_2	R_3	NH st.vib	OH aromatic st.vib	C–H aliphatic st.vib	C=C–H st.vib aromatic	C–H bending	others
XV		H		3300	3450	2800	1550 3050	1440	1050 (C- N)
XVI	H	H		3300	3400	2840	1460 3050	1370	1100 (OCH_3)
XVII		H		3300	3250	2900	1600 3050	1375	1350 (NO_2) asym, 1550 (NO_2) sym
XVIII		H		3310	3400	2870	1500 3050	1450	1550 (NO_2) sym, 1350 (NO_2) asym, 1100 (OCH_3)

XIX		H		3290	3400	2860	1597 3050	1340	1550 (NO_2) asym, 1340 (NO_2) sym
XX	C_3H_7	H		3300	3200	2780	1460 3050	1375	-
XXI	H	H		3314	3270	2880	1517 3050	1375	-
XXII	H	H		3320	3215	2900	1600 3050	1440	1350 (NO_2) sym, 1552 (NO_2) asym
XXIII	H	H		3360	3200	2830	1514 3050	2360	1172 (C – N)
XXIV	H	H		3306	3200	2830	1550 3050	1373	-
XXV		H		3300	3260	2890	1550 3050	1375	1350 (SO_2) asym, 1150 (SO_2) sym
XXVI		H		3300	3220	2800	1600 3050	1375	1150 (SO_2) sym, 1350 (SO_2) asym, 1170 (OCH_3)

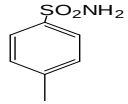
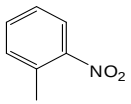
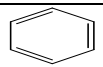
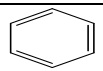
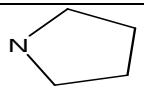
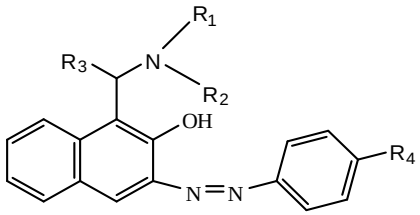
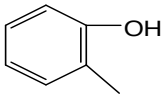
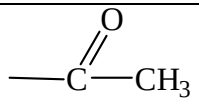
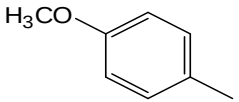
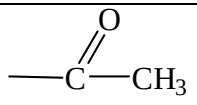
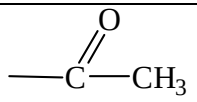
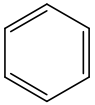
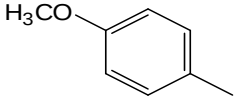
XXVII		H		3350	3200	2850	1600 3050	1375	1350 (SO_2) asym, 1150 (SO_2) sym, 1350 (NO_2) sym, 155o (NO_2) asym
XXVIII	CH_3	H		3300	3265	2900	1583 3050	1375	-
XXIX	C_2H_5	C_2H_5		-	3200	2870	1584 3050	1380	-
XXX		-		-	3385-3000 broad	2860	1522	1440	-
XXXI	C_4H_9	H		3314	3200	2861	1550 3050	1375	-

Table. 2.3.3. IR data (cm^{-1}) of the azo dyes



Cpd No	R_1	R_2	R_3	R_4	N-H st.vib	OH st.vib	C≡C—H st. vib aromatic	C – H bending	C – H st.vib aliphatic	others
XXXII	H	H			3381	3250	1583 3050	1440	2850	1700 (C=O)
XXXIII	H	H			3300	3200	1560 3050	1380	2900	1701 (C=O)
XXXIV	H	C_4H_9			3410	3270	1550 3050	1440	2870	1700 (C=O)
XXXV	H	C_3H_7		SO_2NH_2	3320	3210	1550 3050	1440	2830	1350 (SO_2) asym, 1150 (SO_2) sym
XXXVI	H	H		SO_2NH_2	3400	3200	1600 3050	1375	2920	1380 (SO_2) asym, 1147 (SO_2) sym, 1170 (OCH_3)

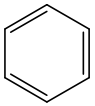
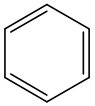
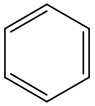
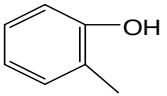
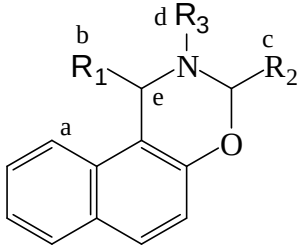
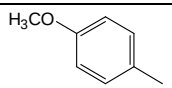
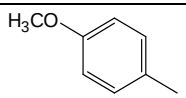
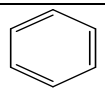
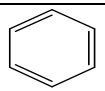
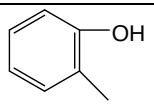
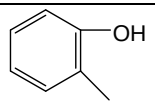
XXXVII	H	C_4H_9		SO_2NH_2	3397	3200	1460 3050	1440	2850	1150 (SO_2) sym, 1350 (SO_2) asym
XXXVIII	H	CH_3		SO_2NH_2	3406	3185	1550 3050	1450	2925	1350 (SO_2) asym, 1150 (SO_2) sym
XXXIX	C_2H_5	C_2H_5		SO_2NH_2	3300	3290	1550 3050	1375	2850	1150 (SO_2) sym, 1350 (SO_2) asym
XXXX	H	H		SO_2NH_2	3308	3200	1600 3050	1375	2890	1140 (SO_2) sym, 1353 (SO_2) asym

Table. 2.4. ^{1}H-NMR data of some synthesized compounds

Table. 2.4.1. ^{1}H-NMR data of the 1,3 – naphthoxazine derivatives



Cpd No	R_1	R_2	R_3	solvent	Chemical shifts (δ) ppm				
					a	b	c	d	e
I				DMSO	6.86-6.89 (m,21H, Ar-H)	6.94-7.17 (m,15H, Ar-H)			2.83 (s,1H, CH), 4.01 (s,1H, CH)
II			H	DMSO	7.18-7.65 (m,6H, Ar-H)	7.71-8.19 (m,8H, Ar-H)	2.96 (s,1H, NH)	3.85 (d, 6H, OCH_3)	2.58 (s, 1H, CH), 4.91 (s,1H, CH)
VI			C_3H_7	DMSO	7.34 – 7.53 (m, 6H, Ar-H)	7.79-7.91 (m,10H, Ar-H)	2.53 (s, 7H, C_3H_7)	-	2.51 (s, 1H, CH), 5.76 (s,1H, CH)
VII			H	DMSO	6.64 – 6.91 (m, 6H, Ar-H)	7.06 – 7.78 (m,8H, Ar-H)	2.01 (s, 1H, NH)	2.56 (s,1H, CH), 4.65 (s,1H, CH)	8.80 (s, H, OH)

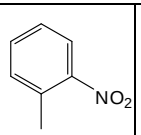
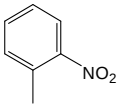
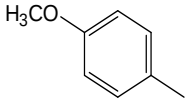
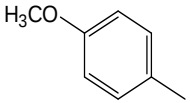
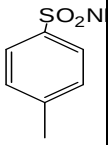
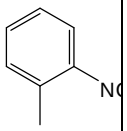
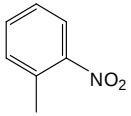
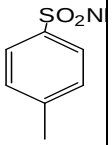
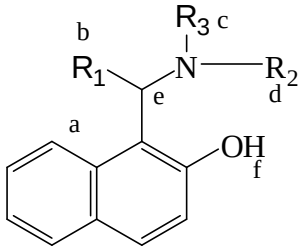
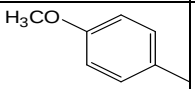
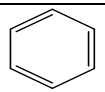
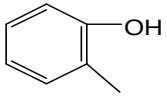
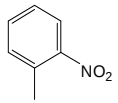
VIII			H	DMSO	6.18 – 6.95 (m, 6H, Ar-H)	7.19 - 7.52 (m, 8H, Ar-H)	2.05 (s, 1H, NH)	-	2.68 (s, 1H, CH), 4.87 (s,1H, CH)
IX			H	DMSO	7.26 – 7.52 (m, 6H, Ar-H)	7.50 – 7.87 (m, 10H, Ar-H)	2.51 (s, 1H, NH)	-	4.51 (s,1 H, CH), 5.56 (s,1H, CH)
XIII				DMSO	7.03 – 7.48 (m, 6H, Ar-H)	7.63 – 7.82 (m, 12H, Ar-H)	2.49 (s, 2H NH_2)	3.88 (s, 6H OCH_3)	4.12 (s, 1H, CH), 5.68 (s,1H, CH)
XIV				DMSO	7.00 – 7.47 (m, 6H, Ar-H)	7.61 – 7.90 (m, 12H, Ar-H)	2.49 (s, 2H NH_2)	-	2.49(s, 1H CH), 4.51 (s,1H, CH)

Table. 2.4.2. ^{1}H-NMR data of the Betti base derivatives



Cpd No	R_1	R_2	R_3	solvent	Chemical shifts (δ) ppm					
					a	b	c	d	e	f
XV		H		DMSO	7.19 – 7.51 (m, 6H, Ar-H)	7.69 – 7.95 (m, 10H, Ar-H)		2.51 (s, 1H ,NH)	4.01 (s, 1H, CH)	9.75 (s,1H, OH)
XVI	H	H		DMSO	6.92 – 7.40 (m, 6H, Ar-H)	7.72 – 7.78 (m, 4H, Ar-H)	2.08 (s, 2H NH_2)	3.69 (s, 6H, OCH_3)	3.31 (s, 1H, CH)	9.75 (d, 1H, OH) J = 2.3 Hz
XX	C_3H_7	H		DMSO	7.81 – 8.00 (m, 6H, Ar-H)	7.30 – 7.50 (m, 5H, Ar-H)	2.20 (s, 7H, C_3H_7)	2.54 (s, 2H, NH_2)	5.05 (s, 1H, CH)	9.53 (s, 1H, OH)
XXI	H	H		DMSO	6.72 – 6.88 (m, 6H, Ar-H)	7.19 – 7.87 (m, 4H, Ar-H)	2.51 (s,2H, NH_2)	-	4.00 (s, 1H, CH)	8.81 (s, H, OH)
XXII	H	H		DMSO	7.36 – 7.65 (m, 6H, Ar-H)	7.81 – 7.96 (m, 4H, Ar-H)	2.08 (s, 2H, NH_2)	-	4.74 (s, 1H, CH)	8.05 (s, 1H, OH)

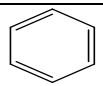
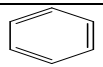
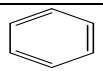
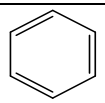
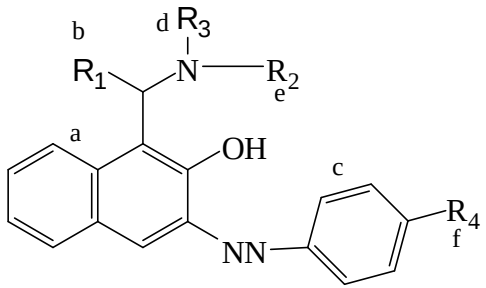
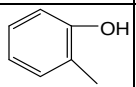
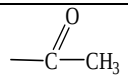
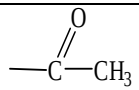
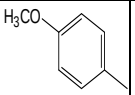
XXIII	H	H		DMSO	7.72 – 7.75 (m, 6H, Ar-H)	6.81 – 7.40 (m, 5H, Ar-H)	2.10 (s,2H, NH_2)	-	2.51 (s, 1H, CH)	9.70 (s, 1H ,OH)
XXVIII	CH_3	H		DMSO	7.69 – 7.92 (m, 6H, Ar-H)	7.14 – 7.40 (m, 5H, Ar-H)	4.08 (s, 3H, CH_3)	2.51 (s, 1H, NH)	5.72 (s, 1H, CH)	9.67 (s, 1H, OH)
XXIX	C_2H_5	C_2H_5		DMSO	7.67 – 7.77 (m, 6H, Ar-H)	7.09 – 7.40 (m, 5H, Ar-H)	3.42 (s, 10H diethyl)	-	2.71 (s, 1H, CH)	9.78 (s, 1H, OH)
XXXI	C_4H_9	H		DMSO	7.67 – 7.92 (m, 6H, Ar-H)	7.06 – 7.54 (m, 11H, Ar-H)	4.71 (s, 9H, butyl)	2.5 (d, 1H, NH) J = 3.83 Hz	5.93 (s, 1H, CH)	9.80 (s, 1H, OH)

Table. 2.4.3. ^{1}H-NMR data of the azo dyes



Cpd No	R_1	R_2	R_3	R_4	solvent	Chemical shifts (δ) ppm					
						a	b	c	d	e	f
XXXII	H	H			DMSO	7.57 – 7.98 (m, 5H, Ar-H)	6.63–7.01(m, 5H, Ar-H)	7.34– 8.17(m, 4H, Ar-H)	2.48 (s, 2H, NH_2)	8.45 (s, 1H, OH), 5.32 (s,1H, CH)	3.63 (s, 3H, OCH_3)
XXXIV	H	C_4H_9			DMSO	7.04 –7.36(m, 5H, Ar-H)	6.62–7.00 (m, 5H, Ar-H)	7.73–8.05 (m, 4H, Ar-H)	2.49 (s, 1H, NH), 3.8 (s, 9H, C_4H_9)	8.89 (s, 1H, OH), 5.52 (s,1H, CH)	3.84 (t, 3H, OCH_3)
XXXVI	H	H		SO_2NH_2	DMSO	7.53 – 7.61 (m, 5H, Ar-H)	7.38–7.45 (m, 4H, Ar-H)	7.83–7.94 (m, 4H, Ar-H)	2.36 (s, 2H, NH_2), 3.21 (s, 2H, NH_2),	6.86 (s, 3H OCH_3), 4.03 (s, 1H, CH)	9.73 (s, 1H OH)

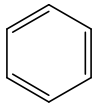
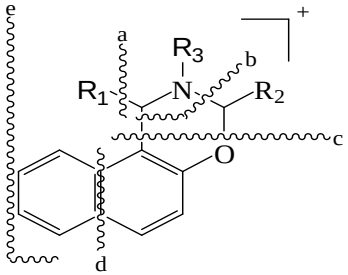
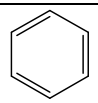
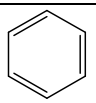
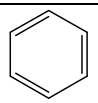
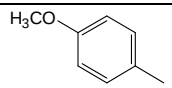
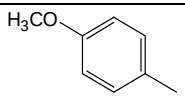
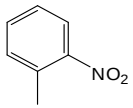
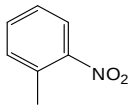
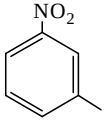
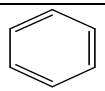
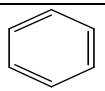
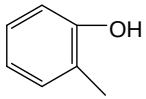
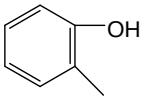
XXXVII	H	C_4H_9		SO_2NH_2	DMSO	7.21 – 7.67 (m, 5H, Ar-H)	7.03 – 7.10 (m, 5H, Ar-H)	7.81 –8.13 (m, 4H, Ar-H)	2.43 (s, 1H NH), 3.27 (s, 2H, NH_2)	4.30 (s, 9H, C_4H_9), 5.26 (s, 1H, CH)	8.61 (s, 1H, OH)
XXXVIII	H	CH_3		SO_2NH_2	DMSO	6.45 – 7.12 (m, 5H, Ar-H)	7.23 – 7.49 (m, 5H, Ar-H)	7.60–8.00 (m, 4H, Ar-H)	2.51 (s, 1H, NH), 3.27 (s, 2H, NH_2)	4.13 (s,3 H, CH_3), 4.24 (s, 1H, CH)	8.01 (s, 1H, OH)

Table .2.5. Mass spectrum data of some synthesized compounds

Table. 2.5.1. Mass spectrum data of the 1,3 – naphthoxazine derivatives



Cpd No	R_1	R_2	R_3	Chemical formula	Molecular weight	M/z (Relative abundance %)				
						a	b	c	d	e
I				$C_{30}H_{23}NO$	413	336 (12)	322 (17)	182 (45)	98 (100)	413(23)
II			H	$C_{26}H_{23}NO_3$	397	320 (20)	247 (14)	166 (44)	82 (100)	397(42)
III				$C_{30}H_{20}N_4O_7$	548	490 (8)	463 (76)	352 (94)	155 (100)	548 (3)
VI			C_3H_7	$C_{27}H_{25}NO$	397	303 (5)	276 (100)	165 (56)	149(90)	397(11)
VII			H	$C_{24}H_{19}NO_3$	369	275 (4)	248 (100)	136 (43)	120 (65)	370(11)

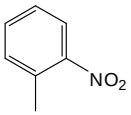
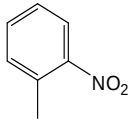
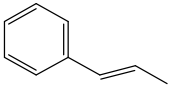
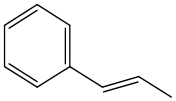
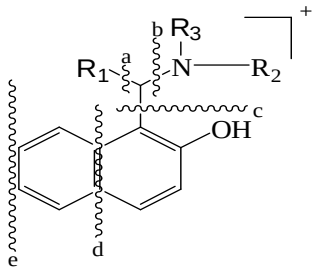
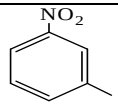
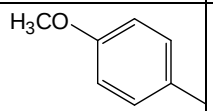
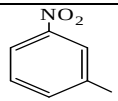
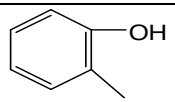
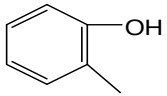
VIII			H	$C_{24}H_{17}N_3O_5$	427	349 (6)	276 (14)	249 (10)	183 (76)	426(100)
IX			H	$C_{24}H_{19}NO$	337	189 (4)	134 (3)	174 (7)	46 (100)	337 (4)
XII			H	$C_{28}H_{23}NO$	389	118 (4)	92 (6)	19 (100)	-	390 (8)

Table. 2.5.2. Mass spectrum data of the Betti base derivatives



Cpd No	R_1	R_2	R_3	Chemical formula	Molecular weight	M/z (Relative abndance)				
						a	B	c	d	e
XV		H		$C_{23}H_{19}NO$	325	205 (27)	183 (7)	169 (11)	92 (100)	326 (13)
XVIII		H		$C_{24}H_{20}N_2O_4$	400	271 (17)	126 (5)	114 (100)	70 (4)	401 (6)
XIX		H		$C_{23}H_{18}N_2O_4$	386	279 (7)	250 (14)	143 (11)	129 (100)	386 (9)
XX	C_3H_7	H		$C_{20}H_{21}NO$	291	184 (4)	155 (3)	119 (7)	29 (22)	290 (100)
XXI	H	H		$C_{17}H_{15}NO_2$	265	157 (3)	130 (16)	35 (6)	-	264 (100)

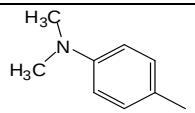
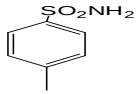
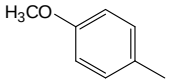
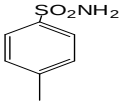
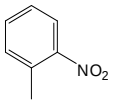
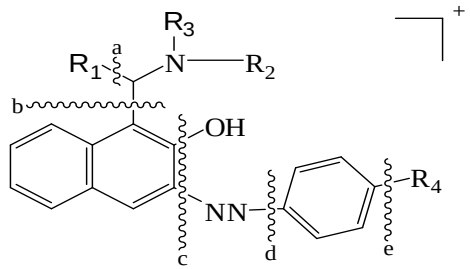
XXIV	H	H		$C_{19}H_{20}N_2O$	292	185 (4)	120 (3)	29 (8)	-	290 (100)
XXVI		H		$C_{24}H_{22}N_2O_4S$	434	343 (10)	327 (21)	279 (23)	144 (100)	432 (3)
XXVII		H		$C_{23}H_{19}N_3O_5S$	449	279 (7)	173 (100)	83 (3)	68 (5)	450 (7)
XXIX	C_2H_5	C_2H_5		$C_{21}H_{23}NO$	305	185 (16)	149 (4)	90 (36)	72 (100)	306 (6)
XXXI	C_4H_9	H		$C_{21}H_{23}NO$	305	114 (5)	100 (21)	90 (42)	72 (100)	303 (19)

Table. 2.5.3. Mass spectrum data of the azo dyes



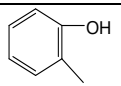
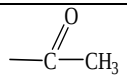
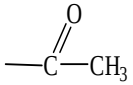
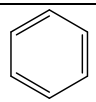
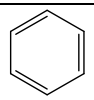
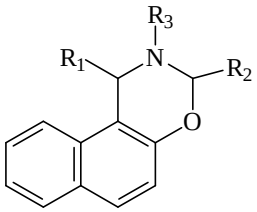
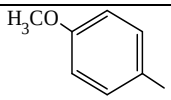
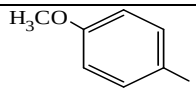
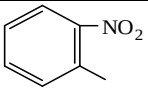
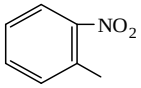
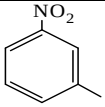
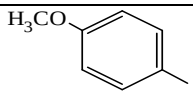
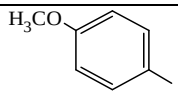
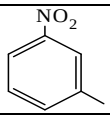
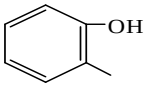
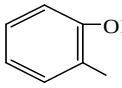
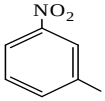
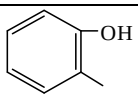
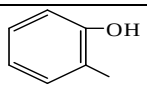
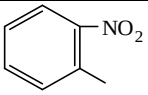
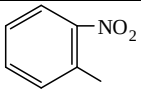
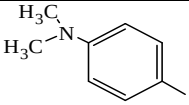
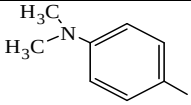
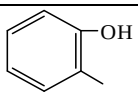
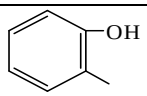
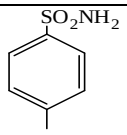
Cpd No	R_1	R_2	R_3	R_4	Chemical formula	Molecular weight	M/z (Relative abndance)				
							a	B	c	d	e
XXXII	H	H			$C_{25}H_{21}N_3O_3$	411	334 (17)	267(100)	96 (68)	46 (34)	409 (29)
XXXIV	H	C_4H_9			$C_{29}H_{29}N_3O_2$	451	349 (3)	-	209 (6)	34 (100)	450 (10)
XXXVI	H	C_3H_7		SO_2NH_2	$C_{26}H_{26}N_4O_3S$	474	462 (7)	341(100)	213 (88)	92 (30)	473 (5)
XXXVIII	H	CH_3		SO_2NH_2	$C_{24}H_{22}N_4O_3S$	446	355 (13)	275 (39)	179 (12)	62 (100)	446 (70)
XXXIX	C_2H_5	C_2H_5		SO_2NH_2	$C_{27}H_{28}N_4O_3S$	488	413 (37)	272(100)	178 (25)	93 (19)	467 (63)

Table. 2.6. R_f values of some synthesized compounds

Table. 2.6.1. R_f values of the 1,3 – naphthoxazine derivatives



Cpd No	R_1	R_2	R_3	Mobile phase	ratio	R_f value
I				methanol : chloroform	1 : 1	0.56
II			H	methanol : chloroform	1 : 1	0.64
III				ethanol : acetone	2 : 0.5	0.43
IV				ethanol : acetone	2 : 0.5	0.52
V				ethanol : chloroform	1.5 : 1	0.73
VI			C_3H_7	methanol : chloroform	1 : 1	0.49
VII			H	methanol : chloroform	1 : 1	0.40
VIII			H	methanol : chloroform	1 : 1	0.60
IX			H	ethanol : chloroform	3 : 2	0.45
X			H	methanol : chloroform	1 : 1	0.67
XI				ethanol : chloroform	1.5 : 1	0.76

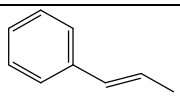
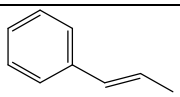
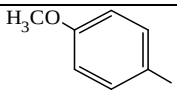
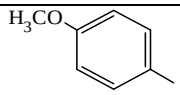
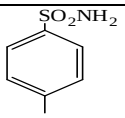
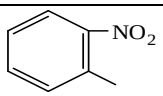
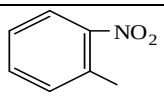
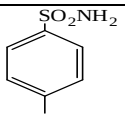
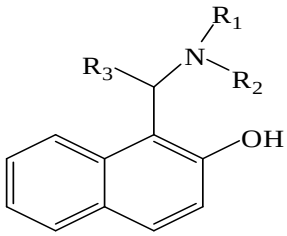
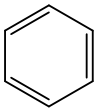
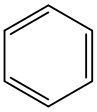
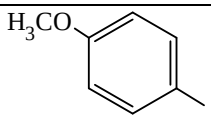
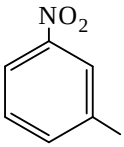
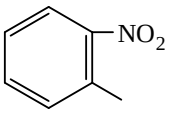
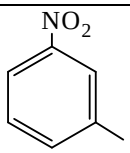
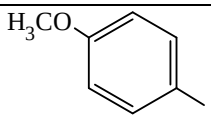
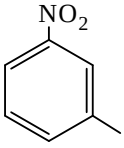
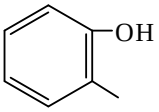
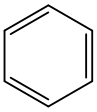
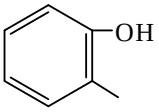
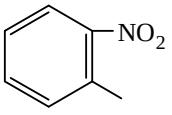
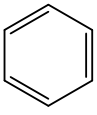
XII			H	ethanol : chloroform	1.5 : 1	0.49
XIII				ethanol : chloroform	3 : 2	0.34
XIV				methanol : n-hexane	3 : 2	0.84

Table. 2.6.2. R_f values of the Betti base derivatives



Cpd No	R_1	R_2	R_3	Mobile phase	ratio	R_f value
XV		H		methanol : chloroform	1 : 1	0.59
XVI	H	H		methanol : chloroform	1 : 1	0.29
XVII		H		ethanol : n-hexane	1 : 1	0.81
XVIII		H		ethanol : n-hexane	2 : 1	0.78
XIX		H		methanol : chloroform	1 : 1	0.53
XX	C_3H_7	H		methanol : chloroform	1 : 1	0.58
XXI	H	H		ethanol : acetone	2 : 1	0.52
XXII	H	H		ethanol : acetone	2 : 1	0.34
XXIII	H	H		methanol : chloroform	1 : 1	0.71

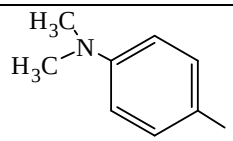
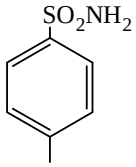
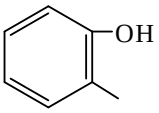
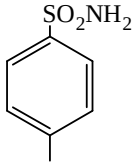
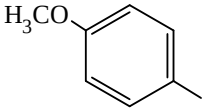
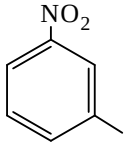
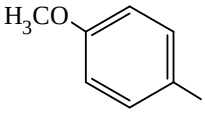
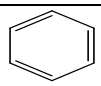
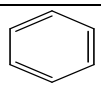
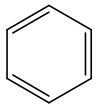
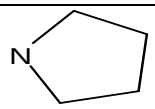
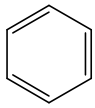
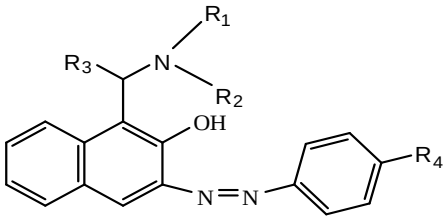
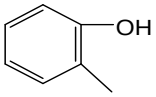
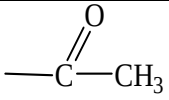
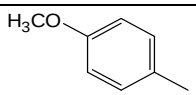
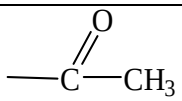
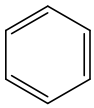
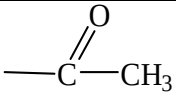
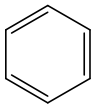
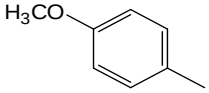
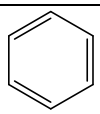
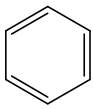
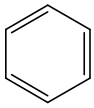
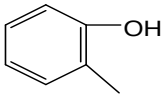
XXIV	H	H		methanol : chloroform	1 : 1	0.24
XXV		H		methanol : chloroform	1 : 1	0.47
XXVI		H		methanol : acetone	3 : 2	0.63
XXVII		H		ethanol : chloroform	3 : 2	0.66
XXVIII		H	CH_3	ethanol : chloroform	3 : 2	0.39
XXIX		C_2H_5	C_2H_5	methanol : chloroform	1 : 1	0.60
XXX			-	methanol : chloroform	1 : 1	0.51
XXXI		H	C_4H_9	methanol : chloroform	1 : 1	0.65

Table. 2.6.3. R_f values of the azo dyes



Cpd No	R_1	R_2	R_3	R_4	Mobile phase	ratio	Rf value
XXXII	H	H			ethanol : acetone	2 : 1	0.52
XXXIII	H	H			ethanol : acetone	2 : 1	0.38
XXXIV	H	C_4H_9			methanol : chloroform	4 : 3	0.59
XXXV	H	C_3H_7		SO_2NH_2	methanol : chloroform	4 : 3	0.71
XXXVI	H	H		SO_2NH_2	ethanol : acetone	2 : 1	0.53
XXXVII	H	C_4H_9		SO_2NH_2	ethanol : acetone	2 : 1	0.47
XXXVIII	H	CH_3		SO_2NH_2	ethanol : acetone	2 : 1	0.64
XXXIX	C_2H_5	C_2H_5		SO_2NH_2	methanol : n-hexane	1 : 1	0.44
XXXX	H	H		SO_2NH_2	methanol : chloroform	3 : 1	0.33

Chapter three

3. Discussion

3.1 Heterocyclic compounds

Heterocyclic compound**,** also called heterocycle, any of a major class of organic chemical compounds characterized by the fact that some or all of the atoms in their molecules are joined in rings containing at least one atom of an element other than carbon (Weissberger, 1975). The presence of the heteroatoms gives heterocyclic compounds physical and chemical properties that are often quite distinct from those of their all-carbon-ring analogs (Elderfield, 1967).

Heterocyclic compounds occur widely in nature and in a variety of non-naturally occurring compounds (Weissberger, 1975). Knowledge of heterocyclic chemistry is useful in biosynthesis and in drug metabolism as well. Nucleic acids are important in biological processes of heredity and evolution (Theophil and Siegried. 2003). There are a large number of synthetic heterocyclic compounds with additional important applications and many are valuable intermediates in synthesis (Katritzky, 1985).

The important methods for synthesizing heterocyclic compounds can be classified under five headings (John and Mills. 2007). Three ways of forming new heterocyclic rings from precursors containing either no rings or one fewer ring than the desired product; one is a way of obtaining a heterocyclic ring from another heterocyclic ring or from a carbocyclic ring; and one involves the modification of substituents on an existing heterocyclic ring (Alan, *et al*. 1996).

Betti's bases are very interesting in the field of asymmetric synthesis in particular; they have provided access to many useful synthetic building blocks. Moreover, they are employed as chiral ligands (Cappannini, *et al*. 2007). Optically active Betti's bases and their derivatives are employed also as chiral auxiliaries for the preparation of enantiopure (Palmieri, 2000). Furthermore, condensation of Betti's base derivatives with aldehydes leads to the formation of the corresponding 1,3-oxazines with different biological properties (Cardellicchio, *etal*. 2010).

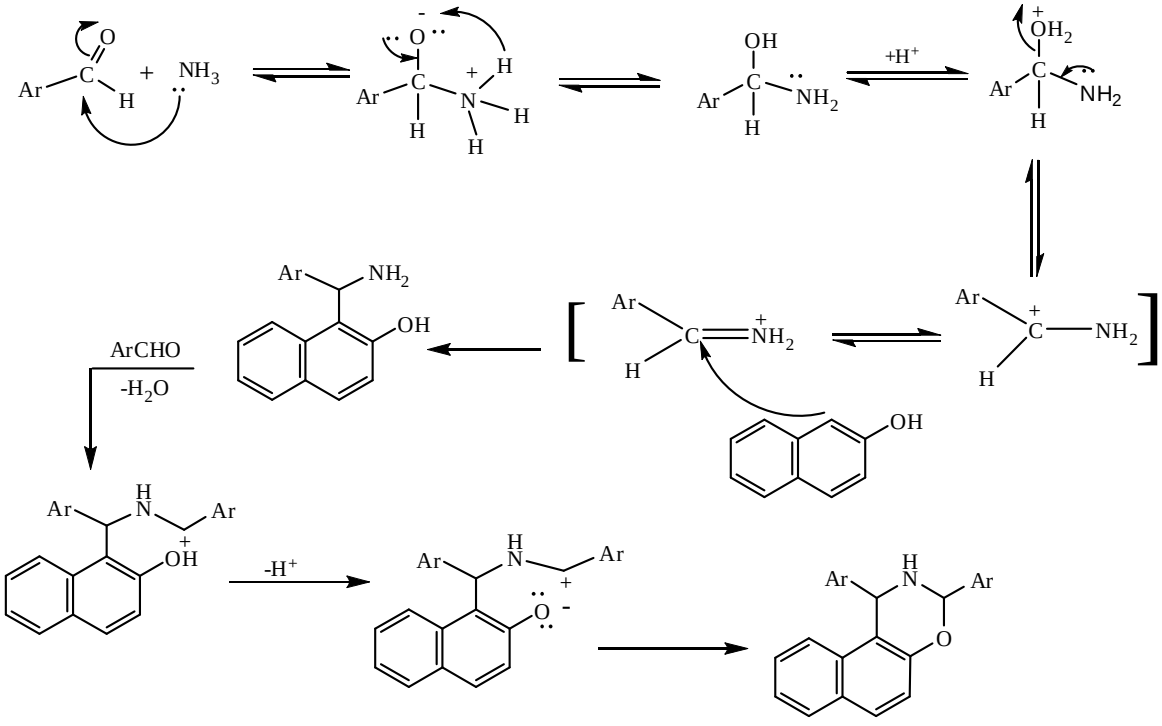
3.2 The retrosynthetic analysis of Betti bases and 1,3-naphthoxazines

Retrosynthesis techniques deal with a particular molecule to be synthesized in order to be able to plane the actual chemical route to be used in the preparation of the target molecule. The task is to devise strategy whereby a particular starting material is converted by series of steps (reactions) to the desired target. One fact must be recognized at the outset – which the target is the compound which must be produced from the starting material and it's the heart of synthetic planning. Whatever its purpose, a target will have particular structural features that must be produced by the synthetic sequence.

The retrosynthetic analysis of the 1,3 oxazine and Betti base reveal naphthol, amine and aldehydes as precursor.

3.3.1 Synthesis of 1,3-naphthoxazines

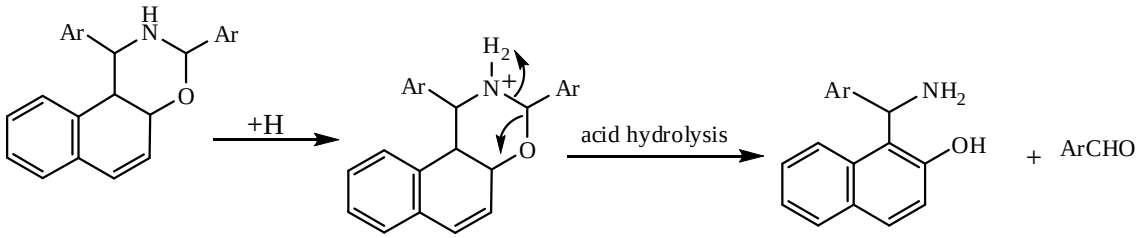
Syntheses of aromatic oxazines were first synthesized through Mannich reactions from phenols, formaldehyde and amines. Synthesis compounds of these classes may be easily obtained by the condensation of β-naphthol, aromatic aldehydes and primary or secondary amines (aromatic or aliphatic) in ratio 1:2:1 in presence of methanol. The Betti bases obtained through acid hydrolysis of 1,3 oxazines by using 20% hydrochloric acid.



Scheme (3.1): Reaction mechanism of synthesis 1,3-naphthoxazine

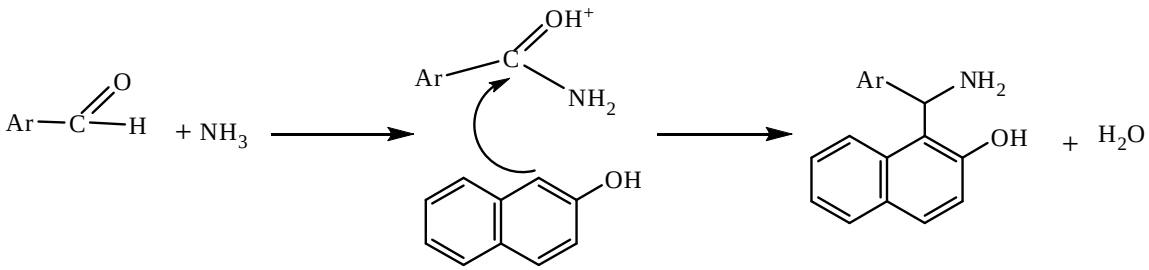
3.3.2 Synthesis of Betti base derivatives

Acid hydrolysis of 1,3-naphthoxazine is widely used for the synthesis of Betti base derivatives



Scheme (3.2): Reaction mechanism synthesis of Betti base derivatives via 1,3-naphthoxazine

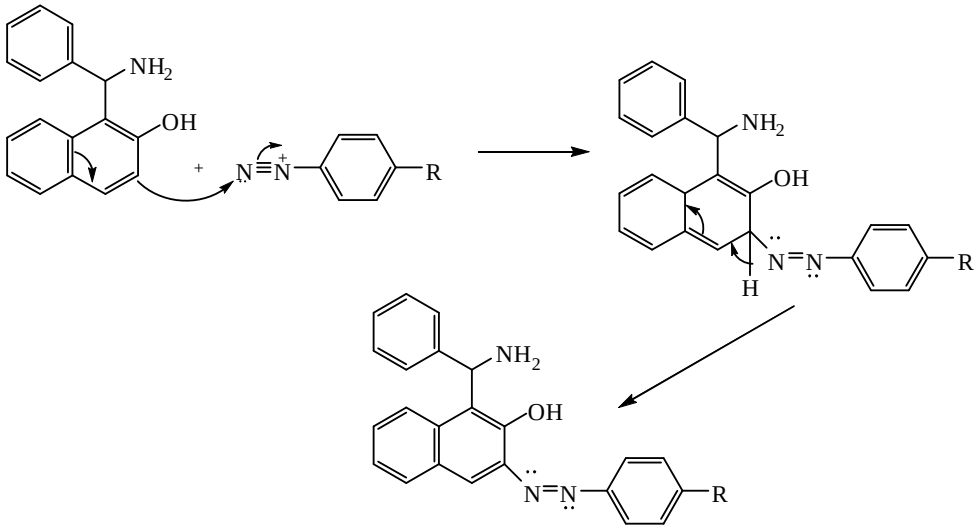
The direct method of synthesis of Betti base derivatives include the reaction between β-naphthol, derivatives of benzaldehyde and ammonia can be followed the bellow scheme.



Scheme (3.3): Reaction mechanism synthesis of Betti base derivatives directly

3.3.3 Synthesis of azo dyes using Betti base derivatives

Reaction of the diazonium salt with various aromatic compounds leads to the formation of azo dye derivatives by what is generally called a coupling reaction, but is mechanistically simply an ordinary electrophilic substitution reaction. The mechanism of the reaction is given bellow:



Scheme (3.4): Reaction mechanism of the Betti base to form azo dye

3.4 Spectroscopic analysis

structure of the synthesized compounds were confirmed by study their properties such as R_f value and melting point or spectroscopic analysis such as IR, NMR, MS, GC – MS and UV techniques.

Most infrared (IR) bands are associated with specific chemical bond. It is usually possible to deduce the functional class of an organic compound from its IR spectrum. The infrared spectrum is the simplest, most rapid and often most reliable means for assigning a compound to its class. Absorption of radiation in the infrared region results in the excitation of bond deformations, either stretching or bending. Nuclear magnetic resonance spectroscopy (NMR) involves transition of a nucleus from one spin state to another with the resultant absorption of electromagnetic radiation by spin active nuclei when they are placed in a magnetic field. The nuclear magnetic resonance spectroscopy is well suited for detecting certain structural units present in the molecule from the characteristic δ values of various types of hydrogens associated with these units. Mass spectrometry (MS) is a microanalytical technique requiring only a few nanomoles of the sample to obtain characteristic information pertaining to the structure and molecular weight of the analyte. In most cases, the molecular ion in the analyte produces fragment ions by cleavage of the bonds and the resulting fragmentation pattern constitutes the mass spectrum. Gas chromatography – mass spectrometry (GC-MS) is a

technique, which combines the separating power of gas chromatography (GC), with the detection power of mass spectrometry.

The IR spectra of the synthesized 1,3-naphthoxazines compounds (II, VII, VII, IX, X, XI, XII, XIII and XIV), all those compounds containing one or more nitrogen atom. These nitrogen atoms refer to secondary amines showed st. vib bands appear around 3300 cm^{-1} (3300 cm^{-1} , 3310 cm^{-1}, 3340 cm^{-1} and 3319 cm^{-1}) due to presence of N – H stretching vibrations of the secondary and tertiary amines. Compounds III, IV, V, VIII and XIV containing nitro groups (NO_2) in *ortho* or *meta* position in aromatic ring. Those compounds showed absorption bands appeared in the range (1310 - 1350 cm^{-1}) for symmetric and in the range (1500 -1550 cm^{-1}) represent the asymmetric stretching of the nitro group (NO_2) in positions *meta* or *ortho* in aromatic rings. Compounds II, IV and XIII containing methoxy group (OCH_3) at *para* position in aromatic ring showed absorption band at 1170 cm^{-1} and 1120 cm^{-1} st. vib. Compounds XI, XIII and XIV containing SO_2 group at *para* position in aromatic ring showed absorption peaks at (1150 – 1180 cm^{-1}) symmetric and at (1340 – 1360 cm^{-1}) asymmetric. The OH group in compounds V, VII and XI showed broad band in the range (3400 – 3000 cm-1), this peak appeared at 3200 cm^{-1} and 3250 cm^{-1}. Absorption bands at 1550 cm^{-1}, 11600 cm^{-1}, 1554 cm^{-1}, 1440 cm^{-1} and 1460 cm^{-1} were indicated for aromatic C=C stretching vibrations of double bonds of benzene system. The aromatic C – H bending showed peaks in range (1430 – 1460 cm^{-1}) and absorption in range (1370 – 1380 cm^{-1}) and for aliphatic C – H st. vib showed bands appears in the range (2810 - 2920 cm^{-1}). The C – N vibration absorption peaks appear at 1250 cm^{-1}, 1216 cm^{-1} and 1236 cm^{-1}. (Table 2.3.1)

The Betti base compounds (XV – XXXI) were synthesized directly or via 1,3-oxazines, they are all containing N – H groups in their structure refer to primary or secondary amines (except compounds XXIX and XXX) this nitrogen atom showed peak appeared st. vib around 3300 cm^{-1} (3310 cm^{-1}, 3340 cm^{-1}, 3350 cm^{-1}, 3314 cm^{-1}, 3314 cm^{-1} and 3106 cm^{-1}). All compounds containing OH group appeared in range (3400 – 3000 cm^{-1}) due OH st. vib in aromatic system. Compounds XVII, XVIII, XIX, XXII and XXVII having NO_2 group in *ortho* or

para position bonded to aromatic rings, appeared at 1550 cm^{-1}symmetric and 1350 cm^{-1} asymmetric stretching. Compounds XVI, XVIII and XXVII containing OCH_3 methoxy group in *para* position attached to aromatic ring showed peaks stretching at 1100 cm^{-1}, 1216 cm^{-1} and 1223 cm^{-1}. The aromatic C – H bending showed peaks appeared at 1440 cm^{-1}, 1370 cm^{-1}, 1375 cm^{-1}, 1460 cm^{-1} and 1450 cm^{-1} consistent with skeletal vibrations of the aromatic system. The aromatic C=C st, vib showed peak at 1550 cm^{-1}, 1560 cm^{-1}, 1600 cm^{-1}, 1514 cm^{-1} and 1584 cm^{-1} in aromatic system. The aliphatic C – H st. vib. gives band at 2800 cm^{-1}, 2840 cm^{-1}, 2861 cm^{-1}, 2900 cm^{-1} and 2880 cm^{-1} is assigned to the aromatic C – H stretching vibrations. Compounds XXV and XXVI containing NO_2 group in their structures, this group showed peaks at 1350 asymmetric and 1150 symmetric. For C – N this group showed absorption appeared at 1050 cm^{-1}, 1020 cm^{-1}, 1240 cm^{-1} and 1237 cm^{-1}. (Table 2.3.2)

The azo dyes compound prepared by diazotization of Betti bases, containing OH group in their structures. This group showed peak in the range (3200 – 3250 cm^{-1}) which indicate aromatic OH. The N –H st. vib showed absorption bands in range (3300 – 3400 cm-1) due to the presence of secondary amines stretching vibrations. The C=C st.vib in aromatic system showed peaks at 1583 cm^{-1}, 1550 cm^{-1}, 1600 cm^{-1} and 1460 cm^{-1}. The aromatic C – H bending showed peaks at 1440 cm^{-1}, 1375cm^{-1}, 1380 cm^{-1} 1550 cm^{-1} and 1600cm^{-1}. Bands at 2850 cm^{-1}, 2830 cm^{-1}, 2900 cm^{-1} and 2890 cm^{-1} those absorption indicate the presence of C – H aliphatic stretching vibrations. Compounds XXXII, XXXIII and XXXIV containing carbonyl group refer to ketone in their structure, this group showed absorption bands at 1740 cm^{-1}, 1701 cm^{-1} and 1760 cm^{-1}. Compounds (XXXV – XXXX) containing SO_2 group in their structures this group showed absorption peak at 1350 cm^{-1} asymmetric and 1150cm^{-1} symmetric. (Table.2.3.3)

^{1}H- NMR spectra data of some synthesized 1,3-naphthoxazines derivatives in DMSO as a solvent. Compound I containing 23 hydrogen showed multiplate at δ = 6.86 – 6.89 ppm equivalent to 6 hydrogen atoms due to aromatic protons, 6.94 – 7.17 ppm for 15 aromatic hydrogen and singlet at δ = 3.34 ppm indicate the

presence of the solvent (DMSO) . The CH protons appeared at δ = 4.79 ppm , 5.63 ppm and 2.86 ppm. Compound II containing two methoxy groups in *para* position to aromatic ring. This compound containing 23 hydrogen atoms showed multiplate at δ = 7.18 – 7.65 ppm due to 6 aromatic hydrogen, 7.71 – 8.19 ppm for 8 aromatic hydrogen and doublet at δ = 3.85 ppm equivalent to six hydrogen atoms represent to the protons of methoxy groups and multiplate at δ = 6.5 – 8 ppm equivalent to 13 hydrogen atoms due to aromatic protons. Compound VI containing propyl group in its structure showed singlet at δ = 2.53 ppm equivalent to 7 hydrogen atoms due to $CH_3CH_2CH_2$ protons and multiplate at δ = 7.34 – 7.91 ppm equivalent to 6 hydrogen atoms due to aromatic protons, δ = 6.64 – 6.91 ppm for 10 aromatic hydrogen, δ = 3.49 ppm for two hydrogen of CH. Compound VII showed singlet at δ = 2.01 ppm equivalent to one hydrogen due to NH, singlet at δ = 3.49 ppm represent to the one hydrogen due to CH, multiplate at δ = 6.64 – 6.91 ppm indicates of the 6 hydrogen atoms due to protons of aromatic rings, δ = 7.07 – 7.78 ppm for 8 aromatic protons, the OH proton showed singlet peak at δ = 8.80 ppm. Compound VIII containing two nitro groups attached to aromatic rings in *ortho* position showed multiplate at δ = 6.18 – 6.85 ppm due to 6 protons indicate the aromatic protons, δ = 7.19 – 7.52 ppm for 8 aromatic hydrogen, the NH proton showed singlet peak appeared at δ = 4.09 ppm. Compound IX showed multiplate peak at δ = 7.26 – 7.52 ppm represent 6 aromatic hydrogen, 7.50 – 7.87 ppm for 10 aromatic protons, the CH proton appeared at δ = 5.56 ppm for two proton. Compound XIII showed singlet at δ = 2.49 ppm equivalent to two hydrogen atoms due to NH_2 protons, singlet at δ = 3.84 ppm equivalent to six hydrogen atoms represent to OCH_3 protons, protons of CH showed peak at δ = 2,51 ppm and multiplate at δ = 7.03 – 7.48 ppm equivalent to 6 hydrogen atoms indicate of the aromatic protons, δ = 7.63 – 7.82 ppm for 12 aromatic protons. Compound XIV containing two nitro group and SO_2 showed singlet at δ = 4.49 ppm equivalent to two hydrogen atoms due to NH_2 protons and multiplate at δ = 7.00 – 7.47 ppm equivalent to six hydrogen atoms represent to aromatic ring protons, δ = 7.61 – 7.90 ppm indicated 12 aromatic protons and singlet at δ = 2.51 ppm equivalent to two hydrogen atoms indicate of the methyl protons. (Table 2.4.1)

The ^{1}H-NMR spectra of the Betti base derivatives which were synthesized directly or through 1,3-oxazines (XV – XXXI) showed spectral data on DMSO as a solvent. Compound XV showed singlet at δ = 2.51 ppm equivalent to one hydrogen indicate the NH proton, singlet at δ = 4.76 ppm, 5.78 ppm and 6.04ppm equivalent to one hydrogen represent to CH group, multiplate at δ = 7.19 – 7.51 ppm equivalent to 6 hydrogen atoms due to aromatic rings protons, δ = 7.69 – 7.95 ppm for 10 aromatic protons and singlet at δ = 9.75 ppm equivalent tone hydrogen atom indicate the hydroxyl protons (OH). Compound XVI containing methoxy group in *para* position to aromatic ring showed singlet at δ = 2.08 ppm equivalent to two hydrogen atoms due to NH_2 protons, singlet at δ = 3.69 ppm equivalent to three hydrogen atoms indicate the OCH_3 group, multiplate at δ = 6.92 – 7.40 ppm equivalent to 6 hydrogen atoms represent to aromatic protons, δ = 7.72 – 7.78 ppm for four aromatic protons and doublet at δ = 9.75 ppm equivalent to one hydrogen atom indicate the hydroxyl protons. Compound XX containing propyl group showed singlet at δ = 2.54 ppm equivalent to one hydrogen atom due to NH proton, singlet at δ = 3.50 ppm equivalent to seven hydrogen atoms represent to the propyl protons, singlet at δ = 4.65 ppm equivalent to one hydrogen atom indicate the methine proton, multiplate at δ = 7.81 – 8.oo ppm equivalent to six hydrogen atoms due to aromatic protons, δ = 7.30 – 7.50 ppm for five aromatic protons and singlet at δ = 8.9 ppm equivalent to one hydrogen atom indicate the hydroxyl proton. Compound XXI containing two hydroxyl groups at *ortho* position in aromatic rings showed singlet at δ = 2.08 ppm equivalent to two hydrogen atoms represent the NH_2 protons, singlet at δ = 4.04 ppm equivalent to one hydrogen atom indicate the methine proton, singlet at δ = 8.81 ppm equivalent to two hydrogen atoms indicate the hydroxyl group and multiplate at δ = 6.72 – 6.88 ppm equivalent to four hydrogen atoms due to aromatic hydrogen, δ = 7.19 – 7.49 ppm for four aromatic protons. Compound XXII containing nitro group in *ortho* position to aromatic rings showed singlet at δ = 2.08 ppm equivalent to two hydrogen atoms due to NH_2 protons, singlet at δ = 6.83 ppm equivalent to one hydrogen atom represent the methyl group protons,

singlet at δ = 8.05 ppm due to OH one proton and multiplate at δ = 7.36 – 65 ppm equivalent to six hydrogen atoms indicate the aromatic protons, δ = 7.81 – 7.96 ppm for four aromatic hydrogen. Compound XXIII showed singlet at δ = 2.10 ppm equivalent to two hydrogen atoms represent the NH_2 protons, singlet at δ = 2.83 ppm equivalent to one hydrogen atom indicate the methine proton, multiplate at δ = 7.72 – 7.75 ppm equivalent to six hydrogen atoms due to aromatic protons, δ = 6.81 – 7.40 ppm for five aromatic protons and singlet at δ = 9.870 ppm equivalent to one hydrogen atom represent the hydroxyl protons. Compound XXVIII showed singlet at δ = 2.08 ppm equivalent to three hydrogen atoms indicate the methoxy protons, singlet at δ = 2.51 ppm equivalent to one hydrogen atom represent the NH proton, singlet at δ = 5.56 ppm equivalent to one hydrogen atom represent to methine proton, multiplate at δ = 7.69 – 7.92 ppm equivalent to six hydrogen atoms due to aromatic protons, δ = 7.14 – 7.40 ppm for four aromatic protons and singlet at δ = 9.76 ppm equivalent to one hydrogen atom indicate the OH proton. Compound XXIX containing double ethyl group showed singlet at δ = 2.51 ppm equivalent to ten hydrogen atoms indicate the $(C_2H_3)_2$ protons, singlet at δ = 3.42 ppm equivalent to one hydrogen atom due to methyl proton, multiplate at δ = 7.67 – 7.77 ppm equivalent to six aromatic protons, δ = 7.09 – 7.04 ppm for five hydrogen atoms indicate the aromatic protons and singlet at δ = 9.78 ppm equivalent to one hydrogen atom represent to OH proton. Compound XXXI containing butyl group in its structure showed doublet at δ = 2.54 ppm equivalent to one hydrogen atom indicate the NH proton, singlet at δ = 5.71 ppm equivalent to nine hydrogen atoms represent the butyl protons, singlet at δ = 2.08 ppm equivalent to one hydrogen atom indicate the methyl proton, multiplate at δ = 7.67 – 7.92 ppm equivalent to six hydrogen atoms due to aromatic protons, δ = 7.06 – 7.54 ppm for five aromatic protons and singlet at δ = 9.80 ppm equivalent to one OH proton. (Table 2.4.2)

H^1-NMR spectra of azo dyes synthesized by coupling of Betti base derivative with diazonium salts showed that at compound XXXII doublet at δ = 2.63 ppm equivalent to three hydrogen atoms indicate methyl (CH_3) protons, singlet at δ = 3.36 ppm equivalent to presence of the solvent. The bands appeared

at δ = 5.42 ppm, 5.53 ppm and 6.24 ppm due to presence of one hydrogen atom represent the methane (CH) proton, multiplate at δ = 7.57 – 7.98 ppm equivalent to six hydrogen atoms due to aromatic protons, δ = 6.60 – 7.01 ppm for four aromatic protons, δ = 7.34 – 8.17 ppm for four aromatic protons and singlet at δ = 8.45 ppm equivalent to two hydrogen atoms indicate the OH protons. Compound XXXIV showed singlet at δ = 2.49 ppm equivalent to one hydrogen atoms indicate the NH protons, triplet at δ = 3.84 ppm equivalent to six hydrogen atoms represent the methoxy protons, multiplate at δ = 7.04 – 7.36 ppm equivalent to six hydrogen atoms indicate the aromatic protons, δ = 6.62 – 7.04 ppm for five aromatic protons, δ = 7.73 – 8.05 ppm for four aromatic protons and singlet at δ = 9.7 ppm equivalent to one hydrogen atom due to OH proton. Compound XXXVI showed multiplate peak at δ = 7.53 – 7.61 ppm due to presence of six aromatic protons, δ = 7.38 – 7.45 ppm for four aromatic protons, δ = 7.83 – 7.94 ppm for four aromatic protons, singlet at δ = 2.36 ppm indicate the two hydrogen of NH_2, peak at δ = 6.86 ppm represent to three protons of methoxy group, the CH protons shoed peak at δ = 5.78 ppm and OH protons appeared at δ = 8.01 ppm. (Table 2.4.3).

The mass spectra of synthesized compounds showed molecular ions corresponding to the molecule formula. Compound (I) showed a molecular ion at m/z 413 corresponding to molecular formula $C_{30}H_{23}O$. The base peak appeared at m/z 315 which is a characteristic for the $C_{22}H_{21}NO$. An ion at m/z 158 is due to $C_{11}H_{10}O$. Compound (II) showed a molecular ion at m/z 397 corresponding to molecular formula $C_{26}H_{23}NO_3$. The base peak appeared at m/z 315 which is a characteristic for the $C_{22}H_{21}NO$. An ion at m/z 58 is due to C_3H_6O. Compound (III) showed a molecular ion at m/z 548 corresponding to molecular formula $C_{30}H_{20}N_4O_7$. The base peak appeared at m/z 261 which is a characteristic for the $C_{18}H_{14}NO$. An ion at m/z 134 is due to $C_9H_{10}O$. Compound (VI) showed a molecular ion at m/z 379 corresponding to molecular formula $C_{27}H_{25}NO$. The base peak appeared at m/z 248 which is a characteristic for the $C_{18}H_{16}O$. An ion at m/z 94 is due to C_6H_8N. Compound (VII) showed a molecular ion at m/z 379 corresponding to molecular formula $C_{17}H_{15}NO_3$. The base peak appeared at m/z

121 which is a characteristic for the $C_8H_{11}N$. An ion at m/z 94 is due to C_6H_6O. Compound (IX) showed a molecular ion at m/z 337 corresponding to molecular formula $C_{24}H_{19}NO$. The base peak appeared at m/z 290 which is a characteristic for the $C_{21}H_{24}N$. An ion at m/z 148 is due to $C_{10}H_{12}O$. Compound (XII) showed a molecular ion at m/z 389 corresponding to molecular formula $C_{28}H_{23}NO$. The base peak appeared at m/z 370 which is a characteristic for the $C_{27}H_{30}O$. An ion at m/z 270 is due to $C_{19}H_{28}N$. Compound (XV) showed a molecular ion at m/z 325 corresponding to molecular formula $C_{23}H_{19}NO$. The base peak appeared at m/z 233 which is a characteristic for the $C_{17}H_{15}N$. An ion at m/z 98 is due to C_7H_{14}. Compound (XVIII) showed a molecular ion at m/z 400 corresponding to molecular formula $C_{24}H_{20}N_2O_4$. The base peak appeared at m/z 286 which is a characteristic for the $C_{21}H_{20}N$. An ion at m/z 98 is due to $C_6H_{10}O$. Compound (XIX) showed a molecular ion at m/z 386 corresponding to molecular formula $C_{23}H_{18}N_2O_4$. The base peak appeared at m/z 257 which is a characteristic for the $C_{17}H_{23}NO$. An ion at m/z 108 is due to C_8H_{12}. Compound (XX) showed a molecular ion at m/z 290 corresponding to molecular formula $C_{20}H_{21}NO$. The base peak appeared at m/z 290 which is a characteristic for the $C_{20}H_{21}NO$. An ion at m/z 136 is due to $C_9H_{12}O$. Compound (XXVI) showed a molecular ion at m/z 434 corresponding to molecular formula $C_{24}H_{22}N_2O_4S$. The base peak appeared at m/z 261 which is a characteristic for the $C_{14}H_{14}NO_2S$. An ion at m/z 92 is due to C_7H_8. Compound (XXVII) showed a molecular ion at m/z 449 corresponding to molecular formula $C_{23}H_{19}N_3O_5S$. The base peak appeared at m/z 275 which is a characteristic for the $C_{19}H_{17}NO$. An ion at m/z 97 is due to $C_6H_{11}N$.Compound (XXIX) showed a molecular ion at m/z 305 corresponding to molecular formula $C_{21}H_{23}NO$. The base peak appeared at m/z 233 which is a characteristic for the $C_{17}H_{15}O$. An ion at m/z 120 is due to C_9H_{12}. Compound (XXXI) showed a molecular ion at m/z 305 corresponding to molecular formula $C_{21}H_{23}NO$. The base peak appeared at m/z 232 which is a characteristic for the $C_{18}H_{16}$. An ion at m/z 215 is due to $C_{15}H_{21}N$. Compound (XXXII) showed a molecular ion at m/z 411 corresponding to molecular formula $C_{25}H_{21}N_3O_3$. The base peak appeared at m/z 266 which is a characteristic for the $C_{17}H_{17}N_2O$. An ion at m/z 96 is due to

C_6H_8O. Compound (XXXIV) showed a molecular ion at m/z 451 corresponding to molecular formula $C_{29}H_{29}N_3O_2$. The base peak appeared at m/z 437 which is a characteristic for the $C_{29}H_{31}N_3O$. An ion at m/z 101 is due to $C_6H_{14}N$. Compound (XXXVI) showed a molecular ion at m/z 462 corresponding to molecular formula $C_{24}H_{22}N_4O_4S$. The base peak appeared at m/z 120 which is a characteristic for the $C_7H_7N_2$. An ion at m/z 432 is due to $C_{23}H_{20}N_4O_3S$. Compound (XXXVIII) showed a molecular ion at m/z 446 corresponding to molecular formula $C_{24}H_{22}N_4O_4S$. The base peak appeared at m/z 32 which is a characteristic for the CH_4O. An ion at m/z 355 is due to $C_{24}H_{25}N_3$. The fragmentation patterns of some synthesized compounds were shown in tables (2.5.1, 2.5.2 and 2.5.3).

Conclusions and recommendations

- 1-(α-aminobenzyl)-2-naphthols (Betti base derivatives) were synthesized by condensation reaction of 2-naphthol, aromatic aldehydes and source of nitrogen such as ammonia or aliphatic and aromatic amines (primary and secondary) in presence of methanol in ratio 1 : 2: 1 to form 1,3-naphthoxazines which were directly hydrolysed with 20% hydrochloric acid.

- Betti base derivatives also synthesized directly in one step by adopting multi component reactions approach using 2-naphthol, aromatic aldehydes and ammonia solution or aliphatic amines in ratio 1: 1: 1 in water.

- Azo dyes in this work were synthesized in moderate to high yield by the coupling reaction of Betti base derivatives with diazonium salts.

- The synthesized compounds were purified by recrystalization and characterized by using different analytical tools (TLC, m.p and spectral analysis).

- The resulting analysis of Betti base derivatives which were synthesized via 1,3-naphthoxazines or directly showed the same physical properties and spectral behavior.

- Syntheses of Betti base derivatives via 1,3-oxazines or directly by using aliphatic aldehydes as a substituent of aromatic aldehydes is highly recommended.

- Testing the antimicrobial activities of the synthesized compounds is also recommended.

- Transformation of the Betti base derivatives to different substituent arylnaphthoxazines in order to study the double substituent effect on the ring – chain tatomeric is recommended.

- Quantitative structure activity relationship (QSAR) analysis is recommended.

CHAPTER FOUR

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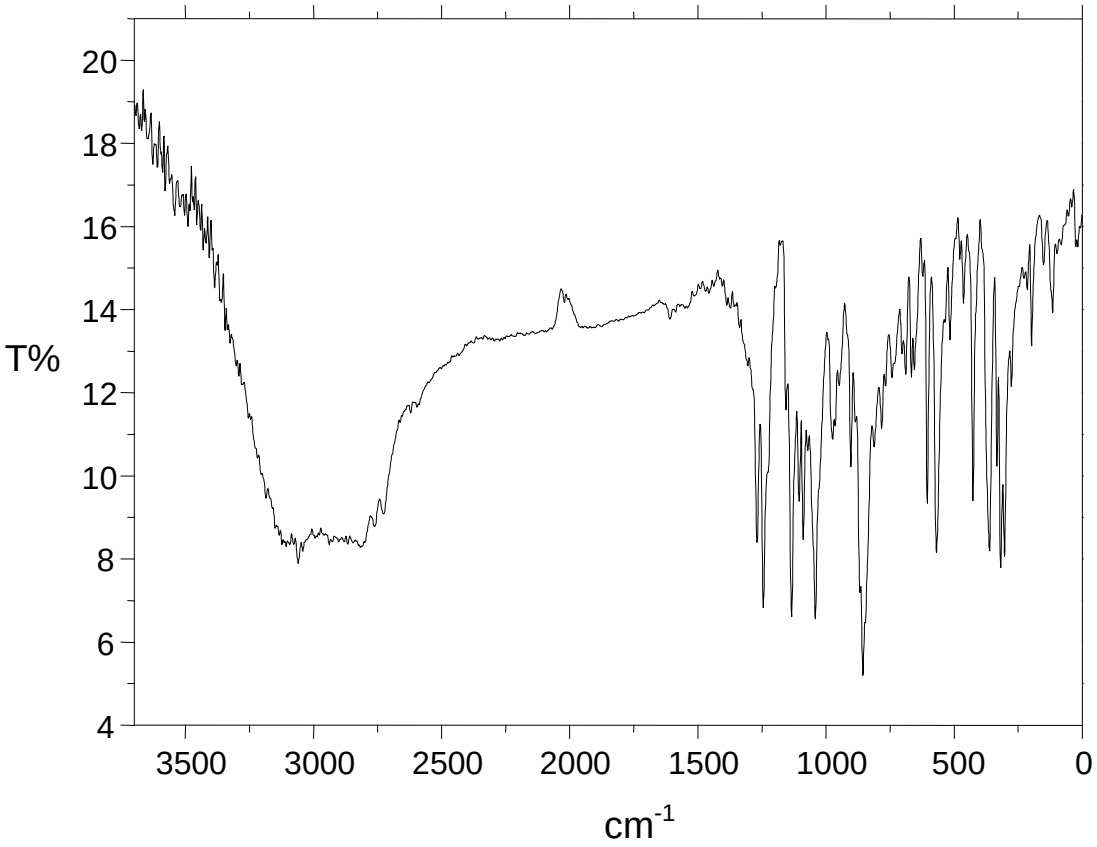
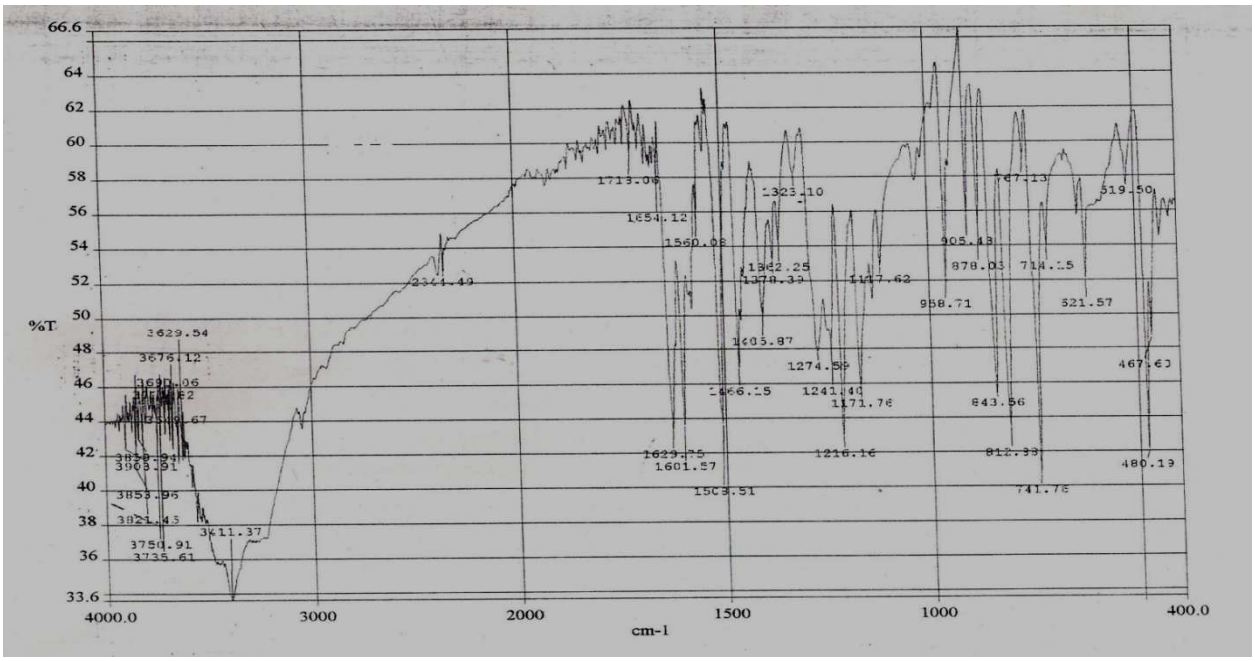
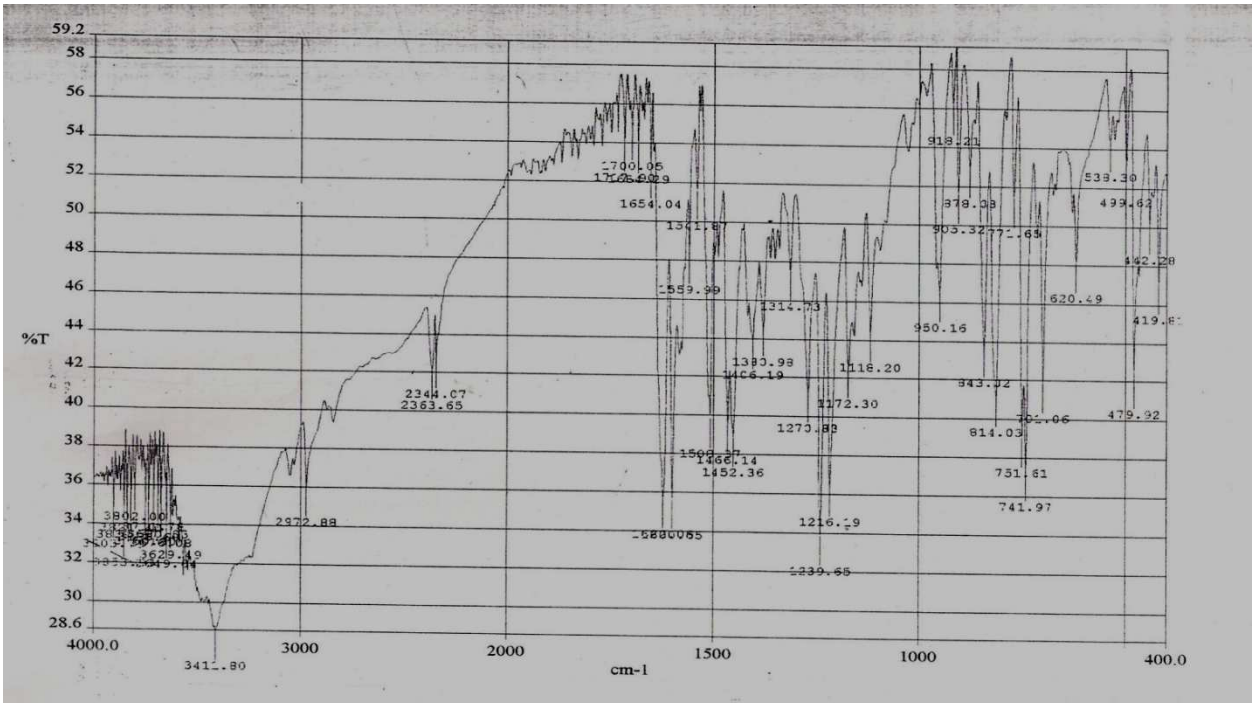
Appendixes



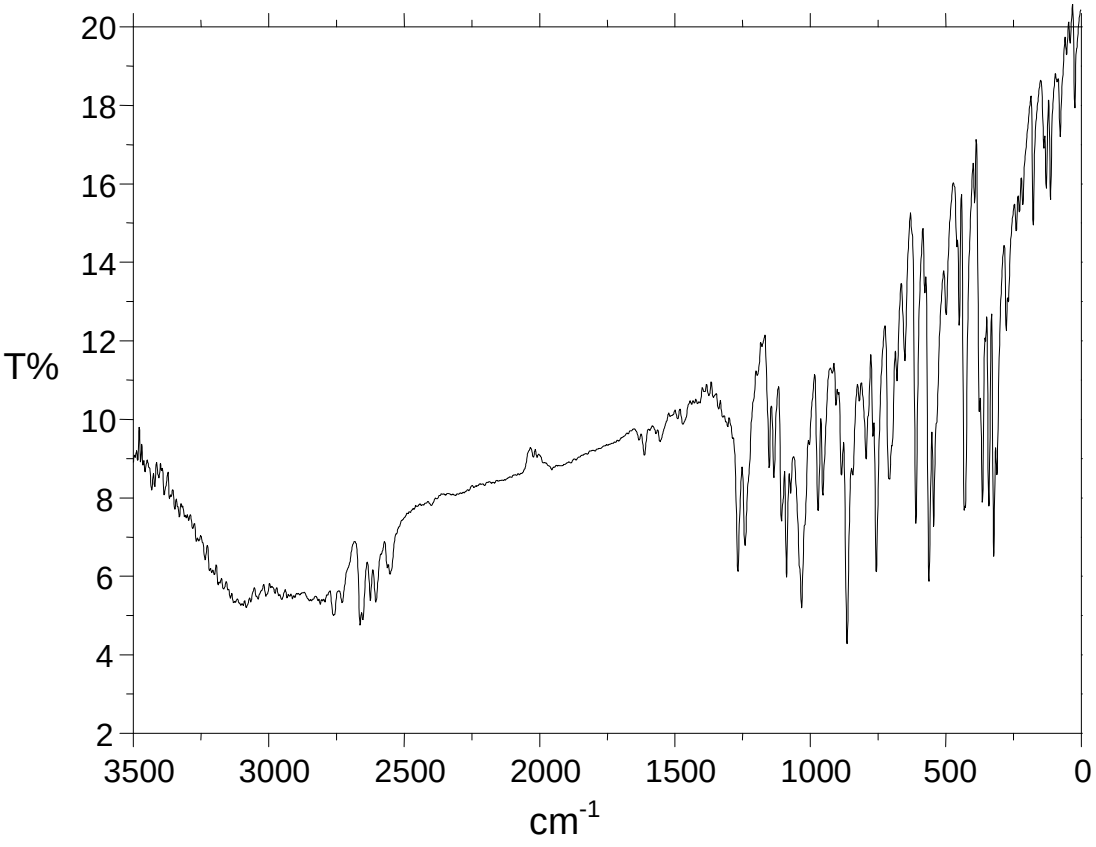
Appendix 1: IR spectra of 1,3-Diphenyl-nitroaniline -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine I



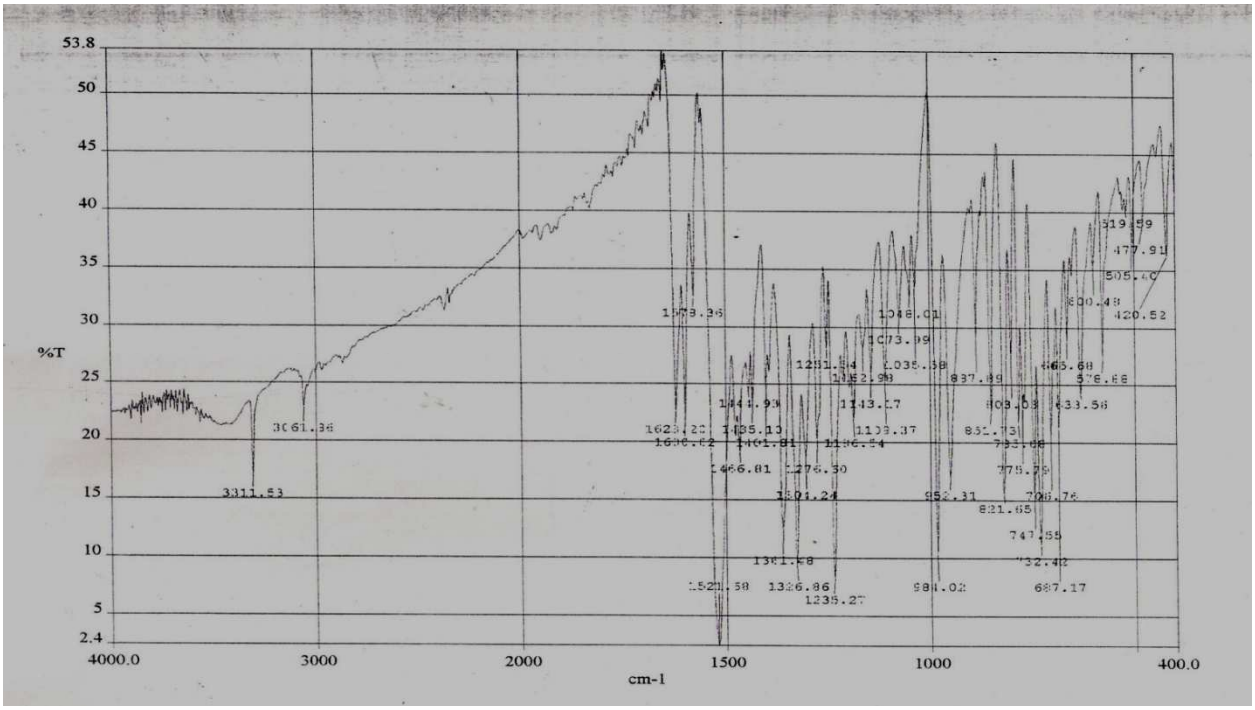
Appendix 2: IR spectra of 1,3-Di-4,4-dimethoxy phenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine II



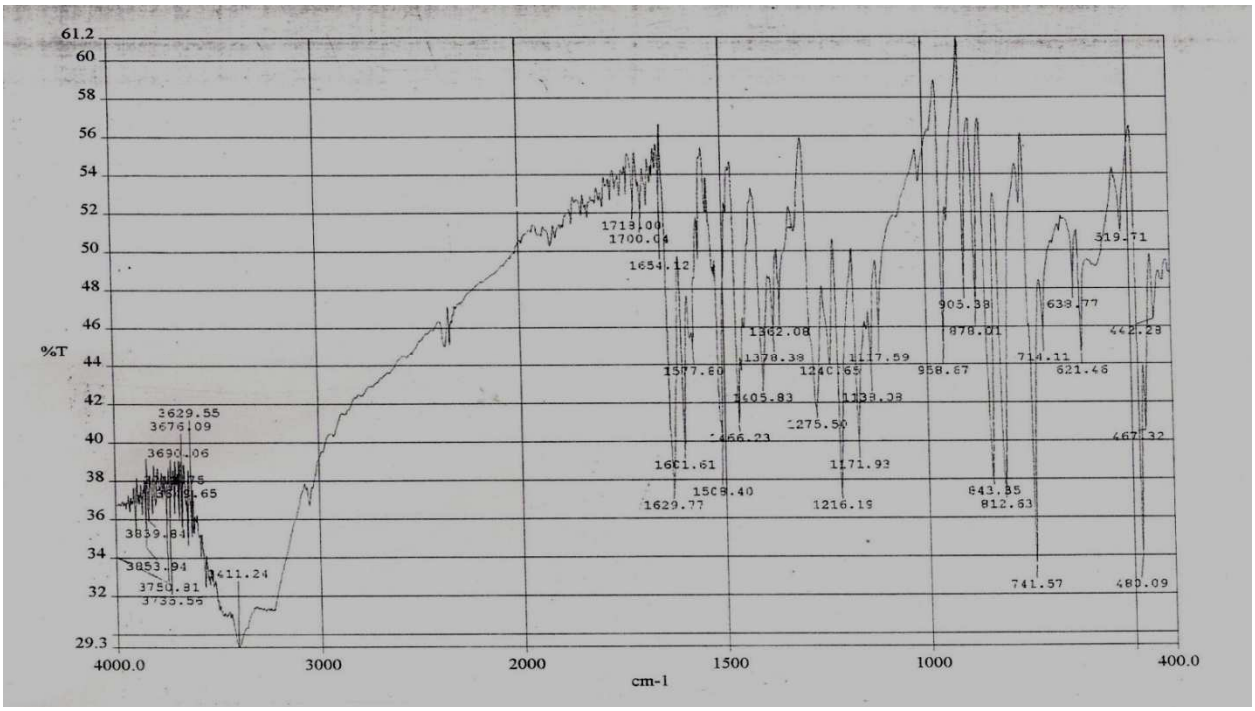
Appendix 3: IR spectra of 1,3-Di-2-nitrophenyl-3-nitrophenyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine III



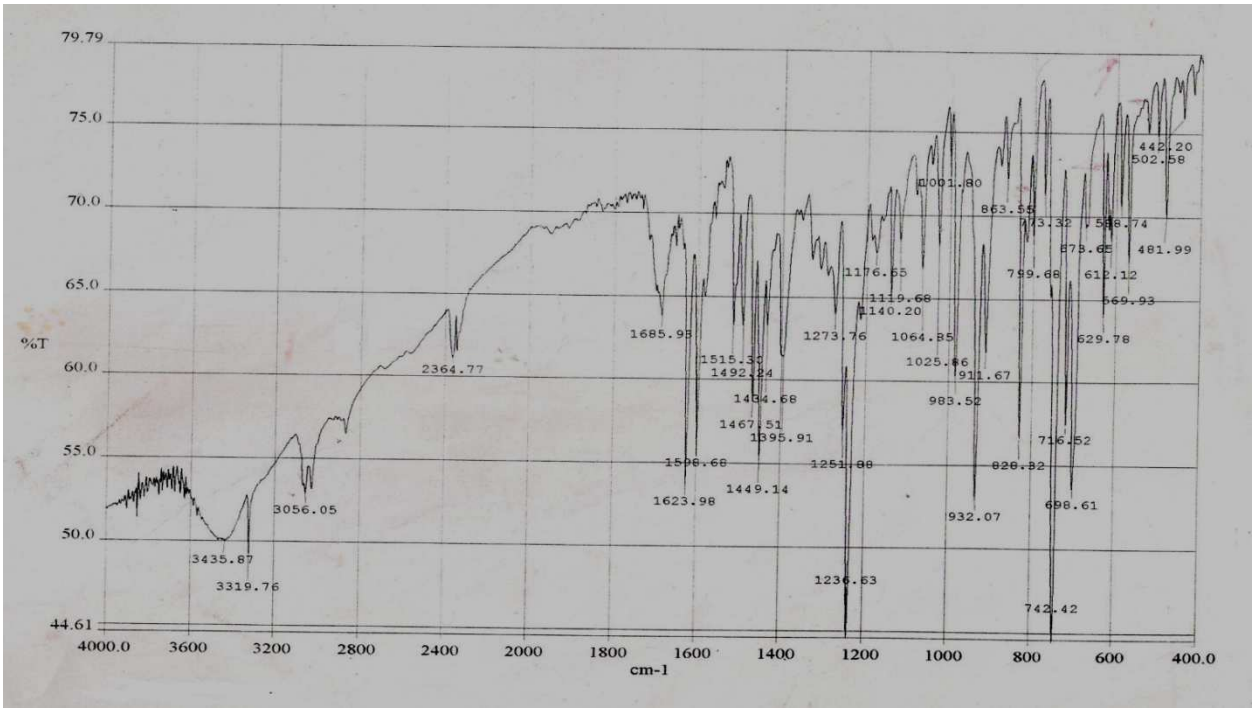
Appendix 4: IR spectra of 1,3-diphenyl-2-propyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine VI



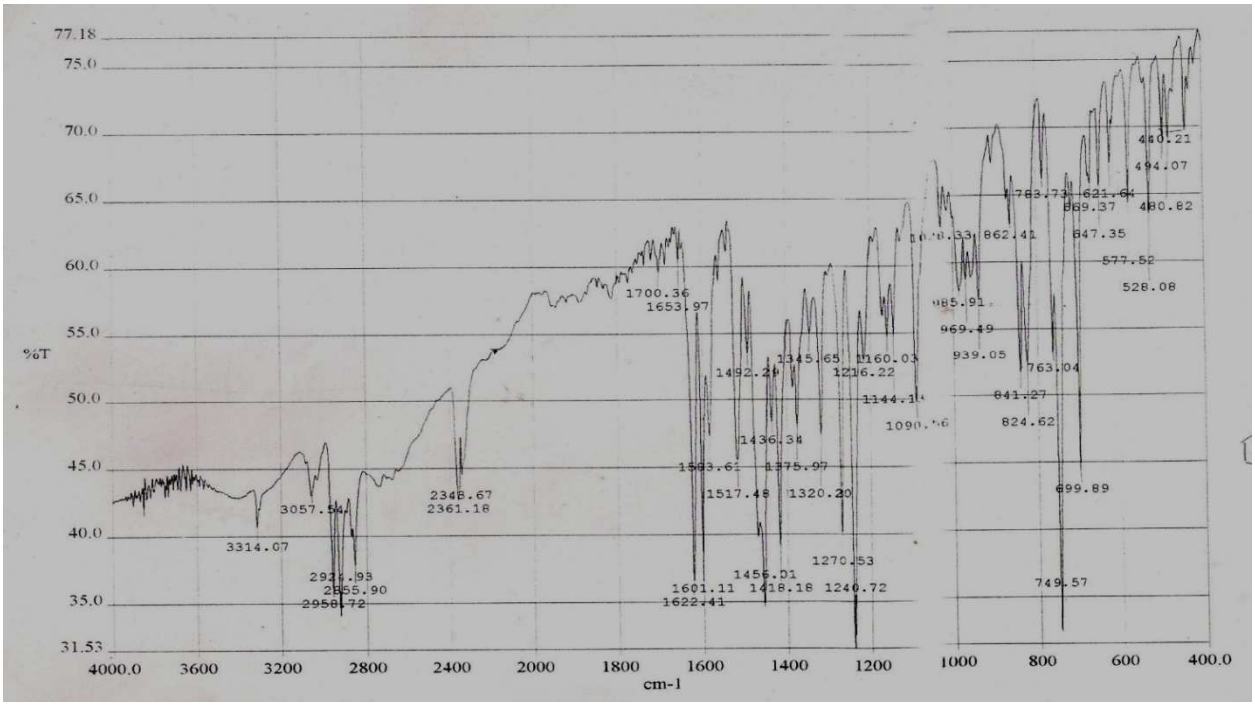
Appendix 5: IR spectra of 1,3-Di-*o*-hydroxyphenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine VII



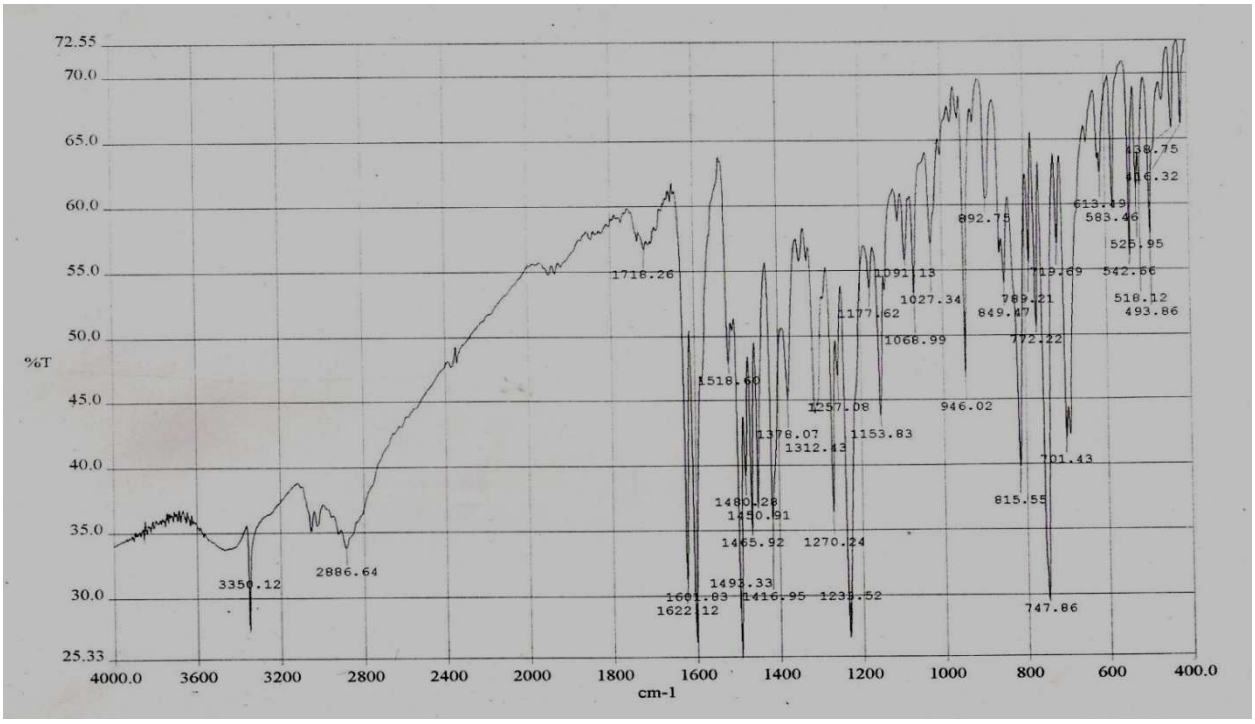
Appendix 6: IR spectra of 1,3-Di-*o*-nitrophenyl-2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine VIII



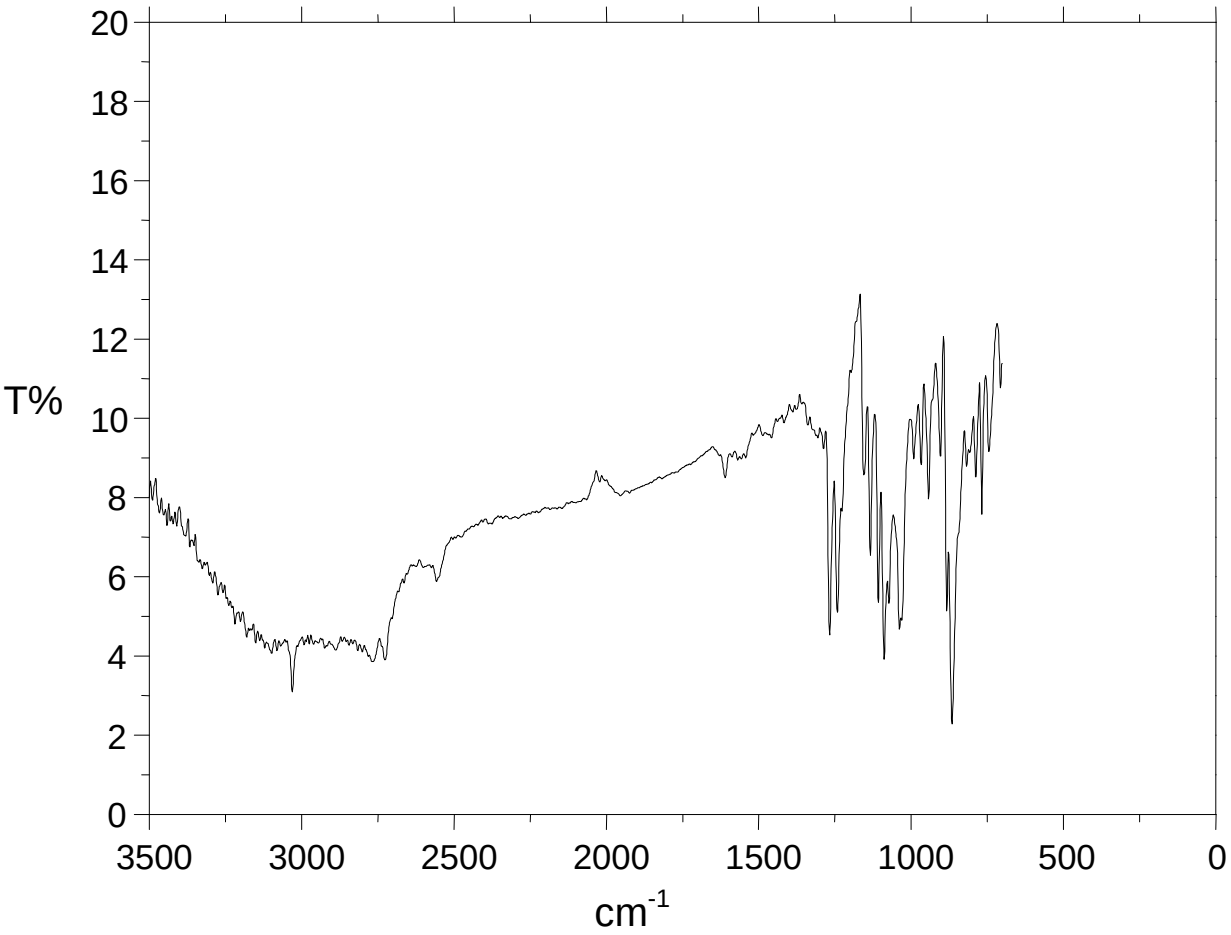
Appendix 7: IR spectra of 1,3-diphenyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine IX



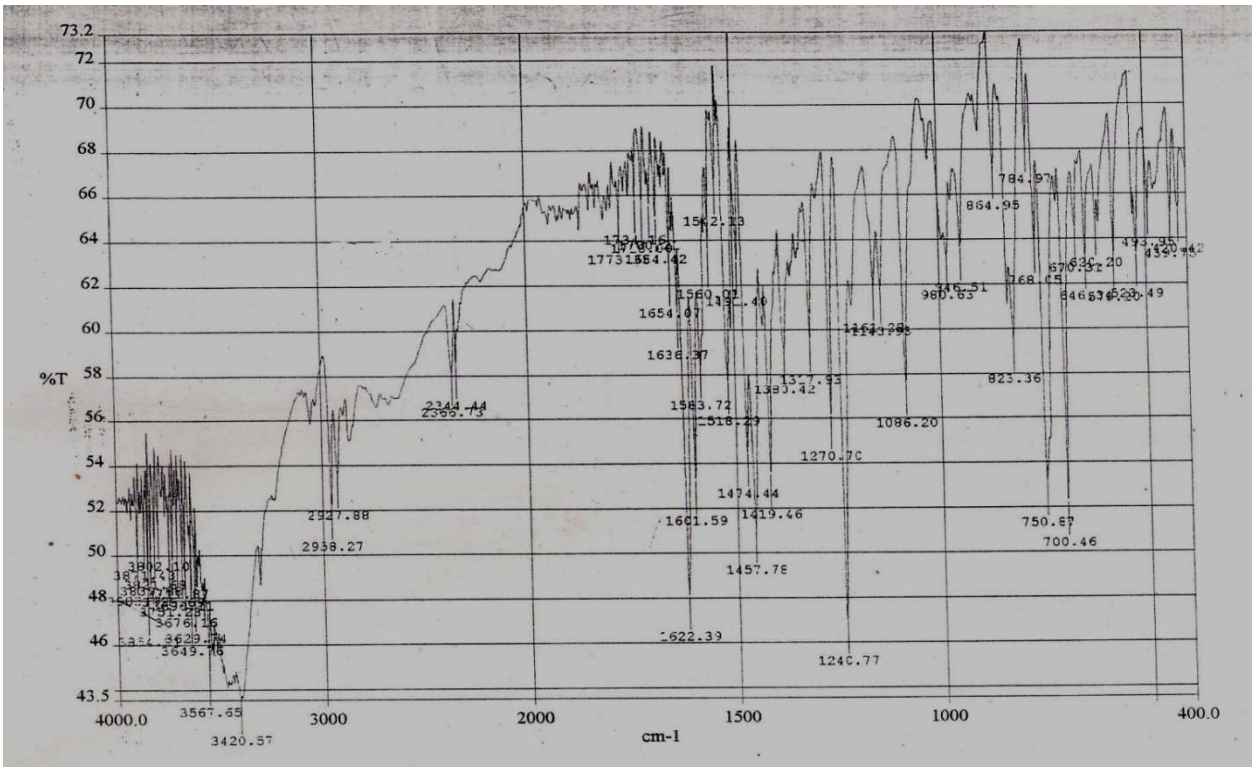
Appendix 8: IR spectra of 1,3-distyryl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3] oxazine XII



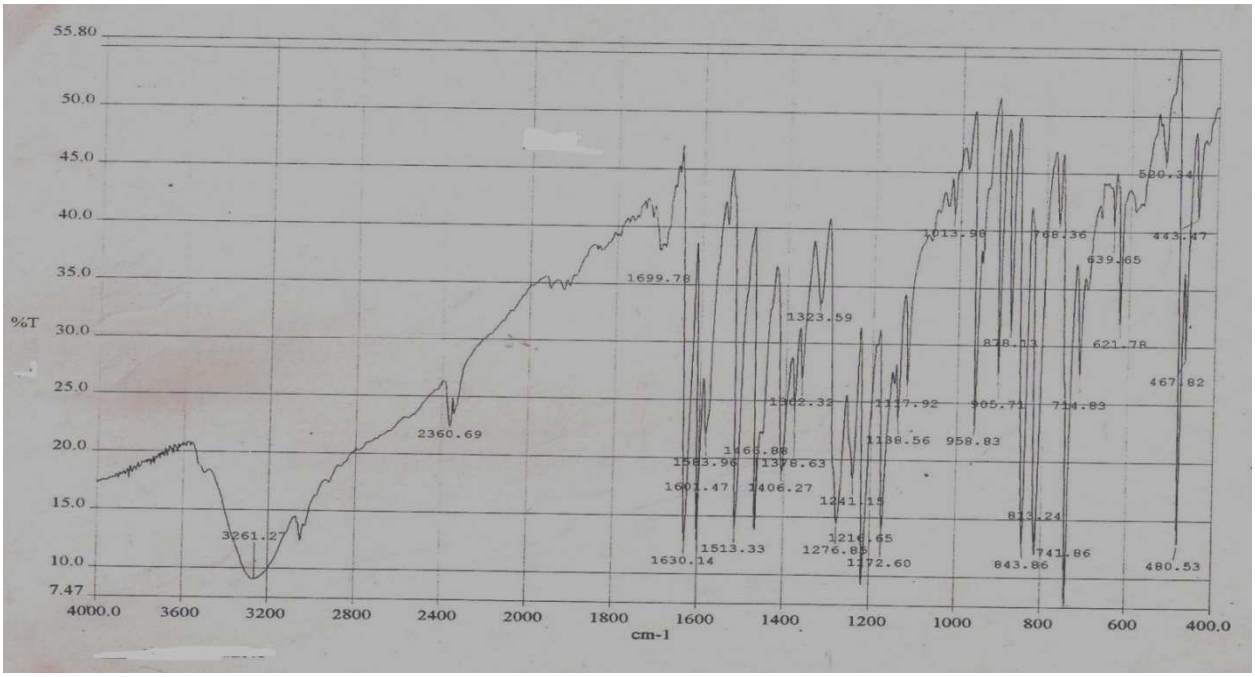
Appendix 9: IR spectra of 1-(α-phenyl-aminobenzyl)-2-naphthol XV



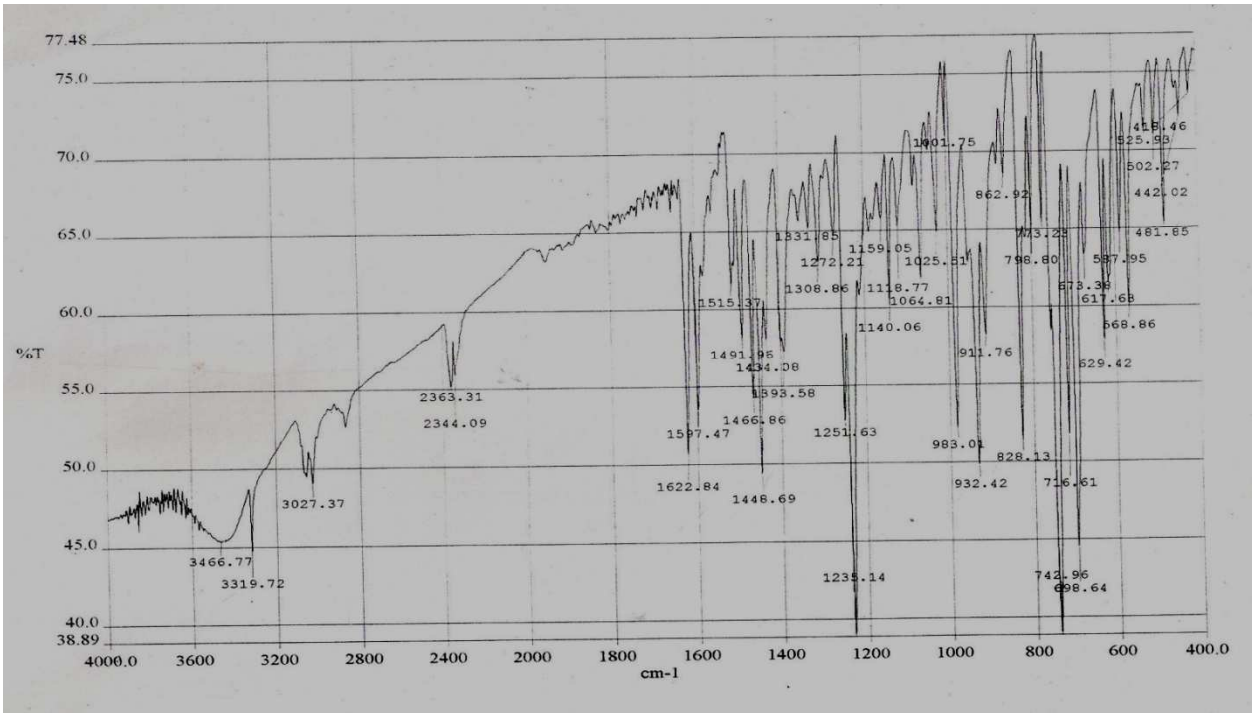
Appendix 10: IR spectra of 1-[α-amino-4-methoxybenzyl]-2-naphthol XVI



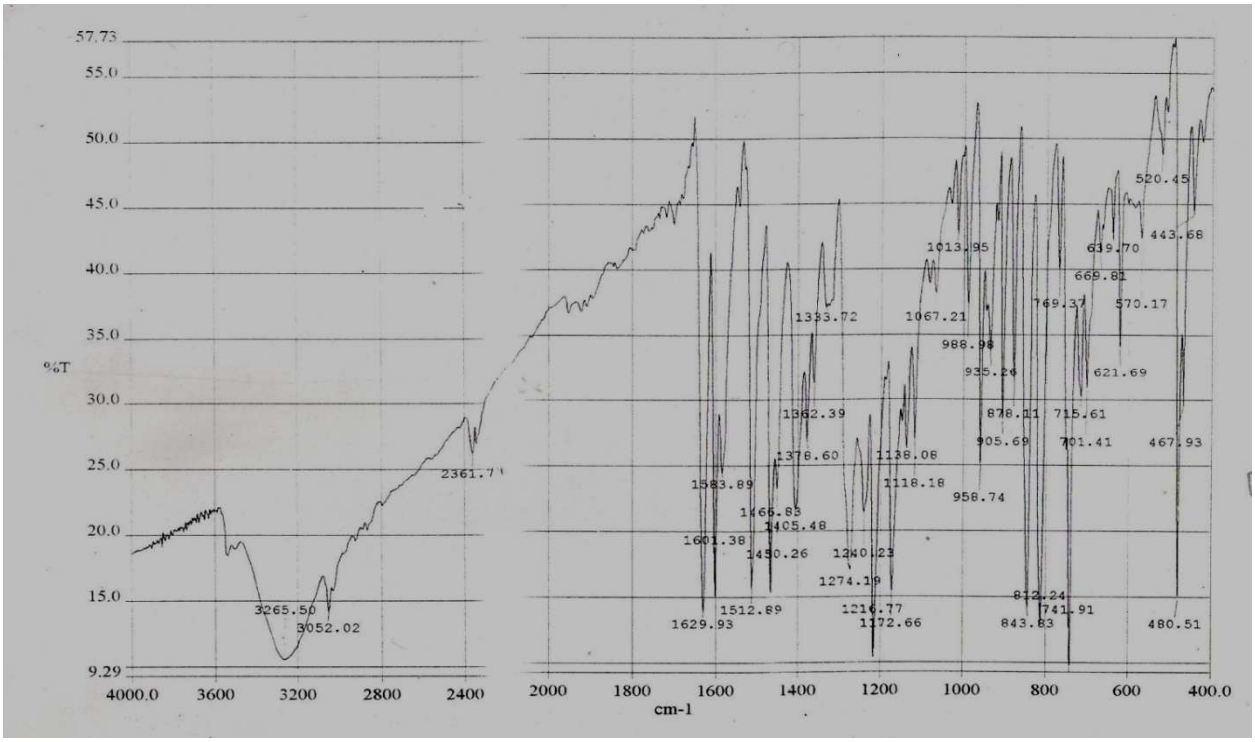
Appendix 11: IR spectra of 1-[α-*N*-propylaminobenzyl]-2-naphthol XX



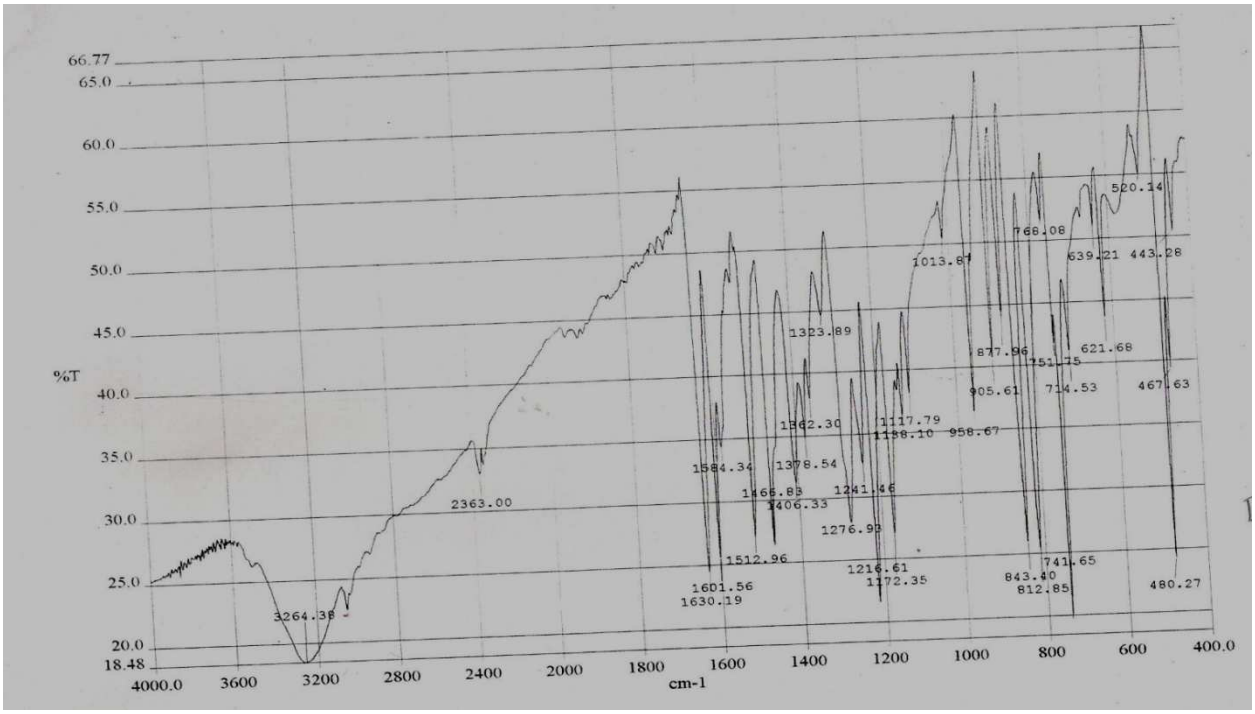
Appendix 12: IR spectra of 1-[α-aminobenzyl]-2-naphthol XXIII



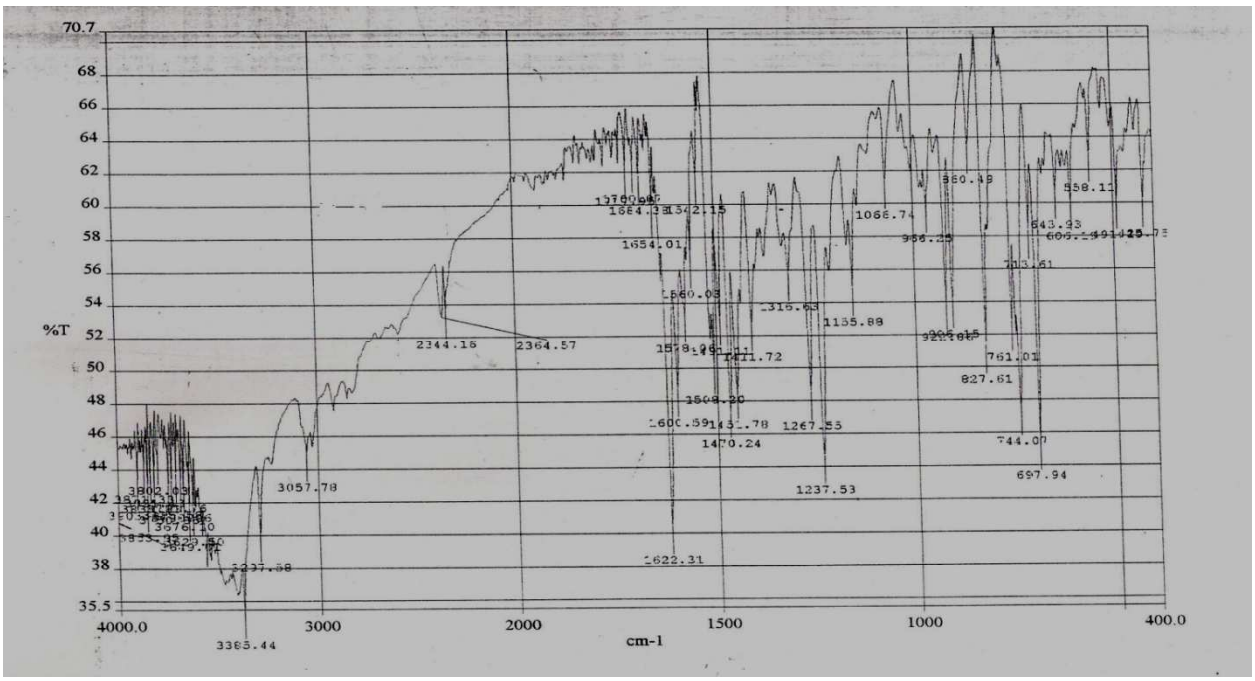
Appendix 13: IR spectra of 3-(α-amino-4-methoxybenzyl-benzene sulfonamide)-2-naphthol XXVI



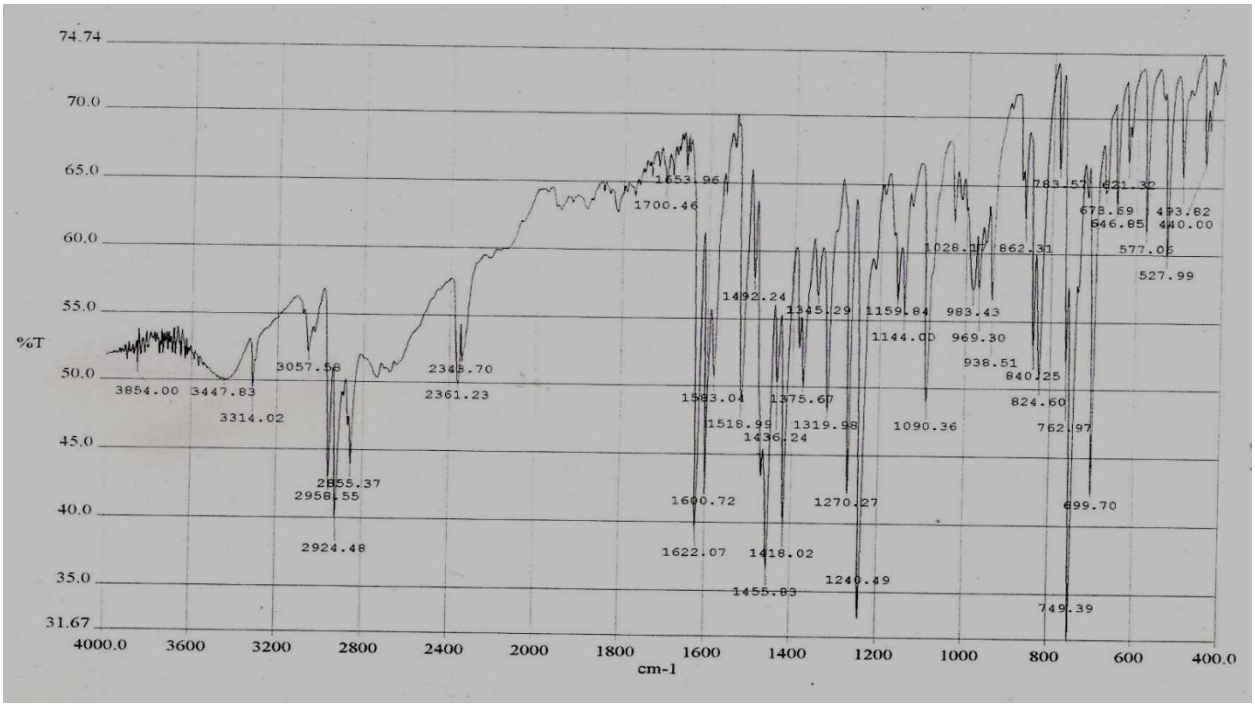
Appendix 14: IR spectra of 1-(α-methylaminobenzyl)-2-naphthol XXVIII



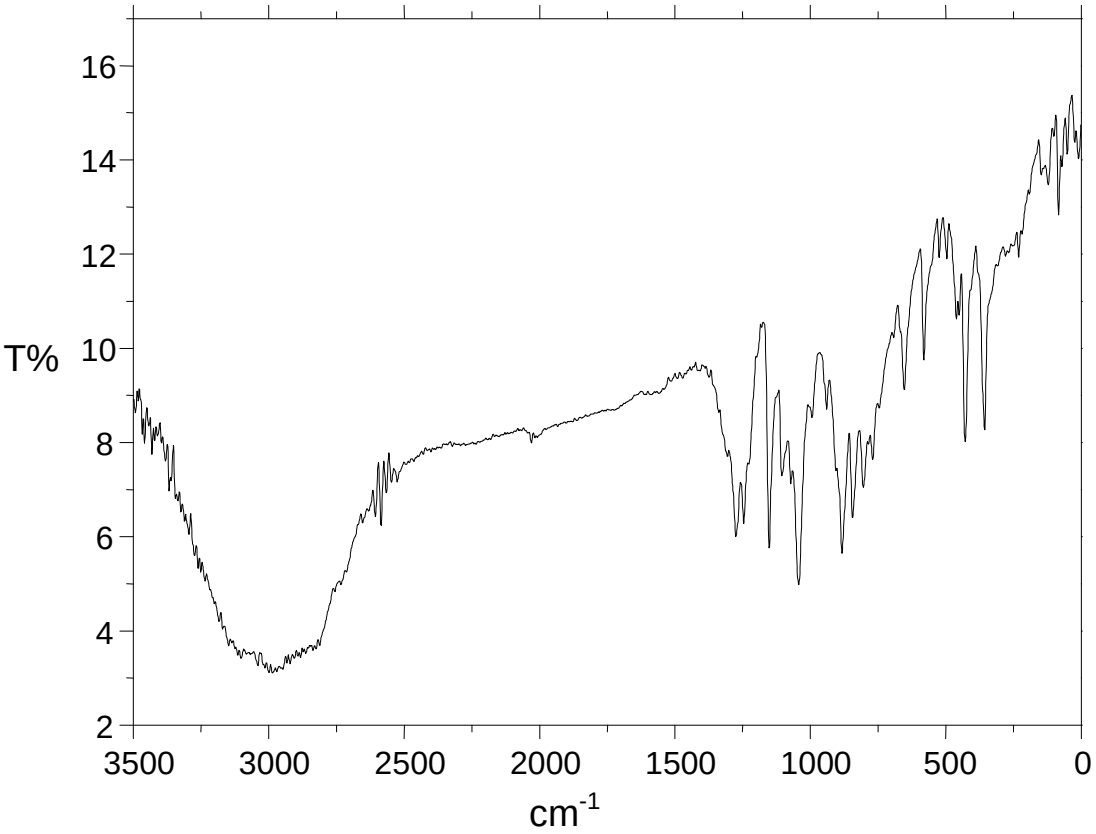
Appendix 15: IR spectra of 1-(α-diethylaminobenzylyl)-2-naphthol XXIX



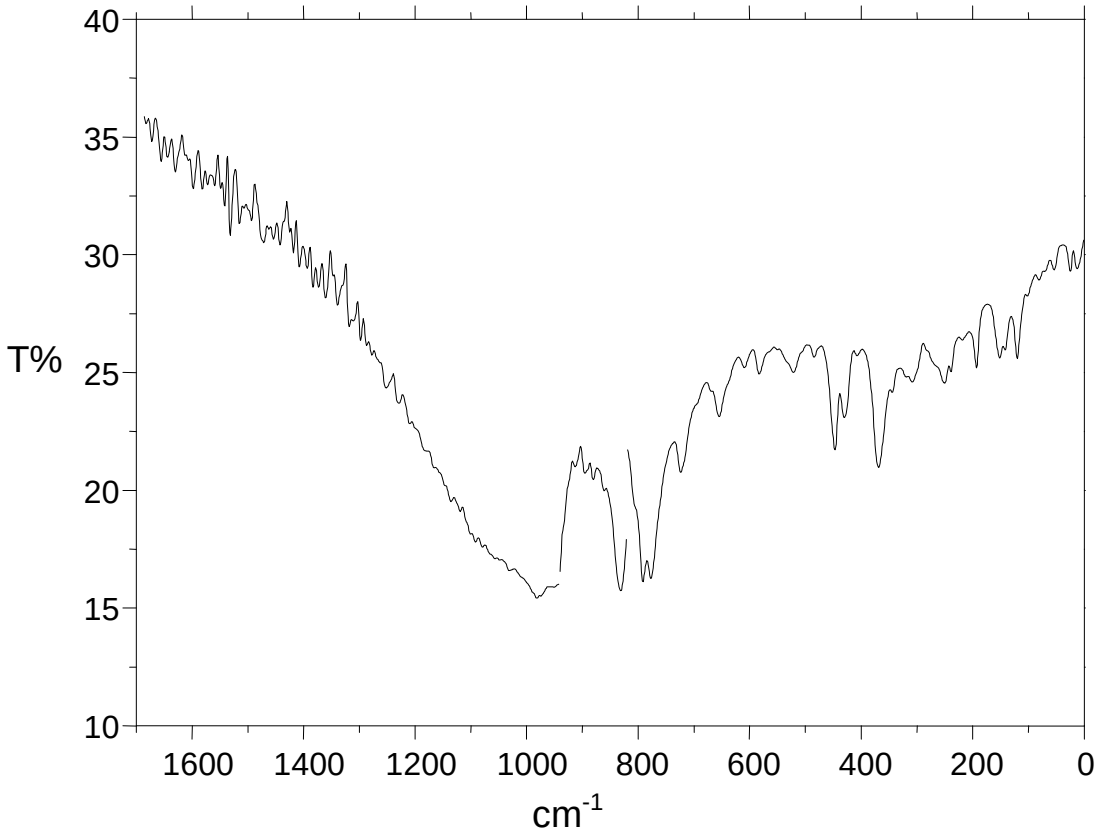
Appendix 16: IR spectra of 1-(α-benzylpyrrolidine)-2-naphthol XXX



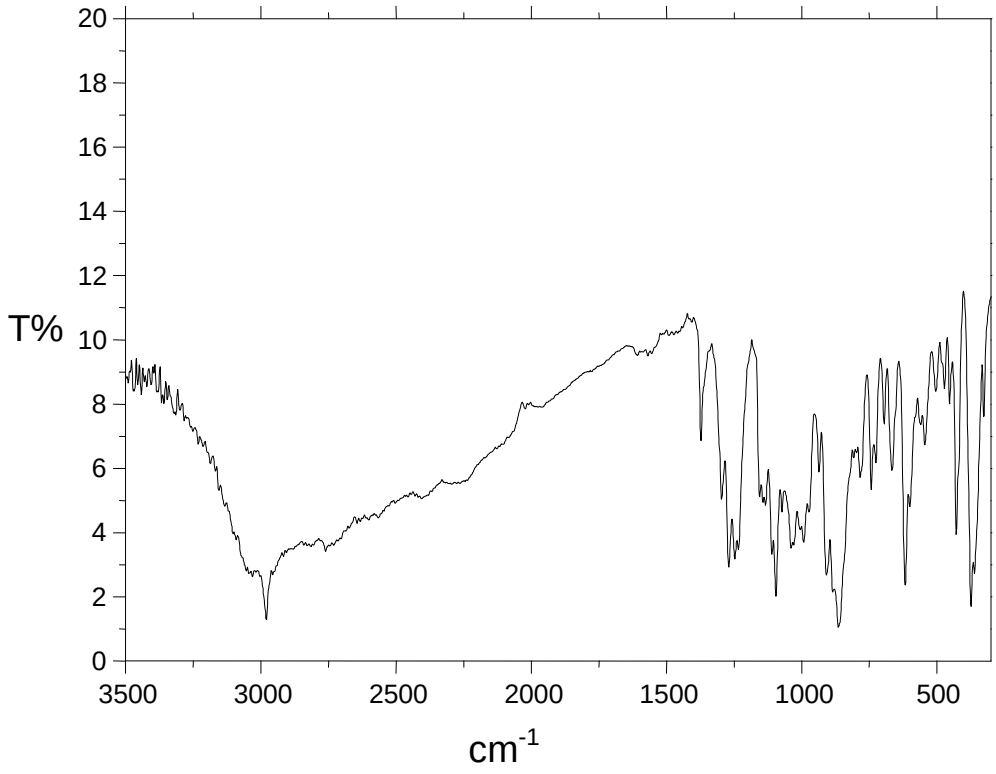
Appendix 17: IR spectra of 1-(α-butylaminobenzyl)-2-naphthol XXXI



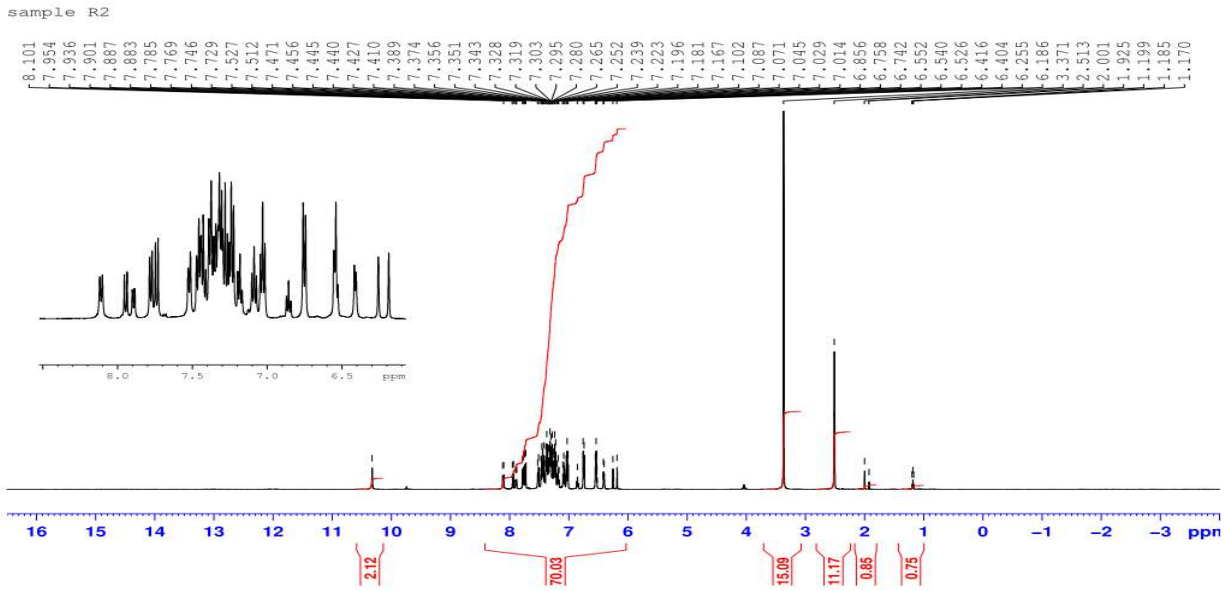
Appendix 18: IR spectra of 1-(amino-4-methoxyphenyl-3-hydroxynaphthol) -diazoniumacetophenone XXXIII



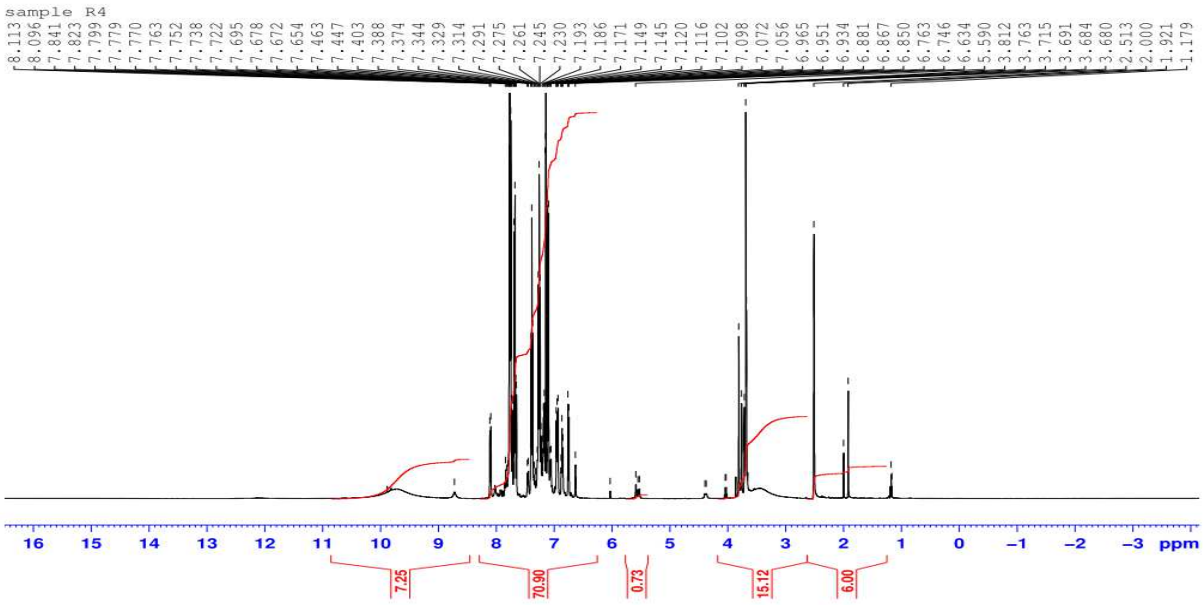
Appendix 19: IR spectra of 4-(3-hydroxy-4-propylaminonaphthol)-diazoniumbezene sulfonamide XXXV



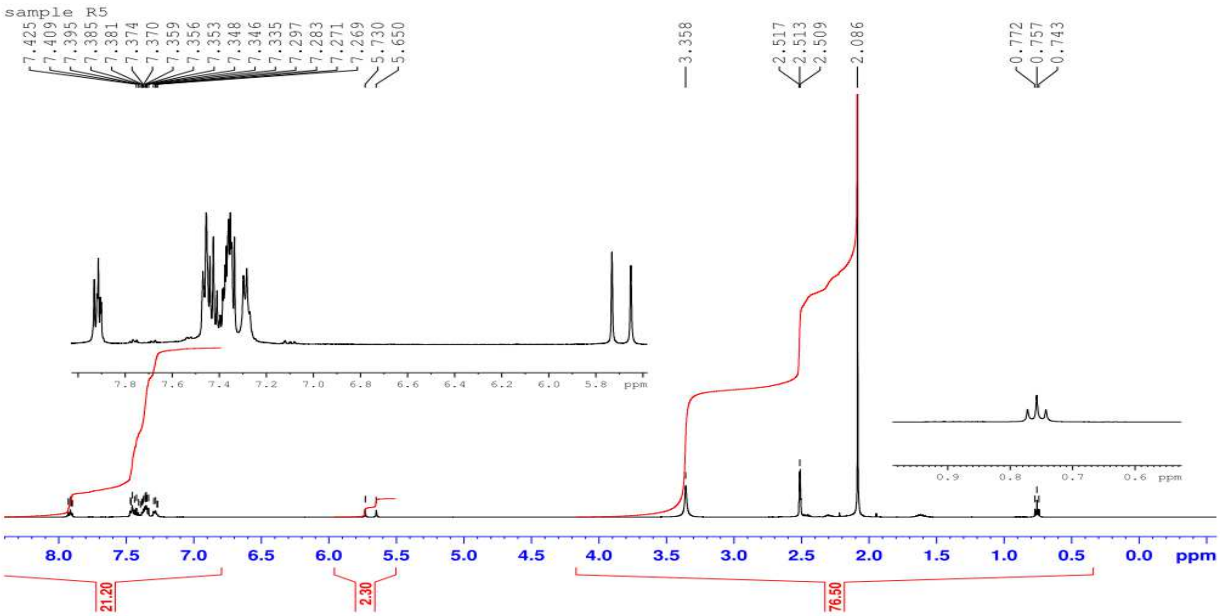
Appendix 20: IR spectra of 4-(aminophenyl-3-hydroxynaphthol)-diazoniumbenzene sulfonamide XXXX



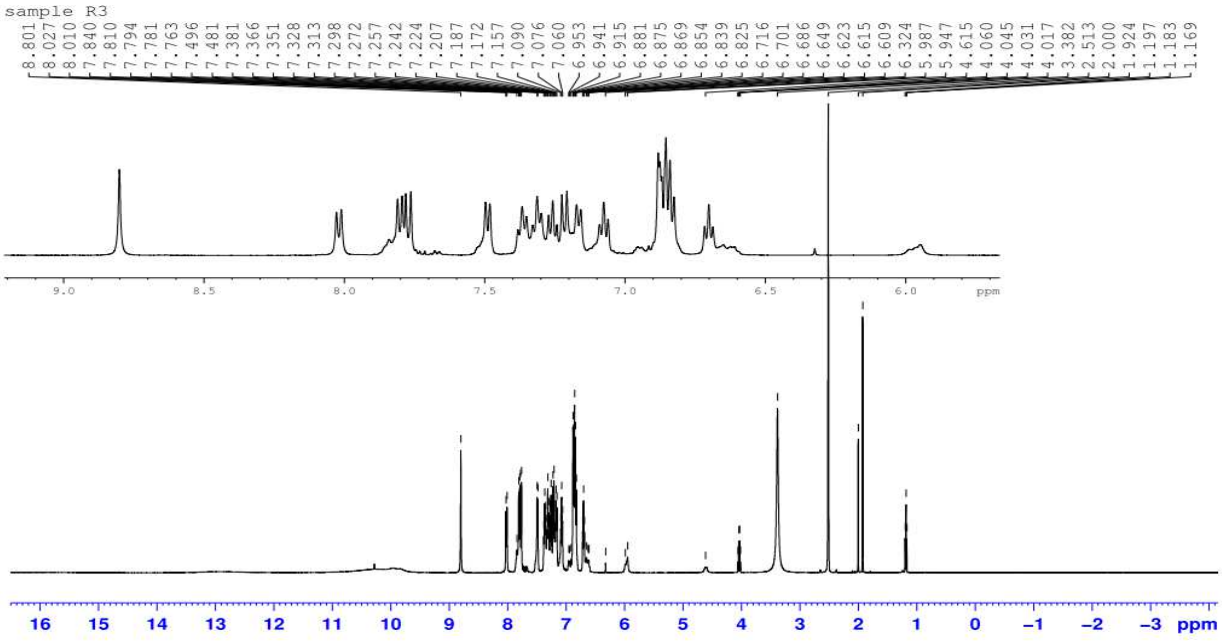
Appendix 21: ^{1}H – NMR spectra of 1,3-Diphenyl-nitroaniline -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine I



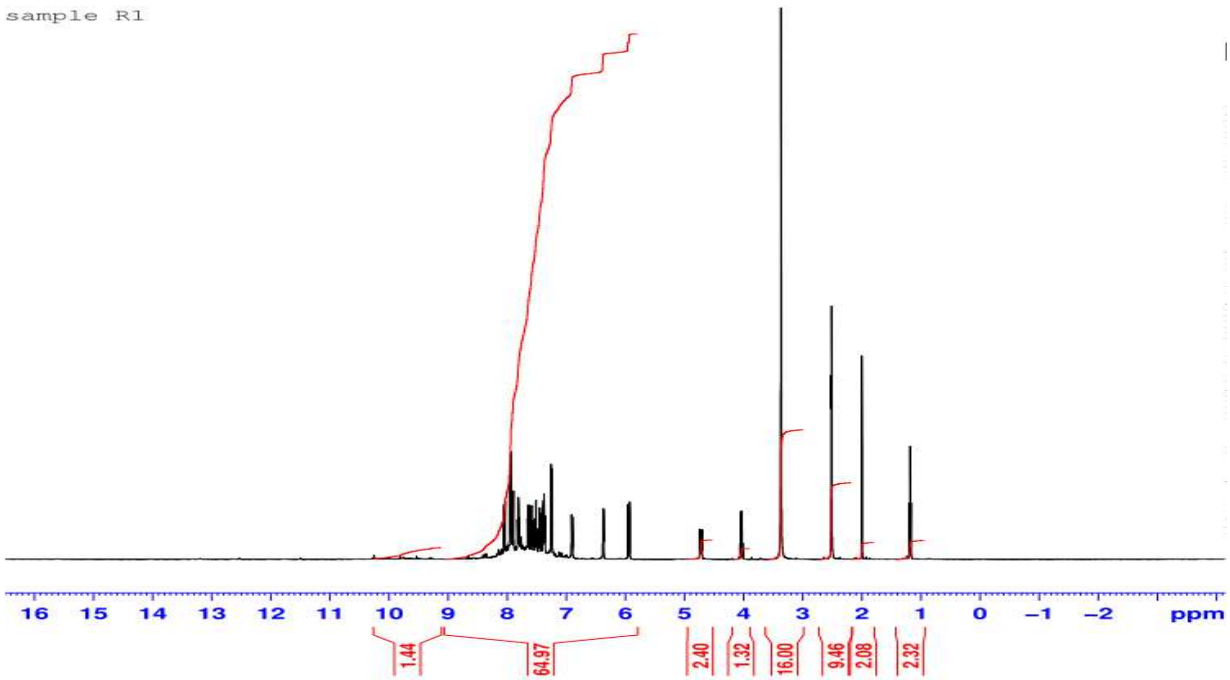
Appendix 22: ^{1}H – NMR spectra of 1,3-Di-4,4-dimethoxy phenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine II



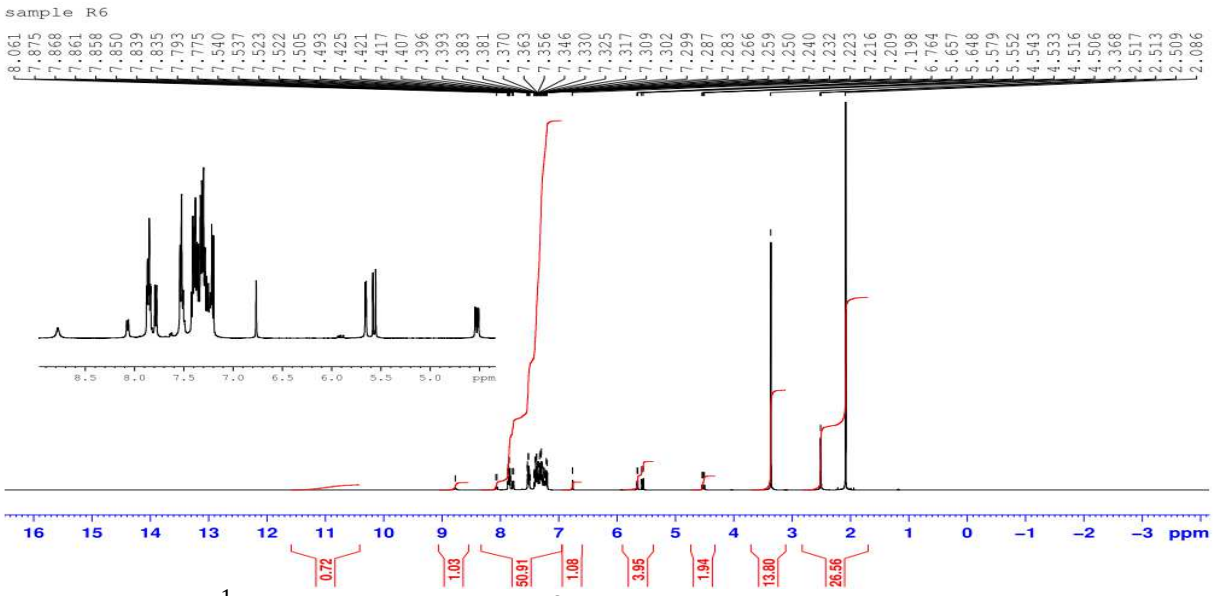
Appendix 23: ^{1}H – NMR spectra of 1,3-diphenyl-2-propyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine VI



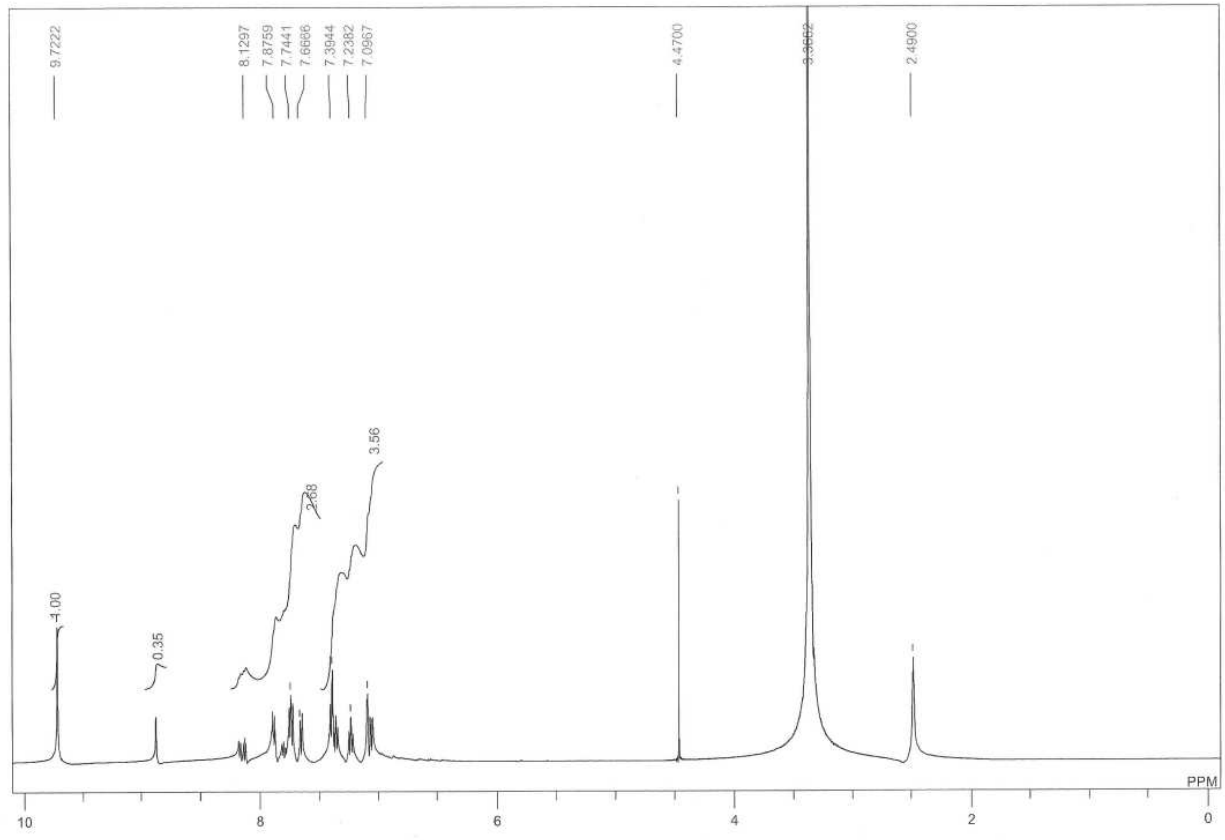
Appendix 24: ^{1}H – NMR spectra of 1,3-Di-*o*-hydroxyphenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine VII



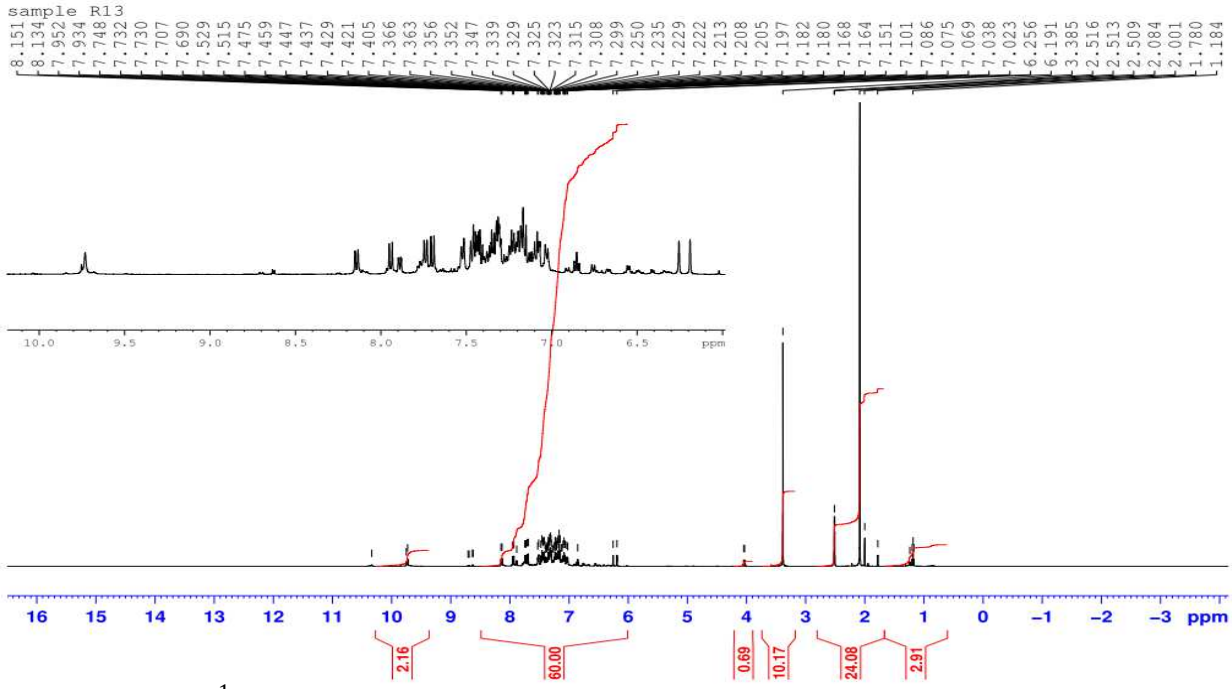
Appendix 25: ^{1}H- NMR spectra of 1,3-Di-*o*-nitrophenyl-2,3-dihydro-1*H*-naphth[1,2-e][1,3] oxazine VIII



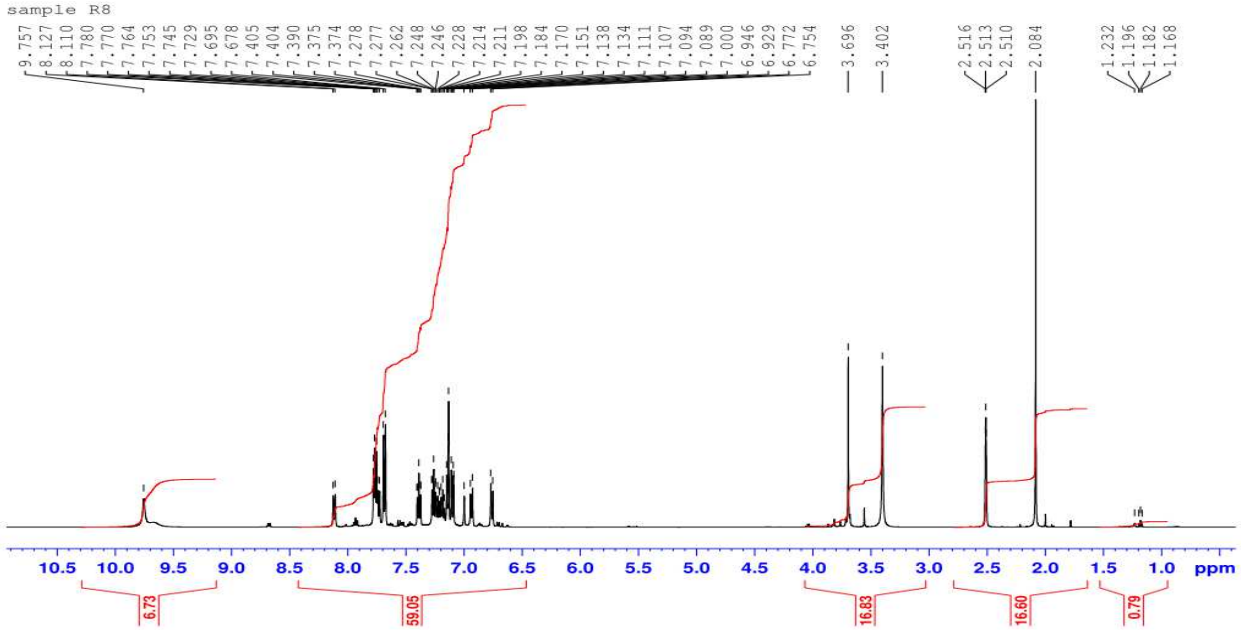
Appendix 26: ^{1}H – NMR spectra of 1,3-diphenyl-2,3-dihydro-1*H*-naphtho [1,2-e][1,3]oxazine IX



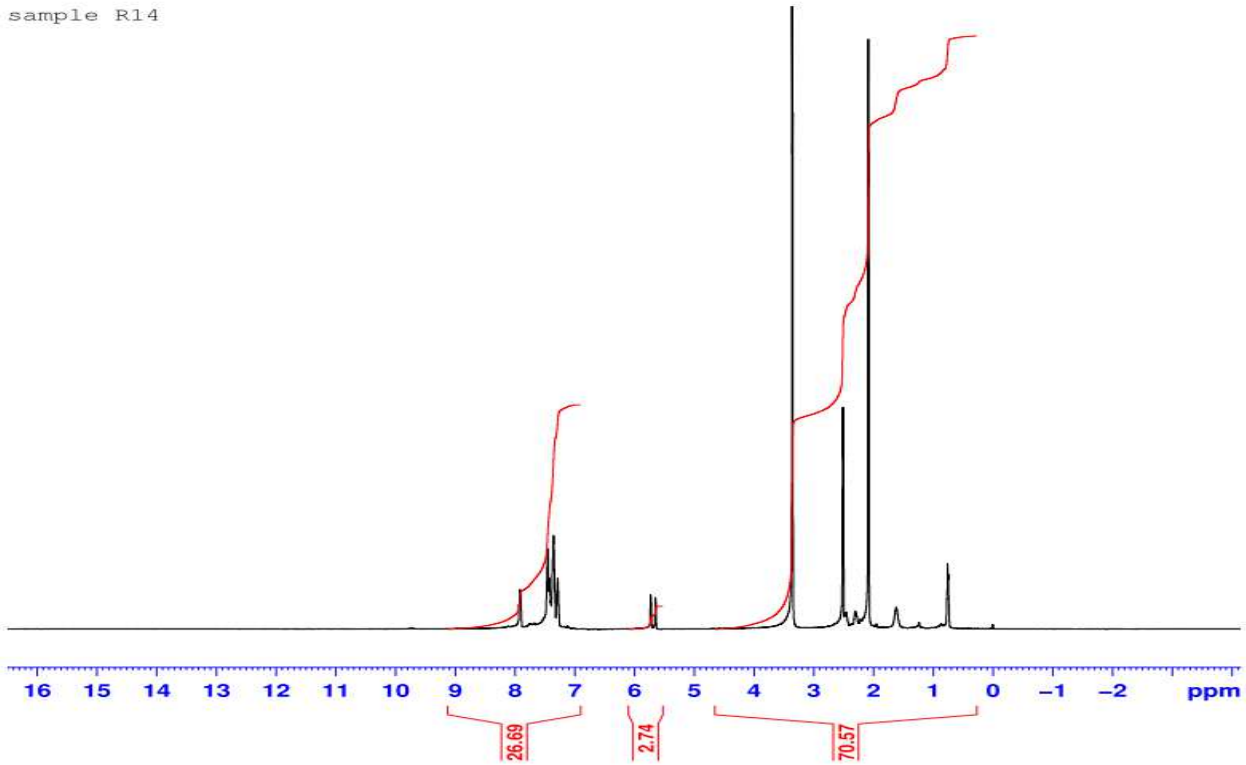
Appendix 27: ^{1}H – NMR spectra of 1,3-Di-*o*-nitrophenyl-2-benzene sulfonamide-1*H*-naphtho[1,2-e][1,3]oxazine XIV



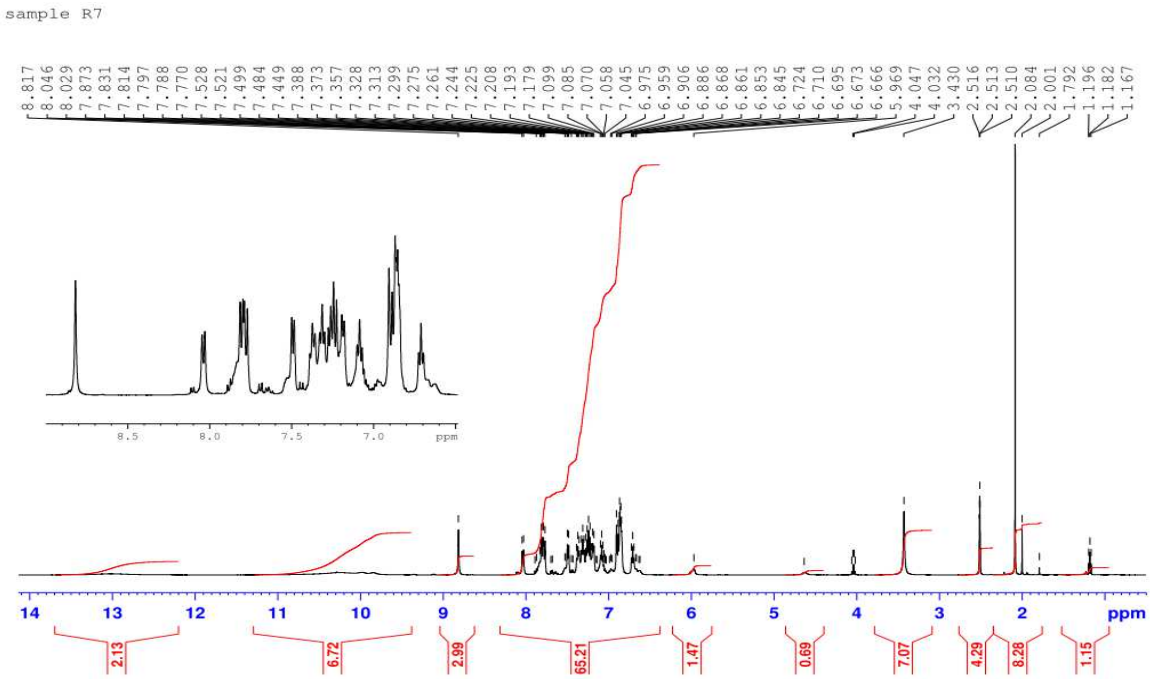
Appendix 28: ^{1}H – NMR spectra of 1-(α-phenyl-phenylamino)-2-naphthol XV



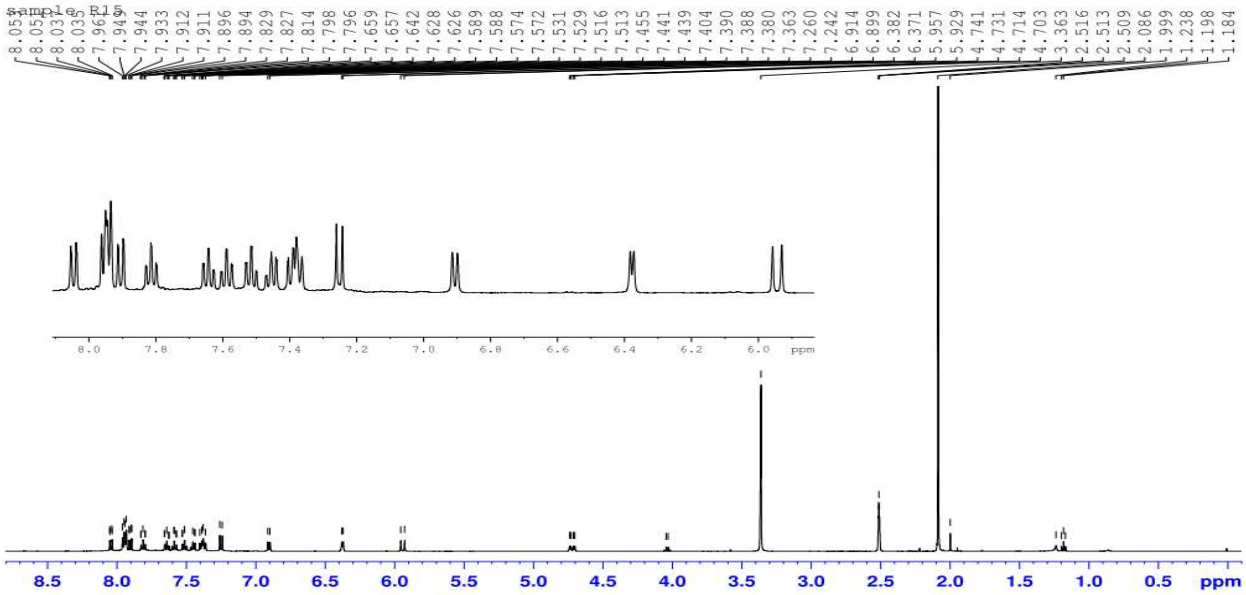
Appendix 29: ^{1}H – NMR spectra of 1-[α-amino-4-methoxybenzyl]-2-naphthol XVI



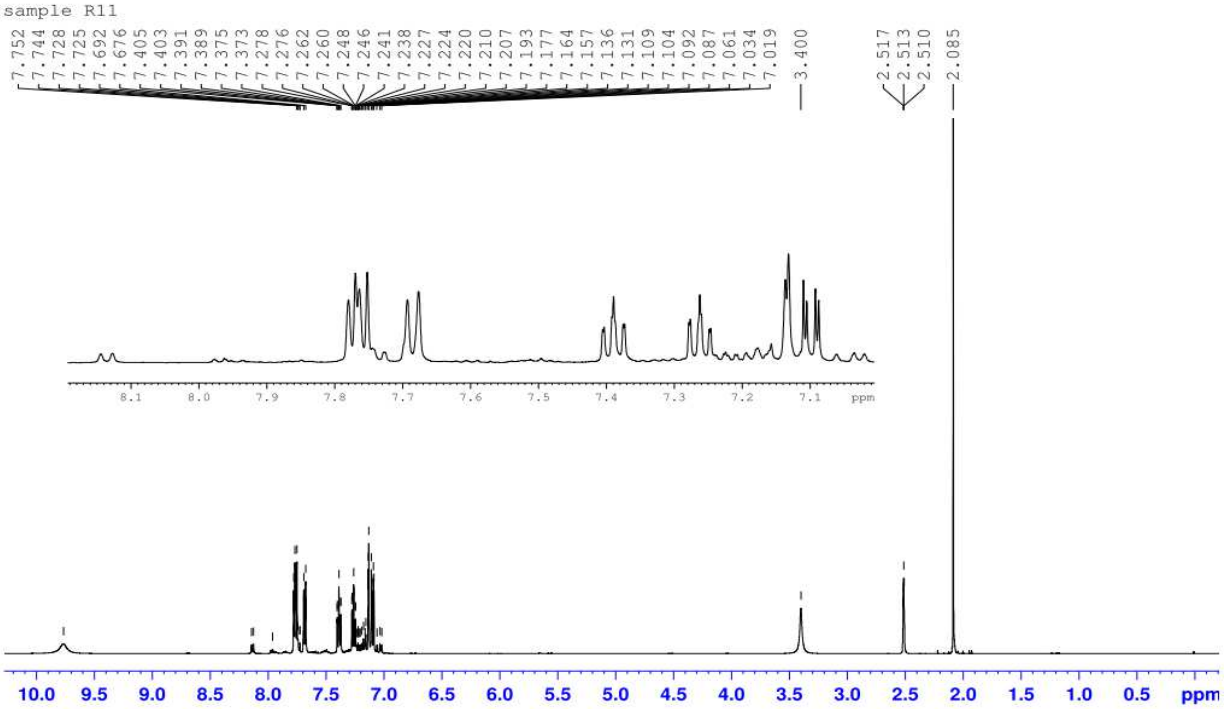
Appendix 30: ^{1}H – NMR spectra of 1-[α-*N*-propylaminobenzyl]-2-naphthol XX



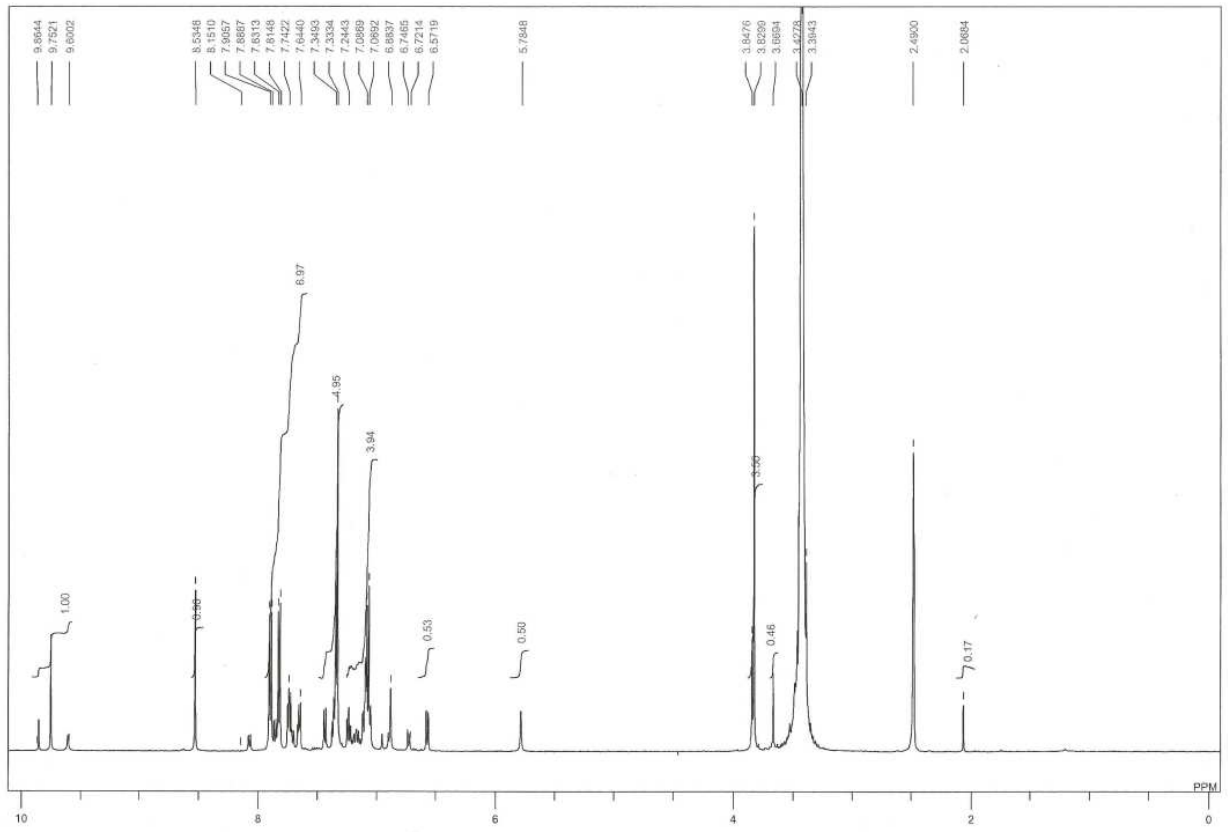
Appendix 31: ^{1}H – NMR spectra of 1-[α-amino-*o*-hydroxybenzyl)]-2-naphthol XXI



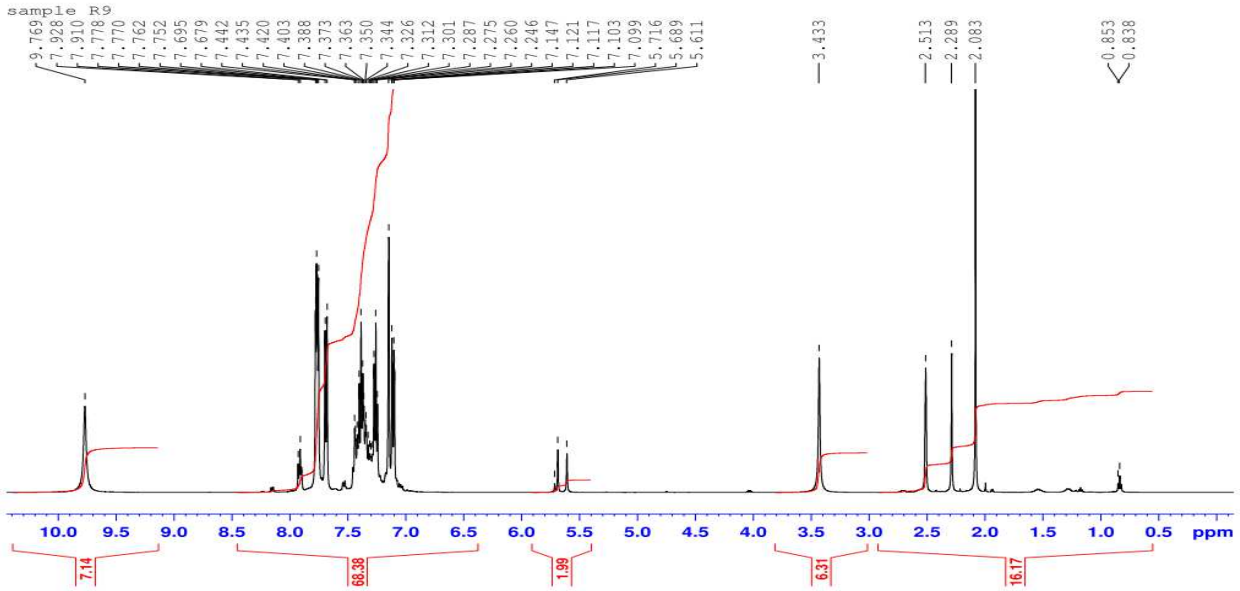
Appendix 32: ^{1}H – NMR spectra of 1-[α-amino-o-nitrobenzyl)]-2-naphthol XXII



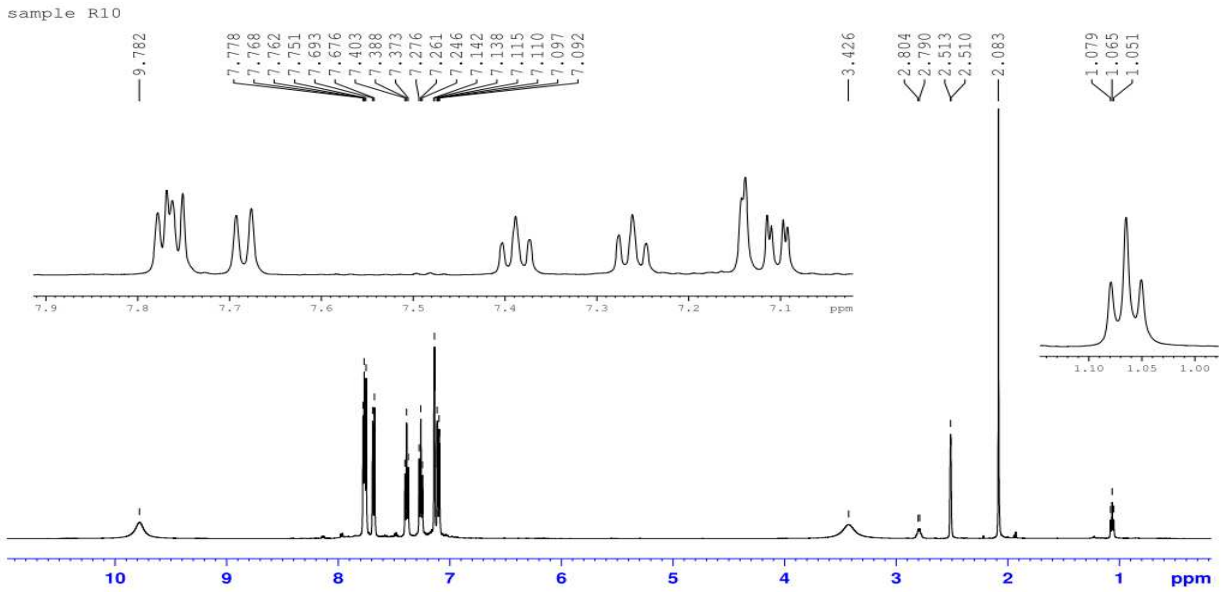
Appendix 33: ^{1}H – NMR spectra of 1-[α-aminobenzyl]-2-naphthol XXIII



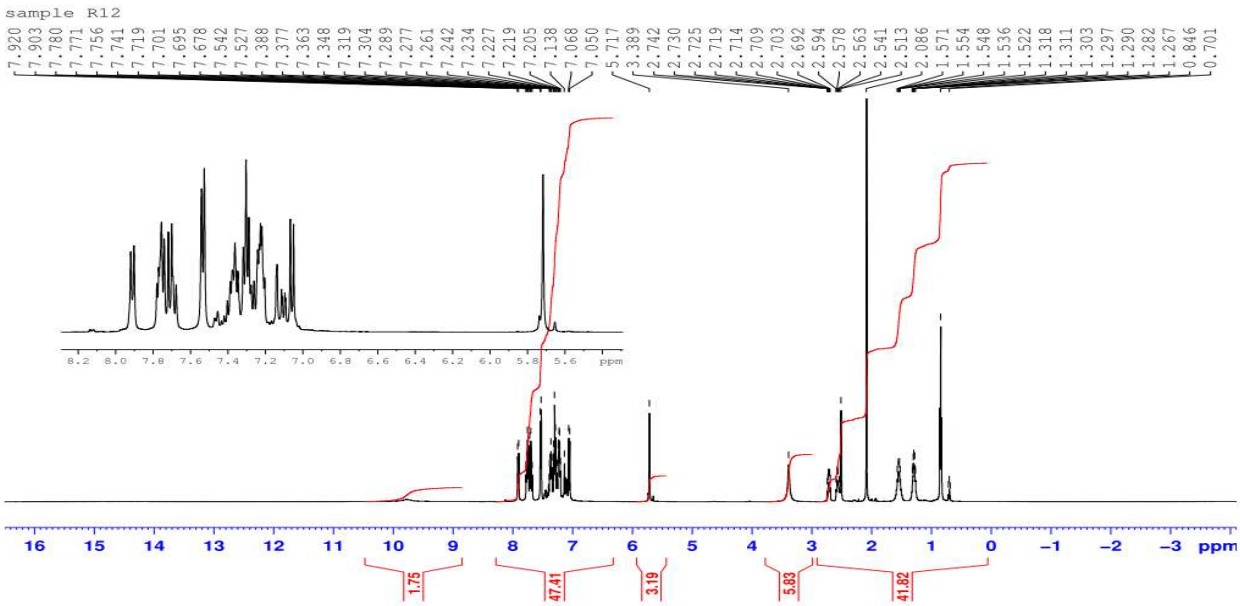
Appendix 34: ^{1}H – NMR spectra of 4-(2-hydroxy-4-methoxyaminobenzyl-benzenesulfonamide)-2-naphthol XXV



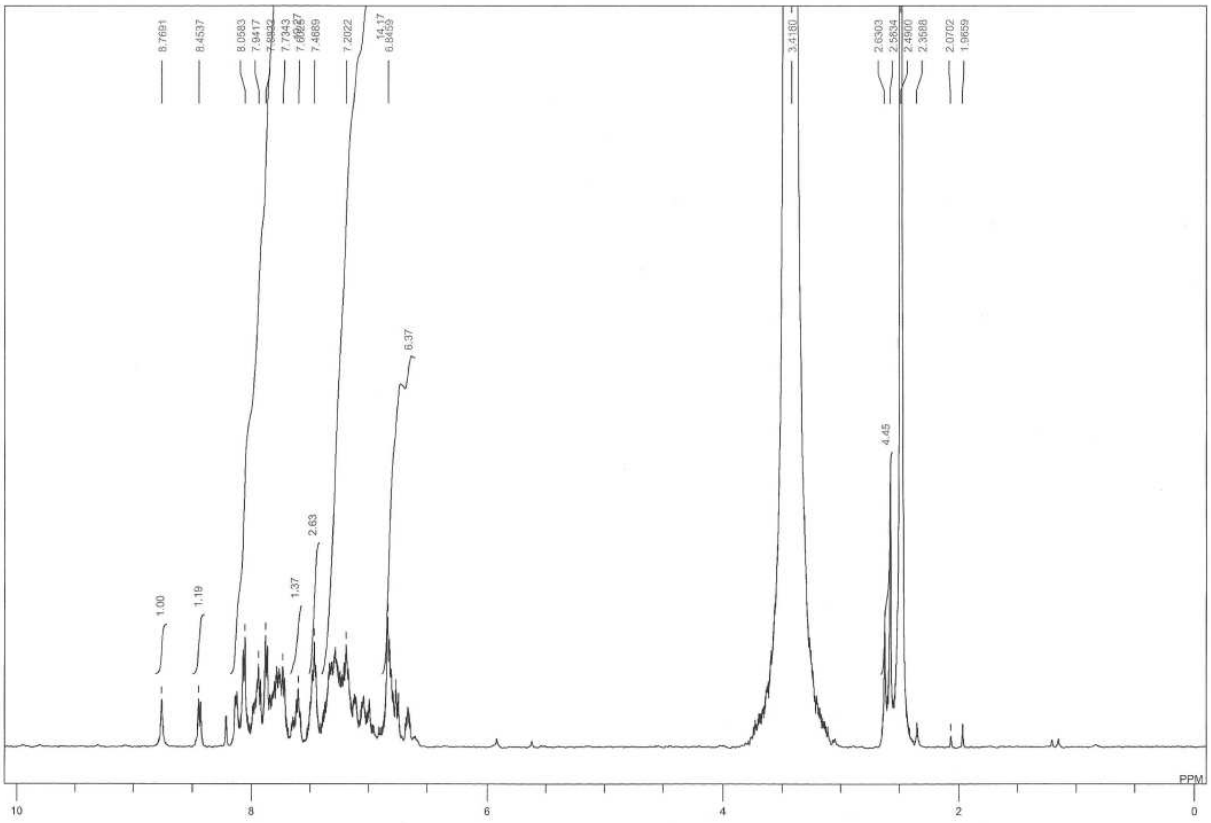
Appendix 35: ^{1}H – NMR spectra of 1-(α-methylaminophenyl)-2-naphthol XXVIII



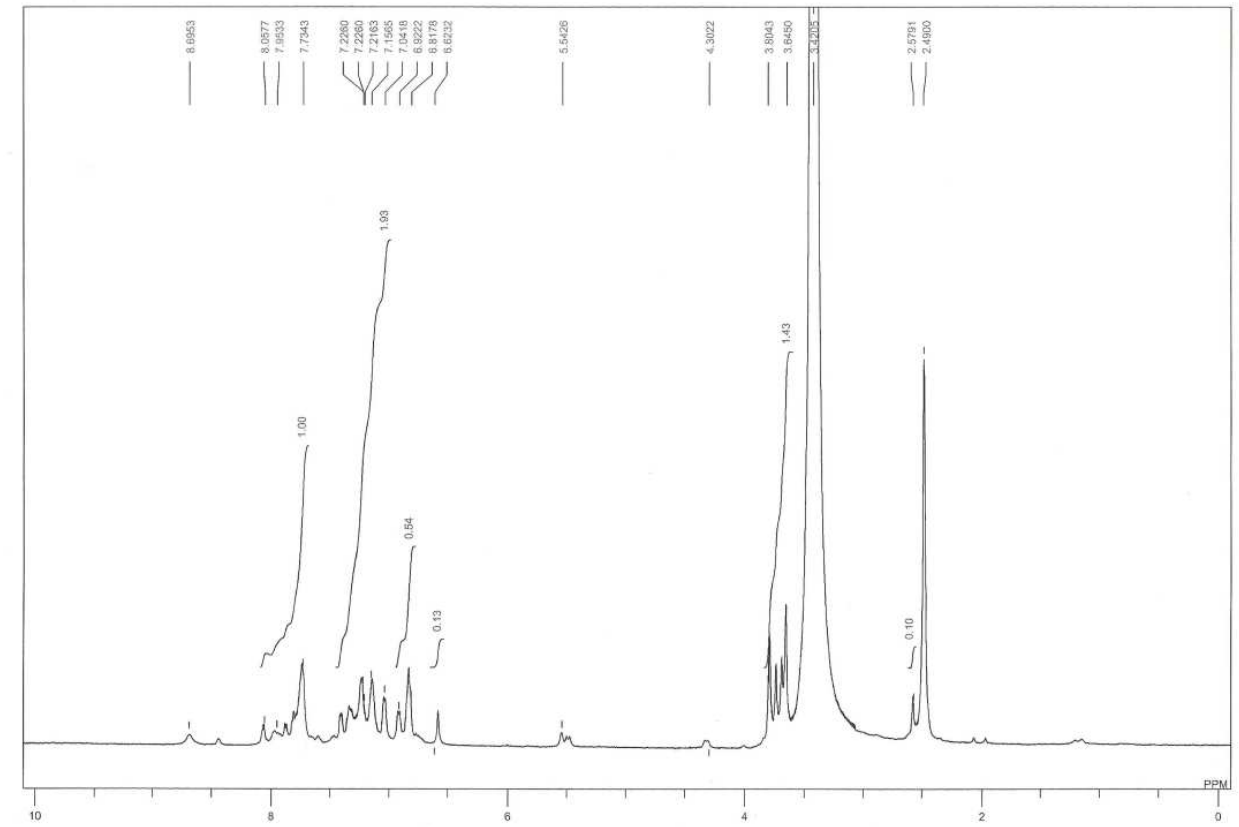
Appendix 36: ^{1}H – NMR spectra of 1-(α-diethylaminobenzyl)-2-naphthol XXIX



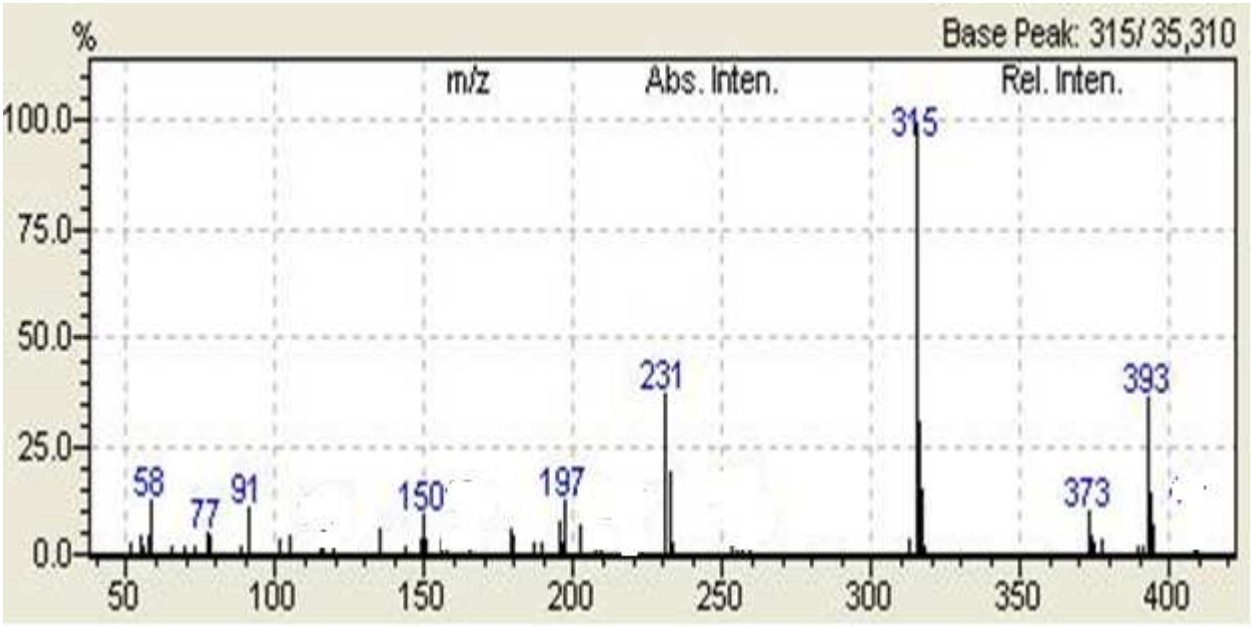
Appendix 37: ^{1}H – NMR spectra of 1-(α-butylaminophenyl)-2-naphthol XXXI



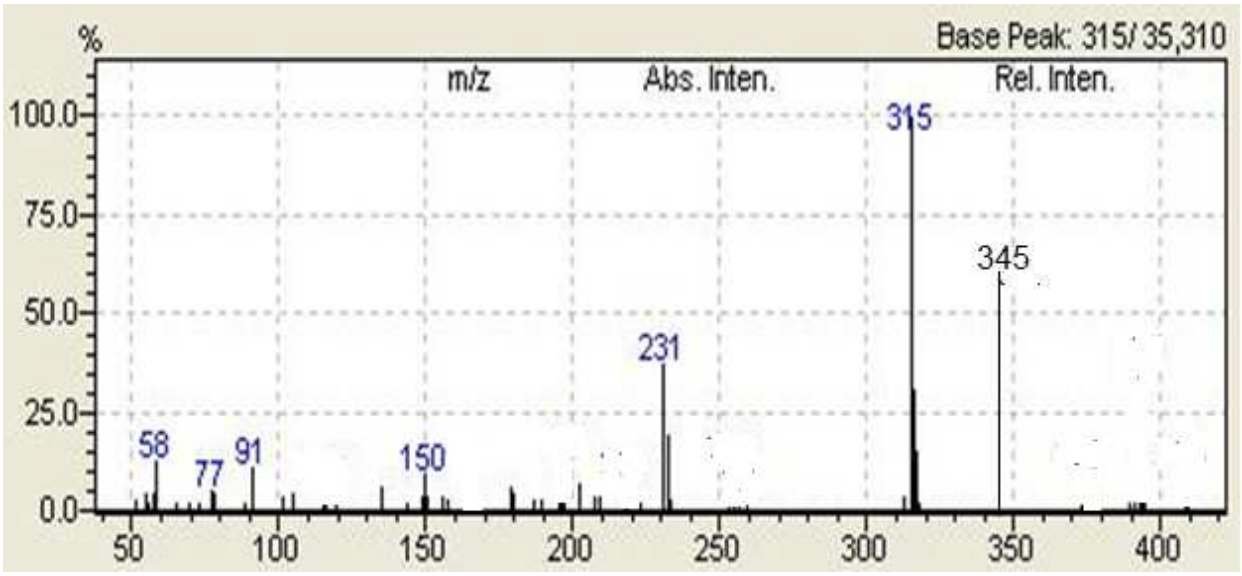
Appendix 38:^{1}H – NMR spectra of 1-(4-amino -3-hydroxynaphthol)-diazonium acetophenone XXXII



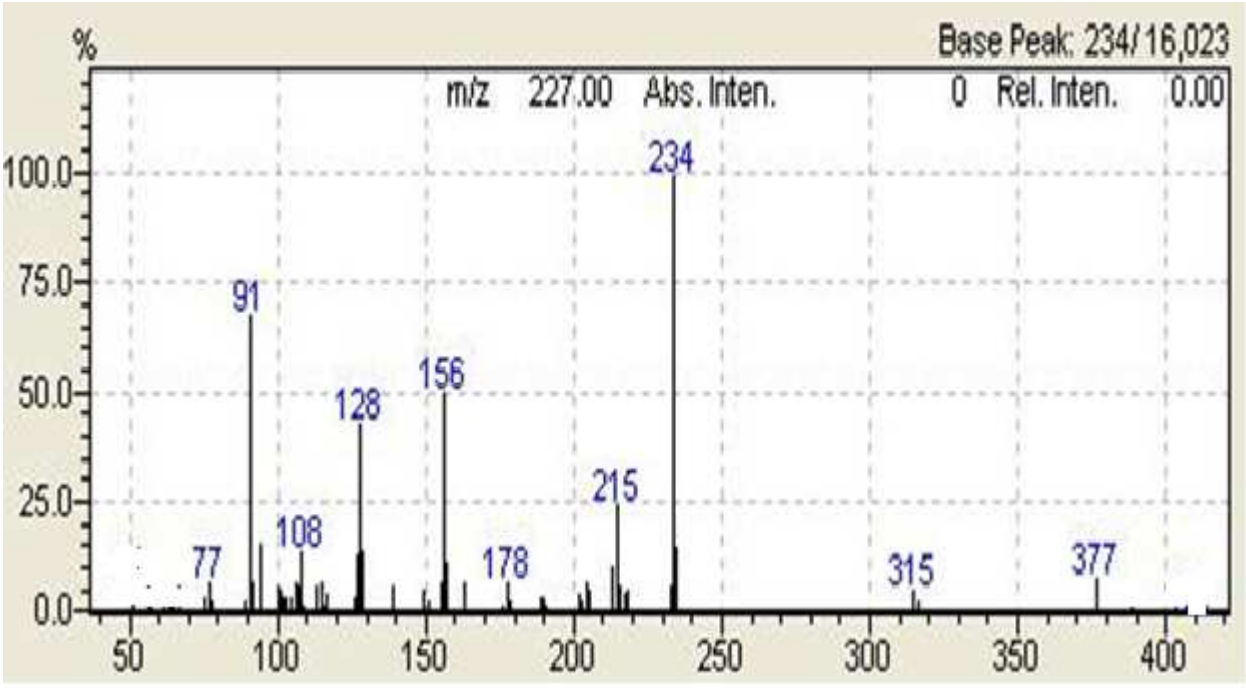
Appendix 39:[1]H – NMR spectra of 1-(amino-4-methoxyphenyl-3-hydroxynaphthol)-diazoniumacetophenone XXXIV



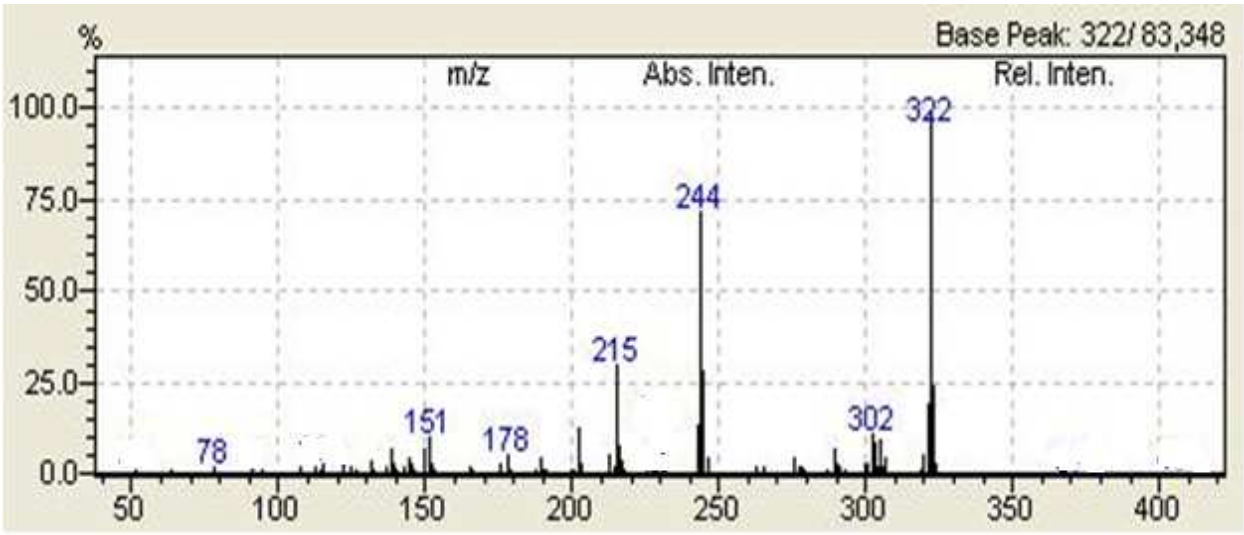
Appendix 40: MS of 1,3-Diphenyl-nitroaniline -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine compound I



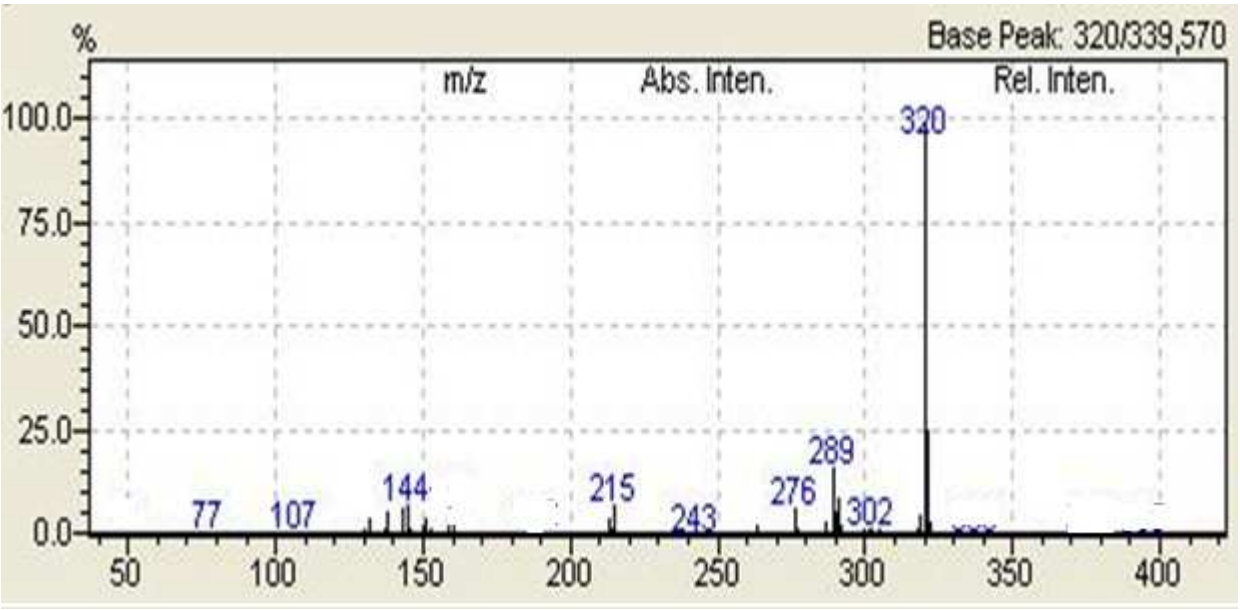
Appendix 41: MS of 1,3-Di-4,4-dimethoxy phenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine compound II



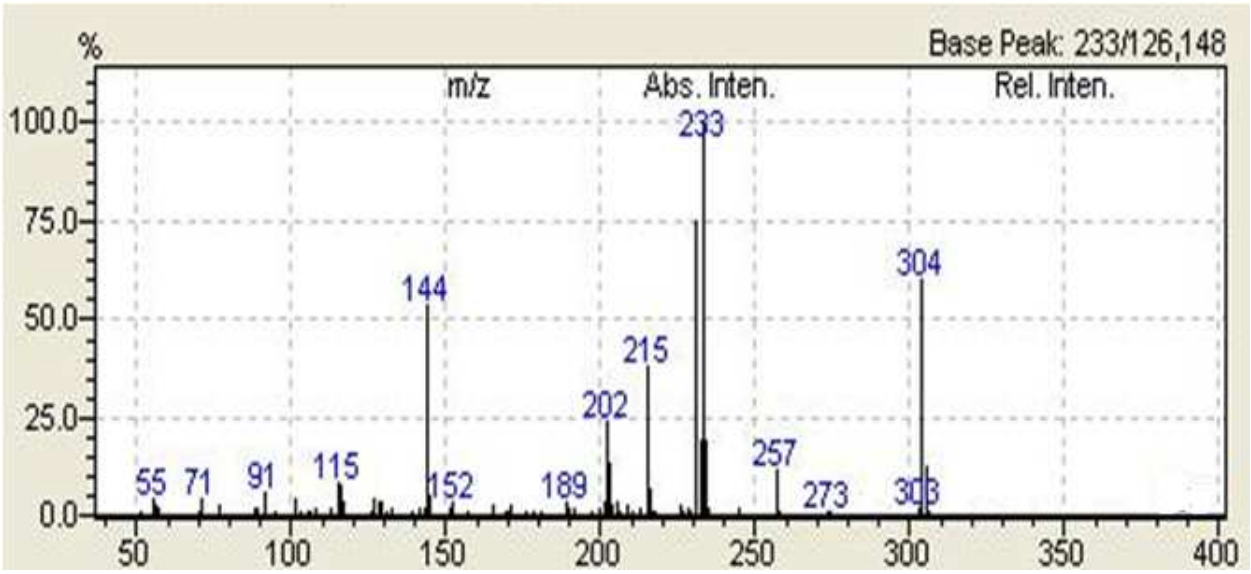
Appendix 42: GC – MS of 1,3-diphenyl-2-propyl-2,3-dihydro-1*H*-naphth [1, 2-e][1,3]oxazine VI



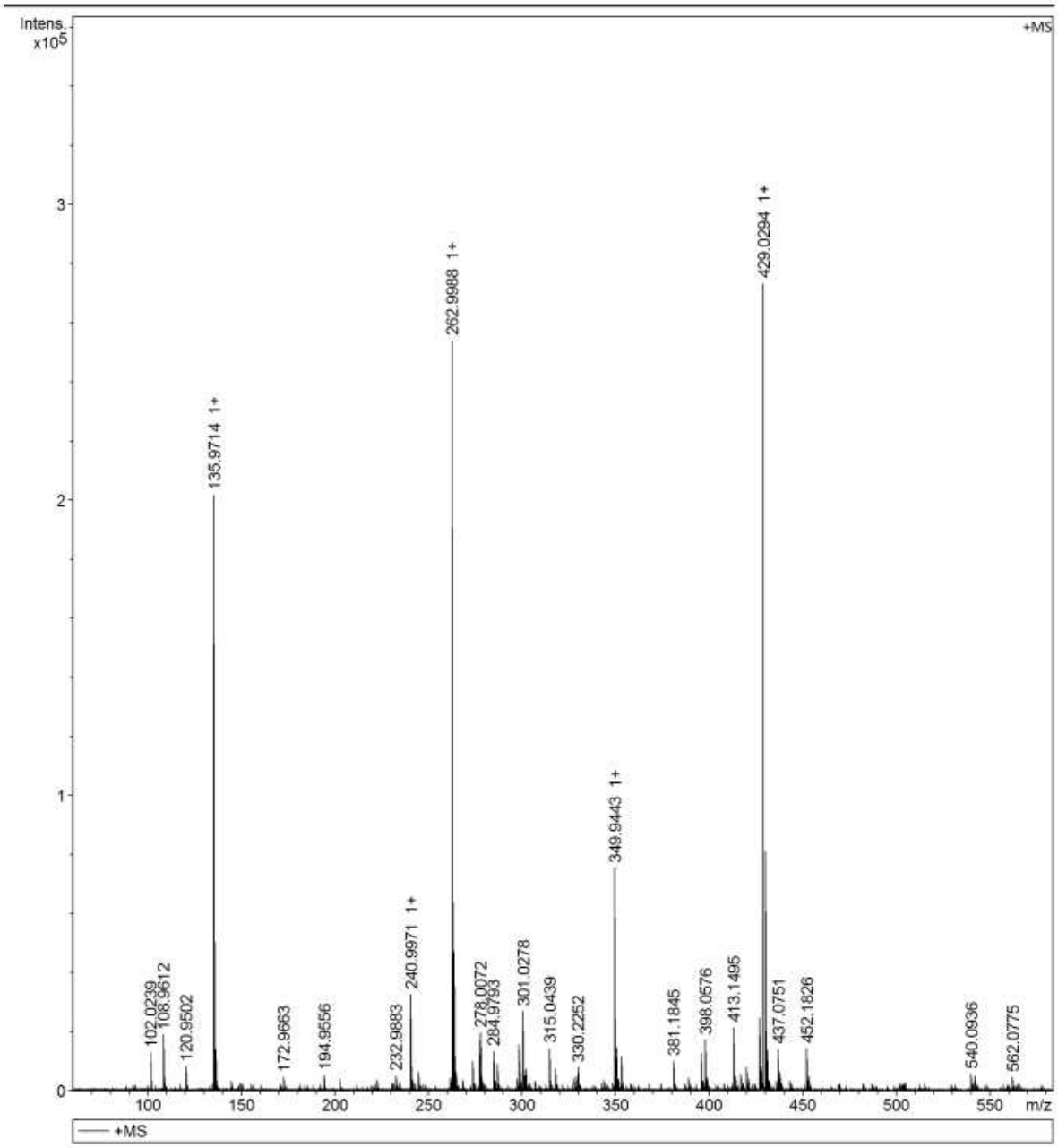
Appendix 43: MS of 1,3-Di-*o*-nitrophenyl-2,3-dihydro-1*H*-naphth[1,2-e][1,3] oxazine compound VIII



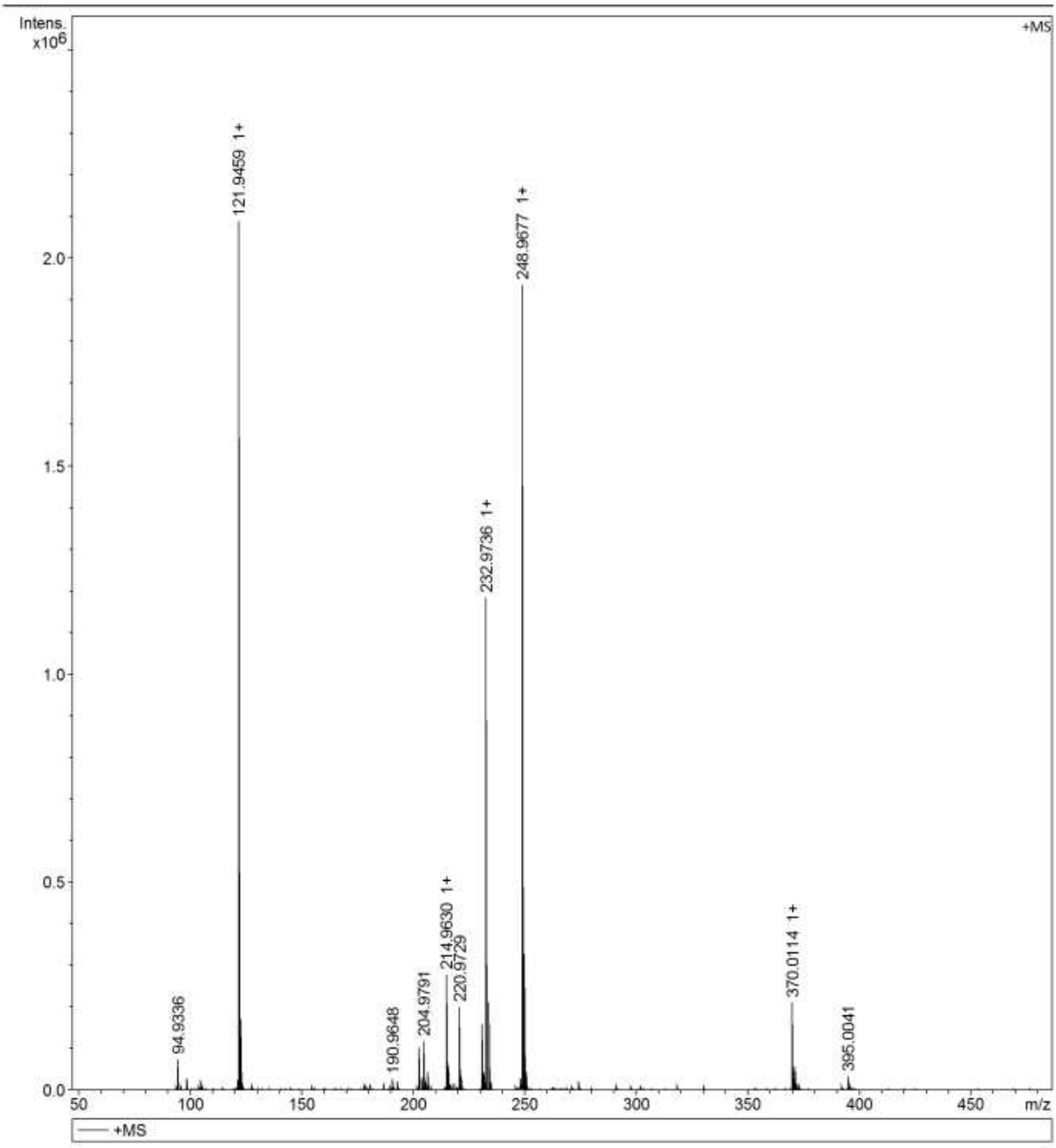
Appendix 44: GC – MS of 1-(α-phenyl-phenylamino)-2-naphthol XV



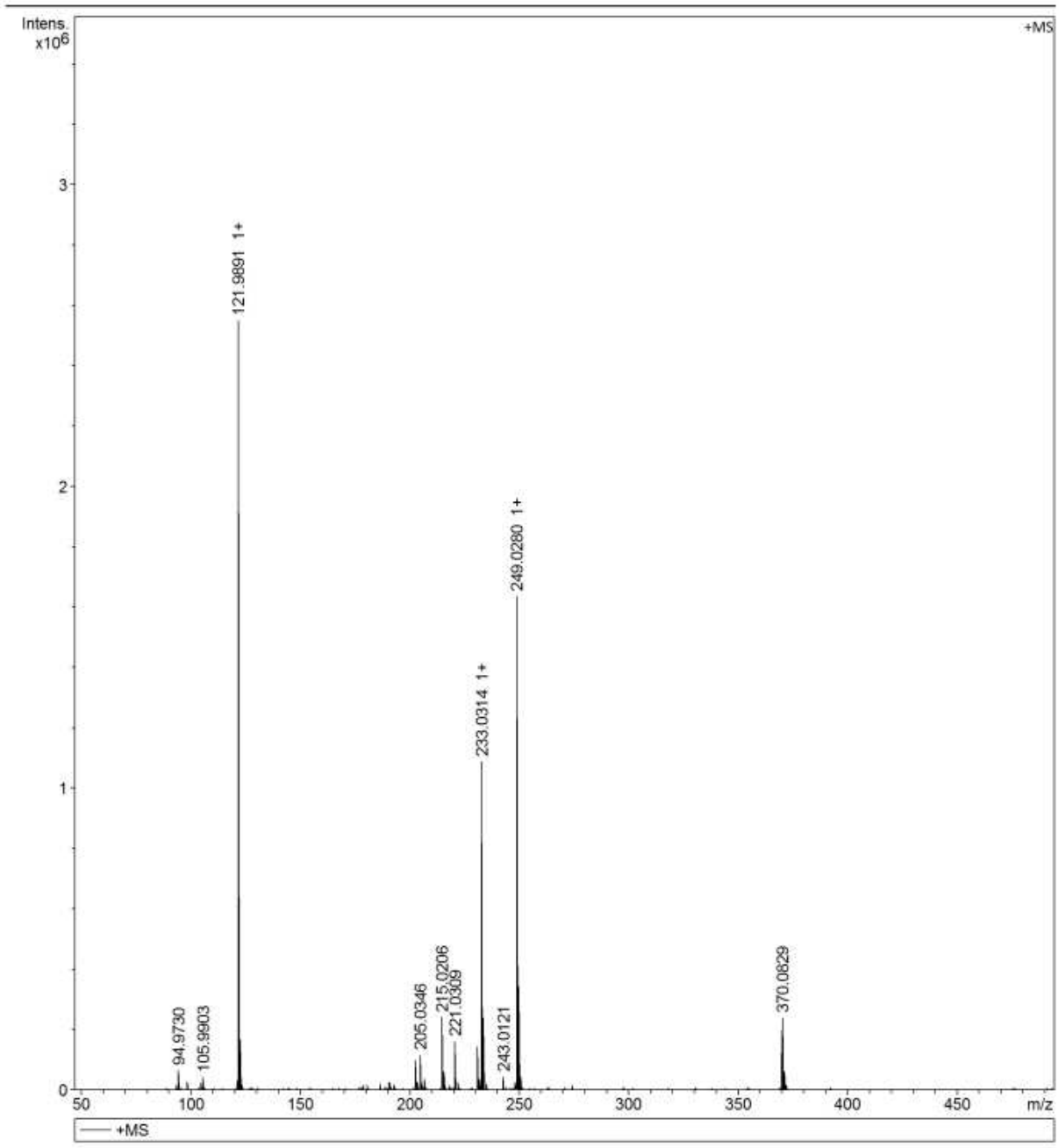
Appendix 45: GC-MS of 1-(α-butylaminophenyl)-2-naphthol XXXI



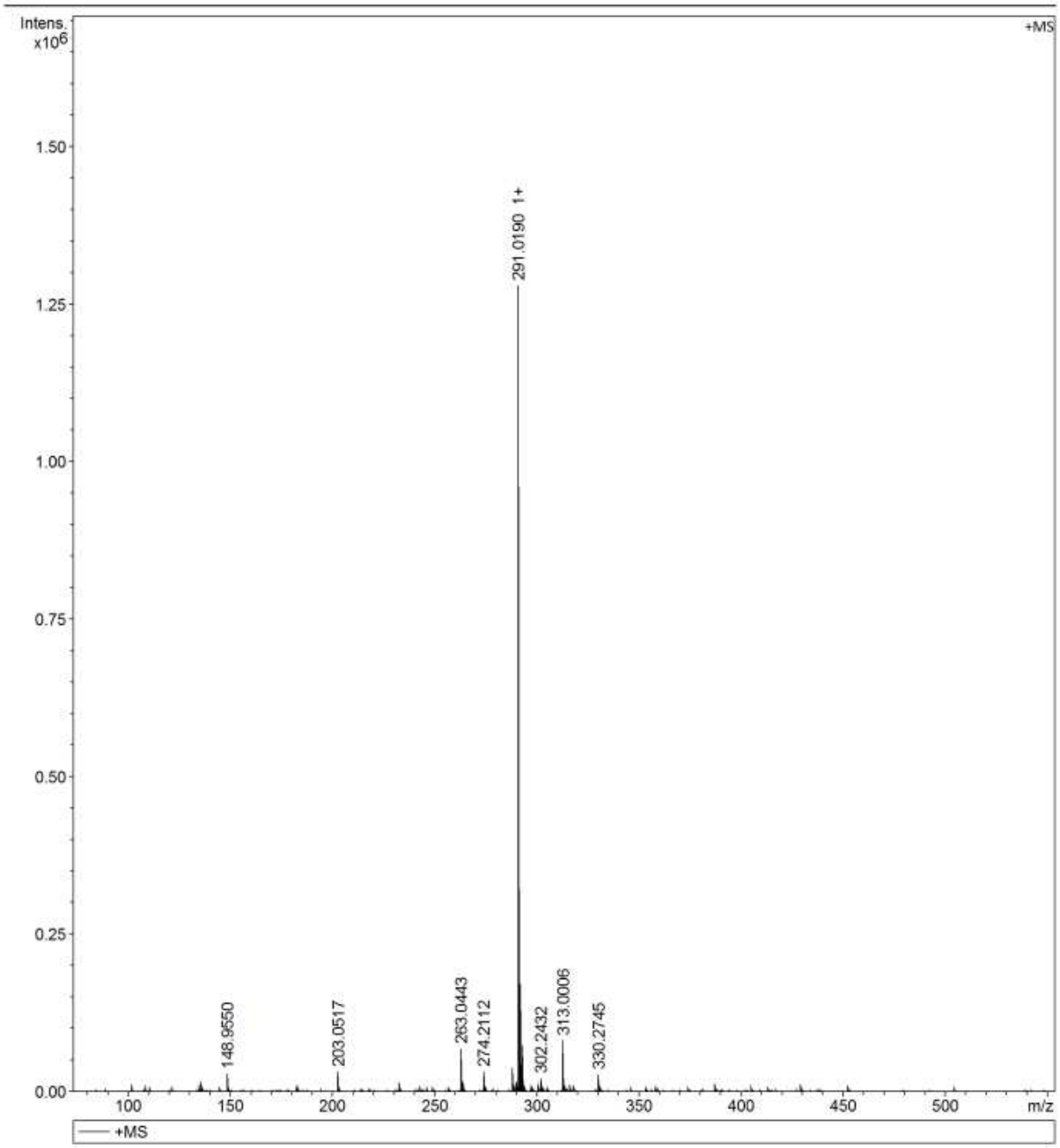
Appendix 46: MS of 1,3-Di-2-nitrophenyl-3-nitrophenyl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3] oxazine III



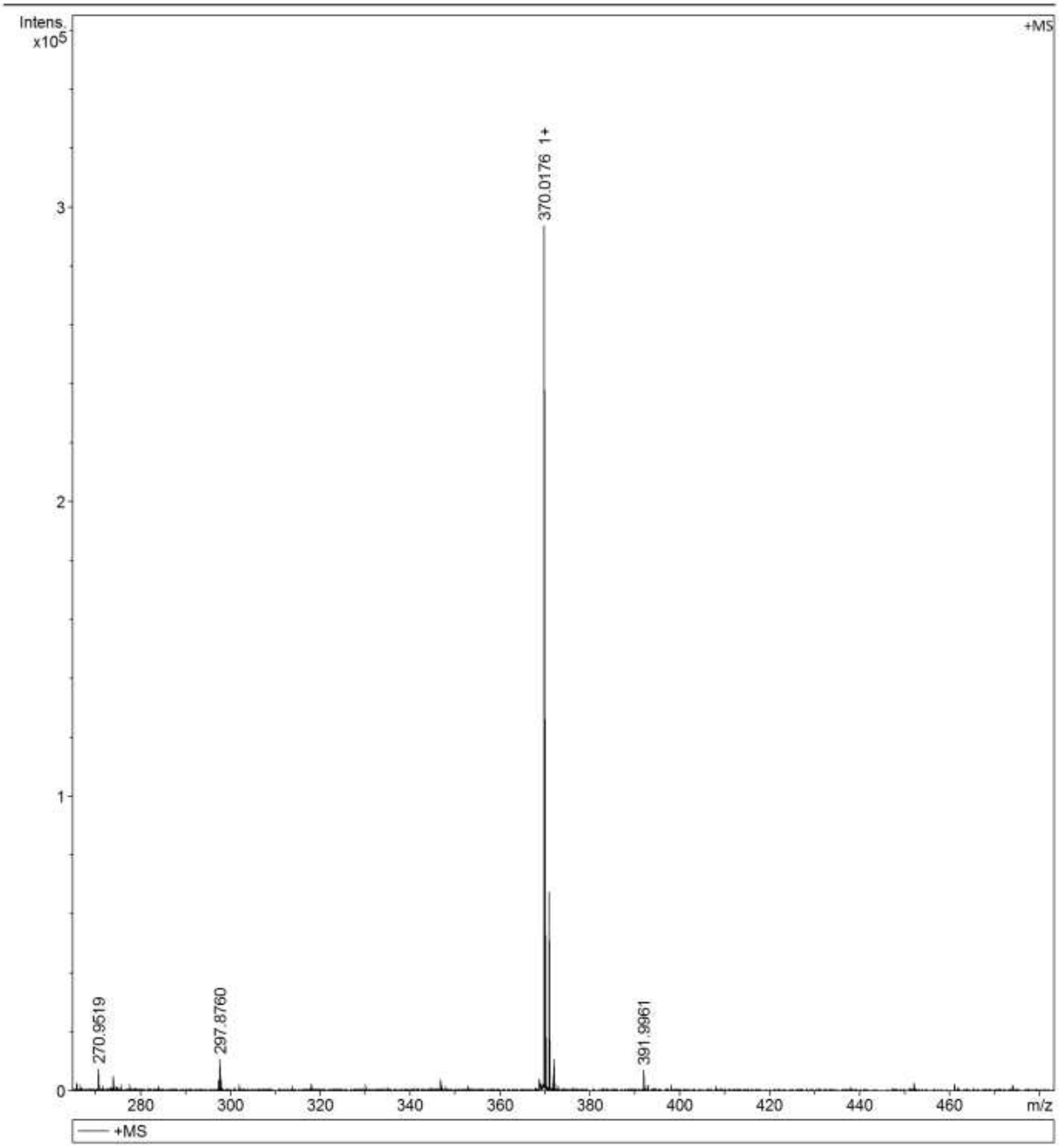
Appendix 47: MS of 1,3-Diphenyl-2-propyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine VI



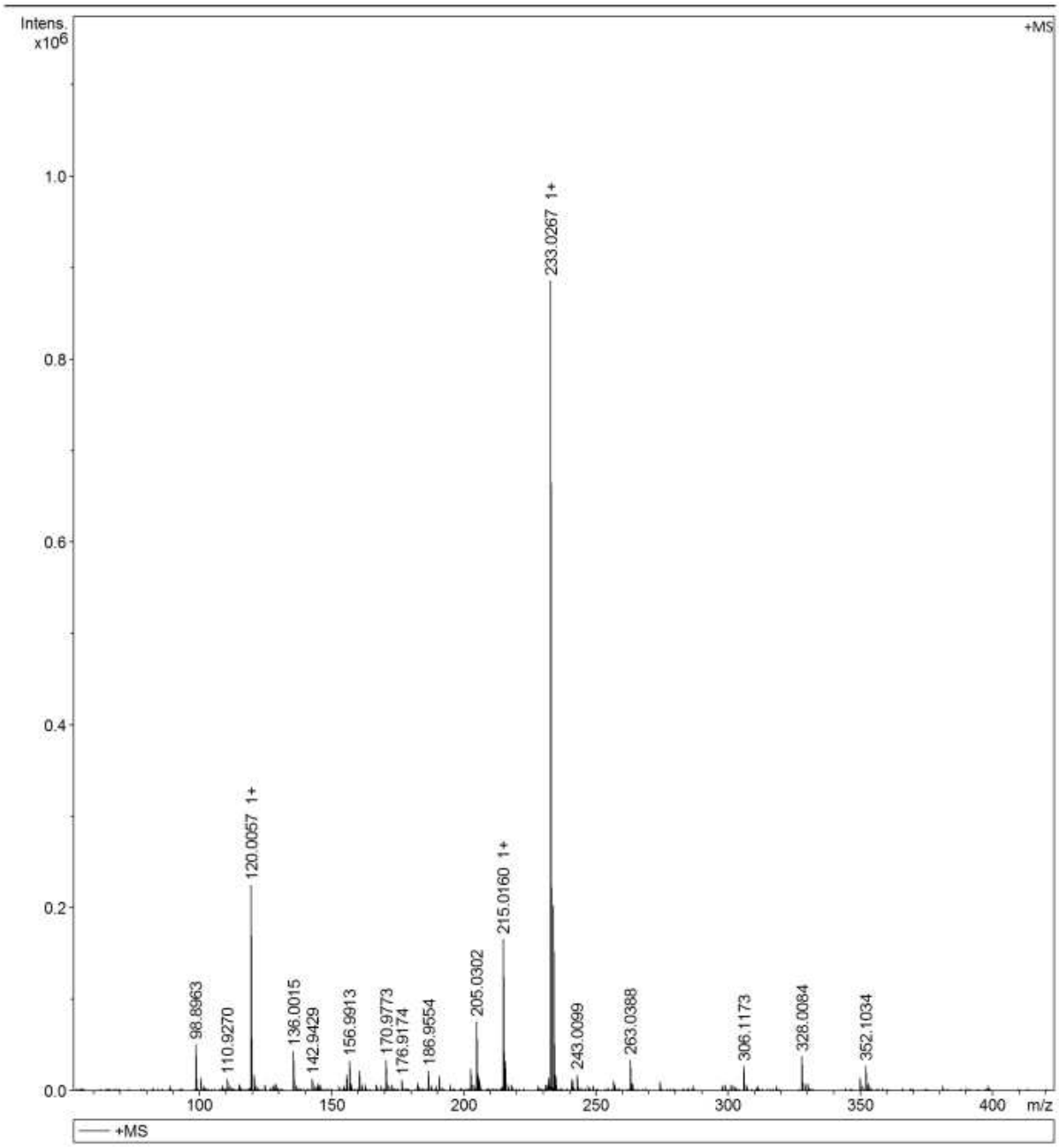
Appendix 48: MS of 1,3-Di-*o*-hydroxyphenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3] oxazine compound VII



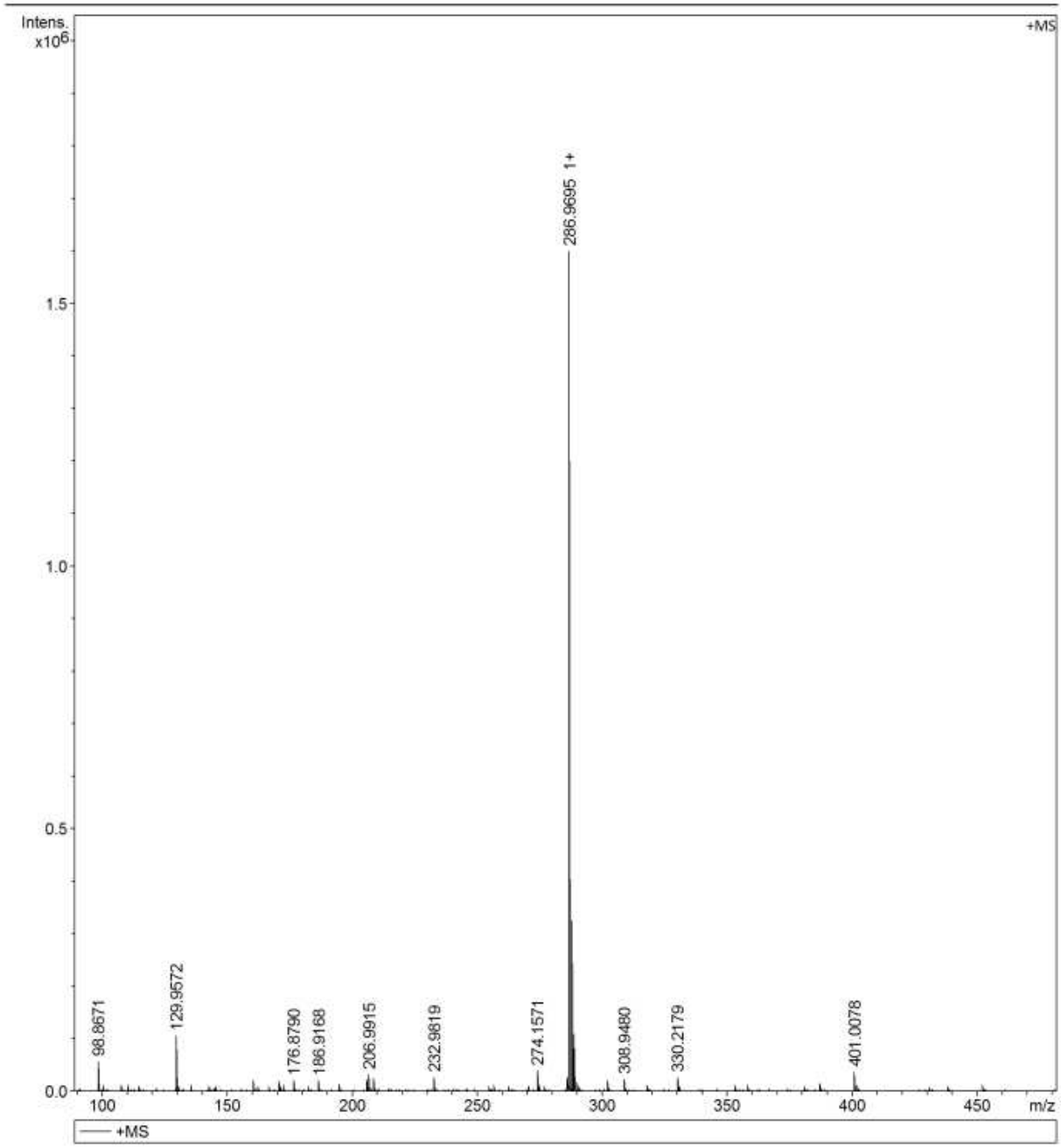
Appendix 49: MS of 1,3-Di-phenyl -2,3-dihydro-1*H*-naphth [1,2-e][1,3]oxazine IX



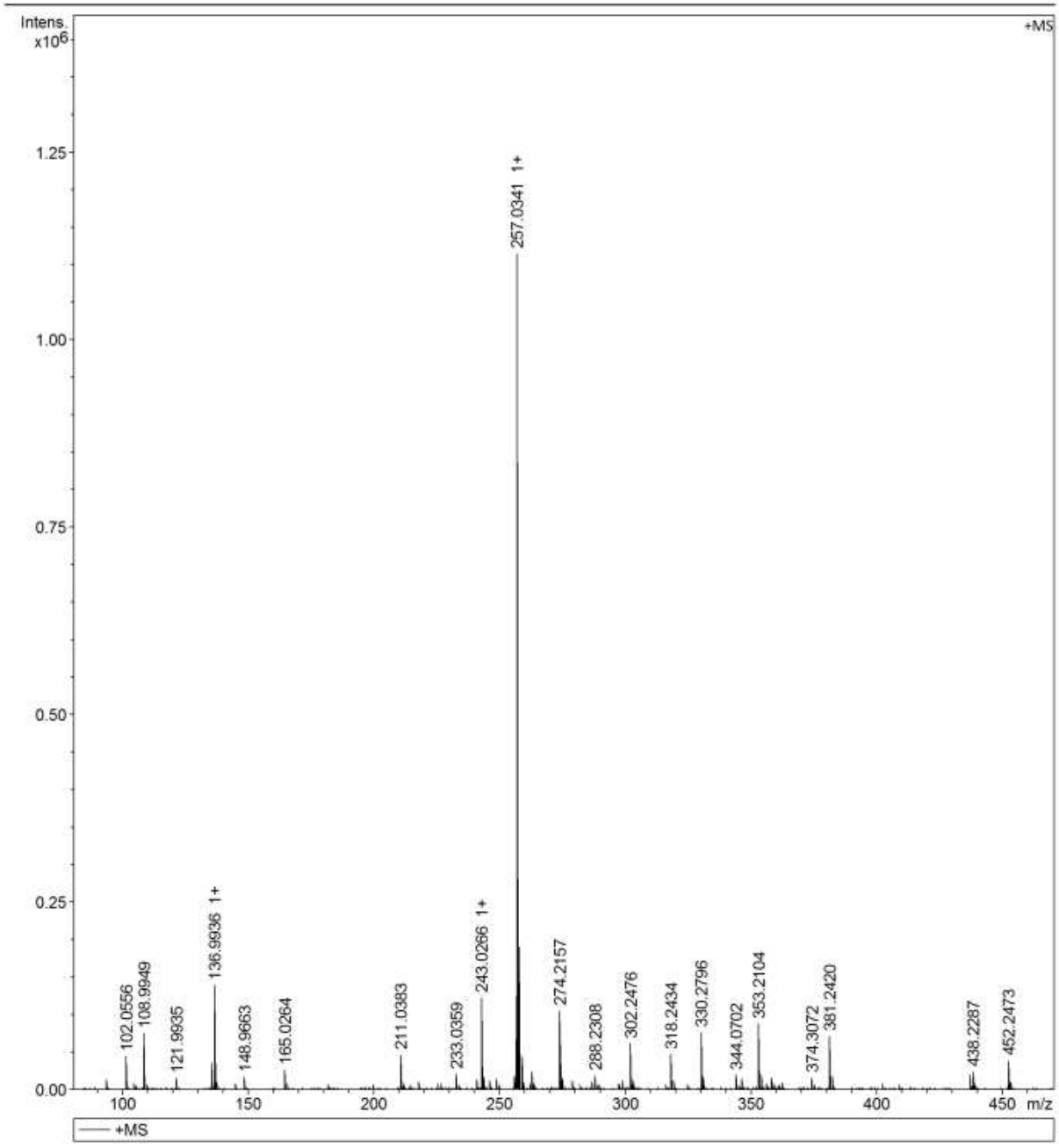
Appendix 50: MS of 1,3-distyryl-2,3-dihydro-1*H*-naphtho[1,2-e][1,3]oxazine compound XII



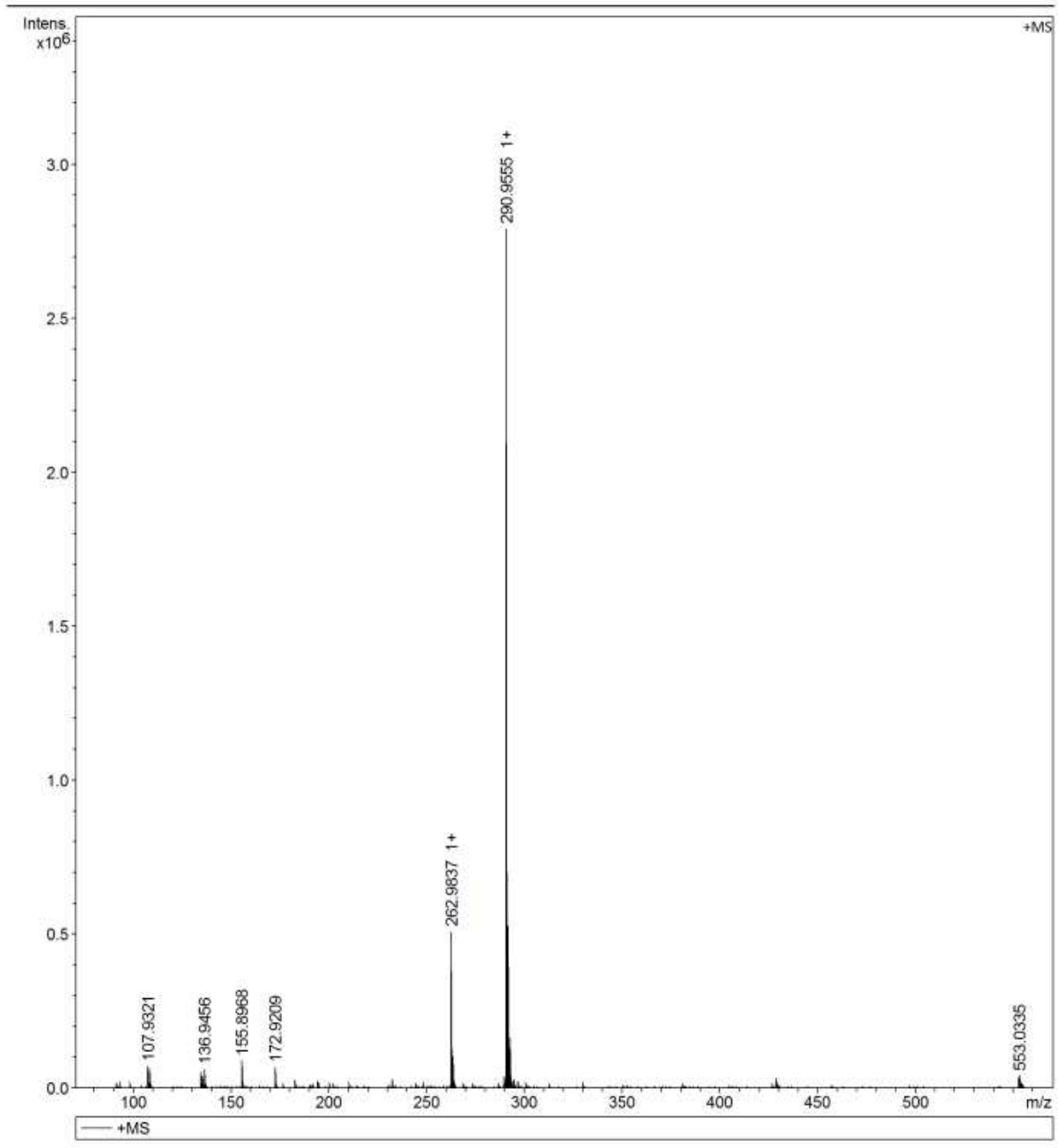
Appendix 51: MS of 1-(α-phenyl-phenylamino)-2-naphthol XV



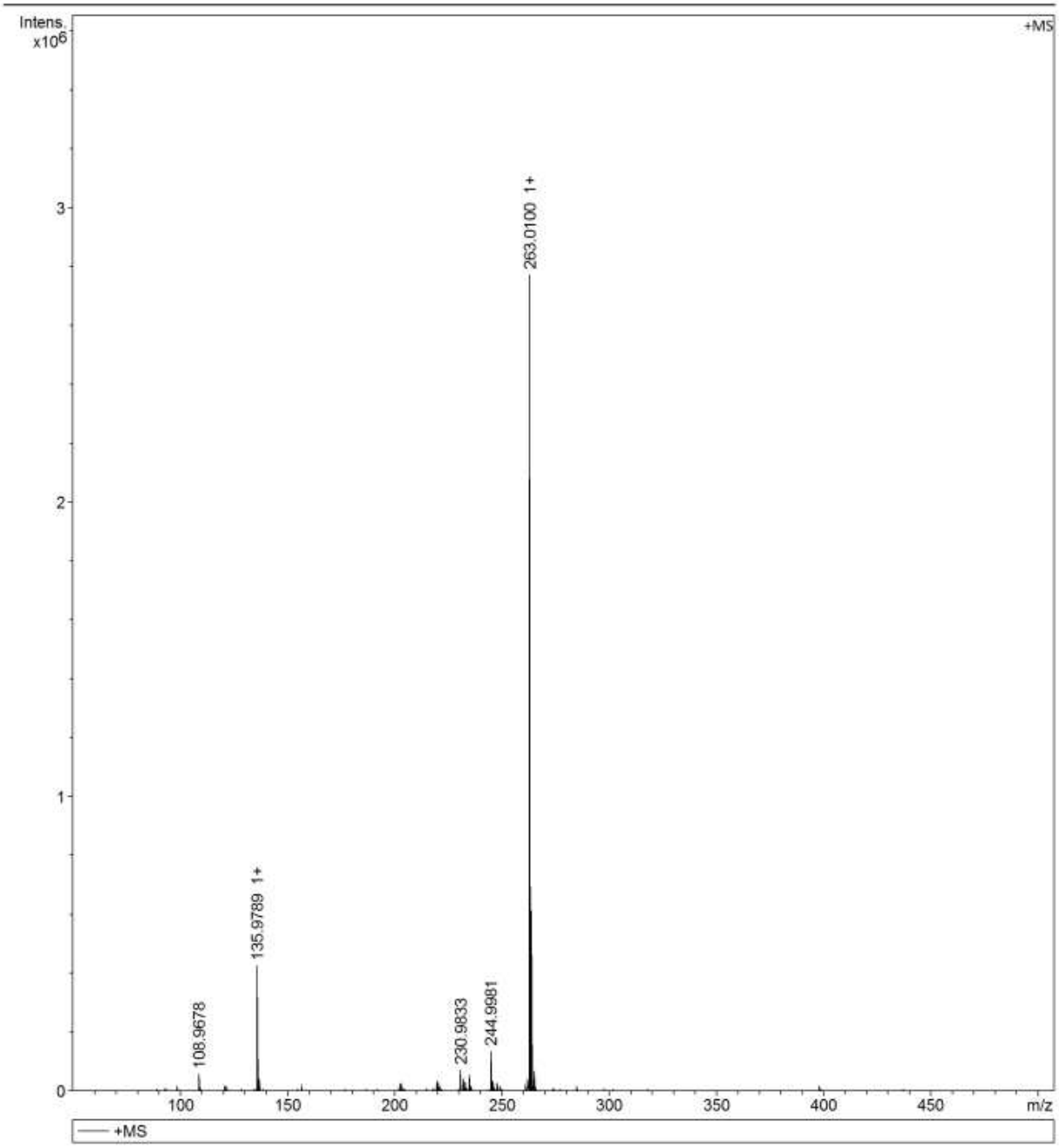
Appendix 52: MS of 1-(α-amino-4-methoxyphenyl-4-nitrobenzyl)-2-naphthol compound XVIII



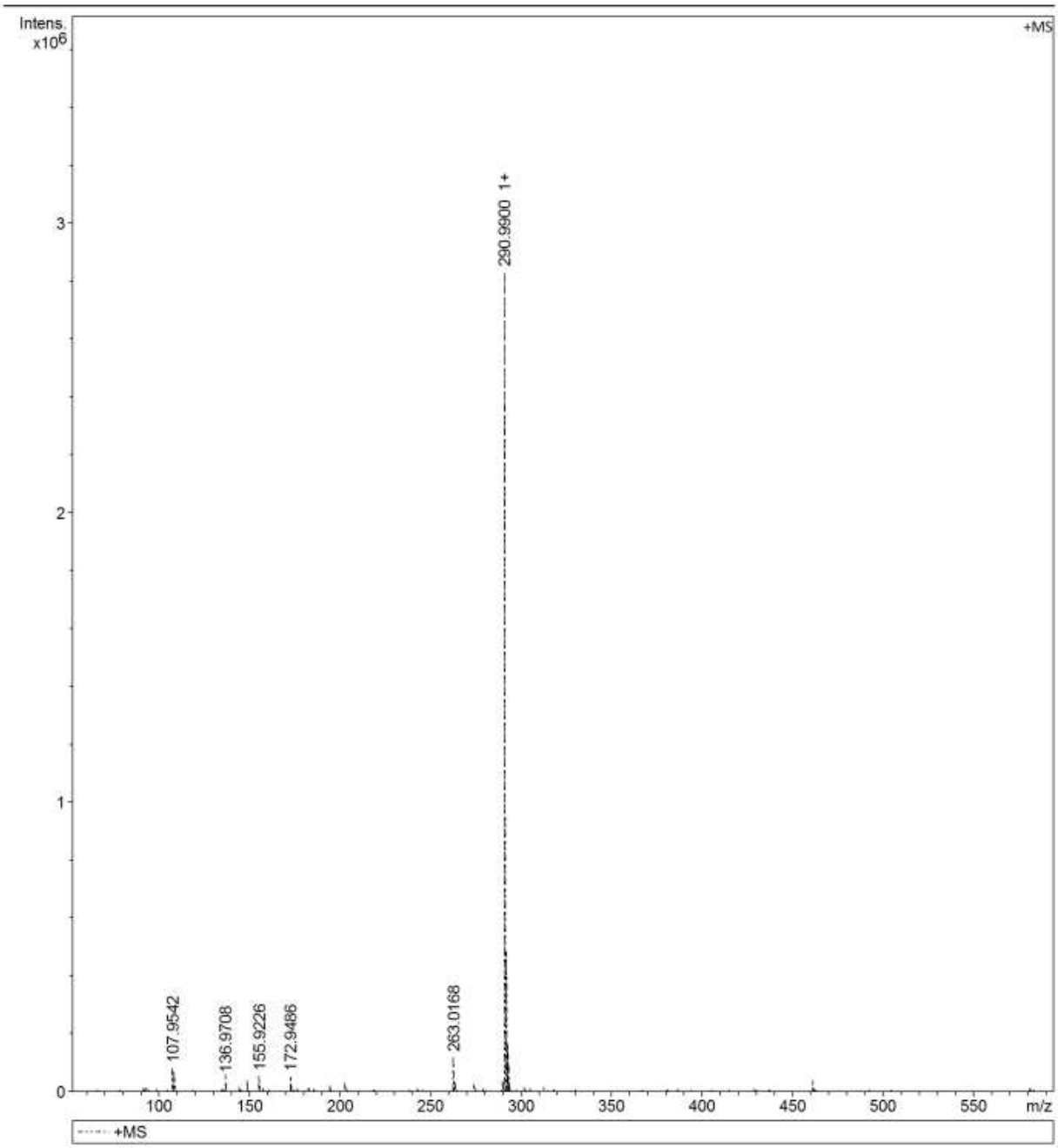
Appendix 53: MS of 1-(α-amino-2-hydroxyphenyl-4-nitrobenzyl)-2-naphthol XIX



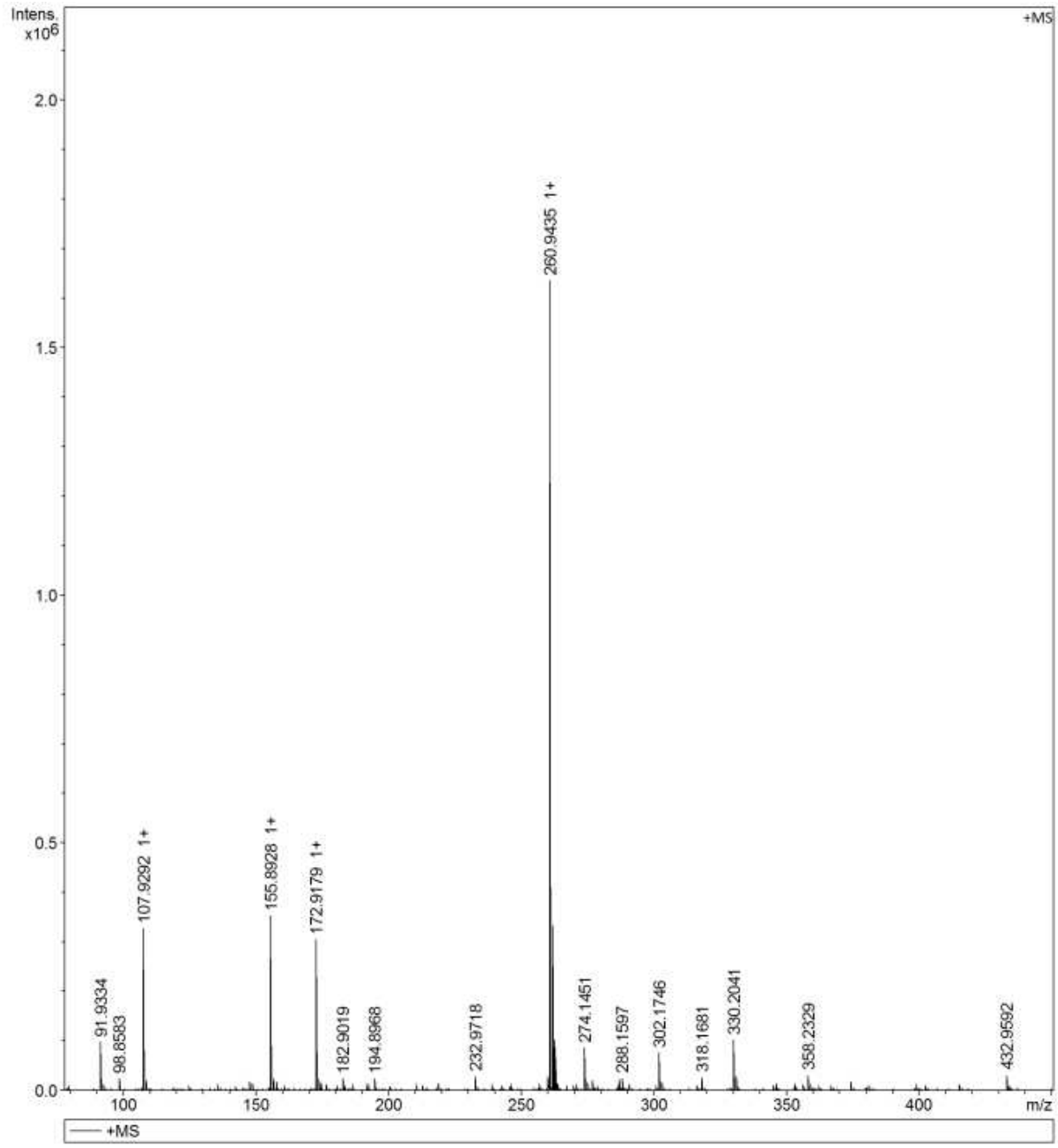
Appendix 54: MS of 1-[α-*N*-propylaminobenzyl]-2-naphthol compound XX



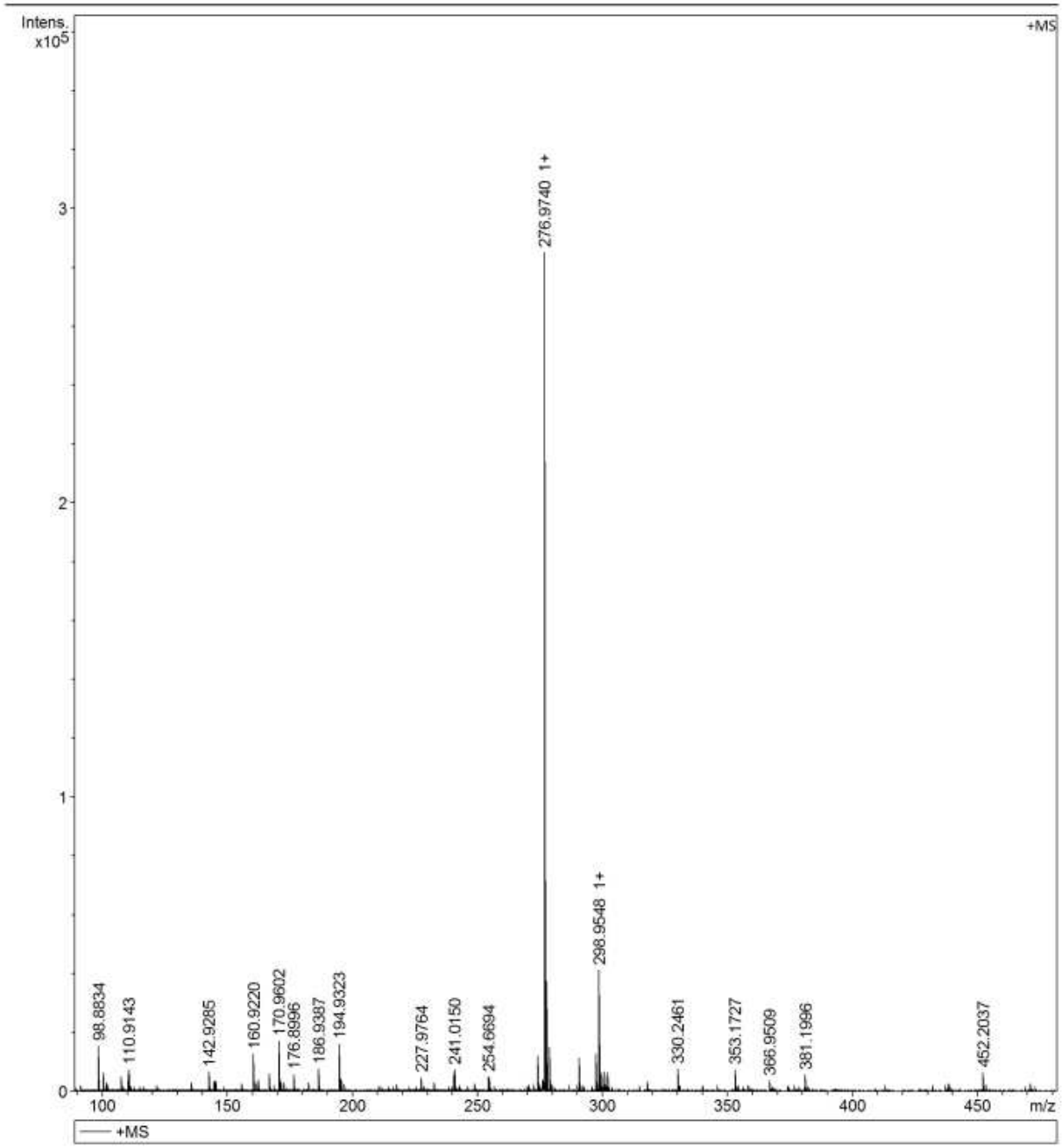
Appendix 55: MS of 1-[α-amino-*o*-hydroxybenzyl)]-2-naphthol compound XXI



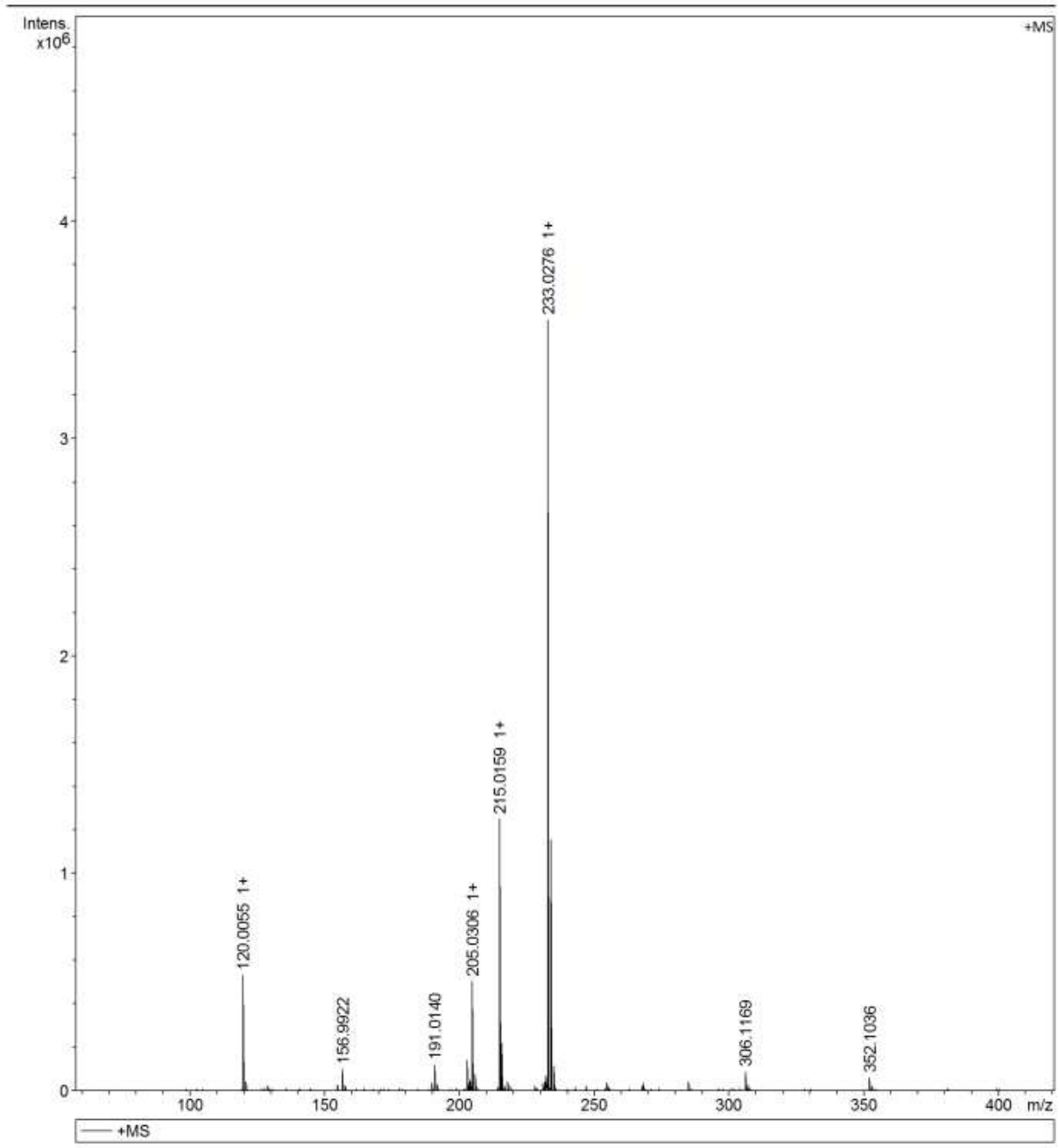
Appendix 56: MS of 1-(α-amino-4-dimethylaminobenzylyl)-2-naphthol XXIV



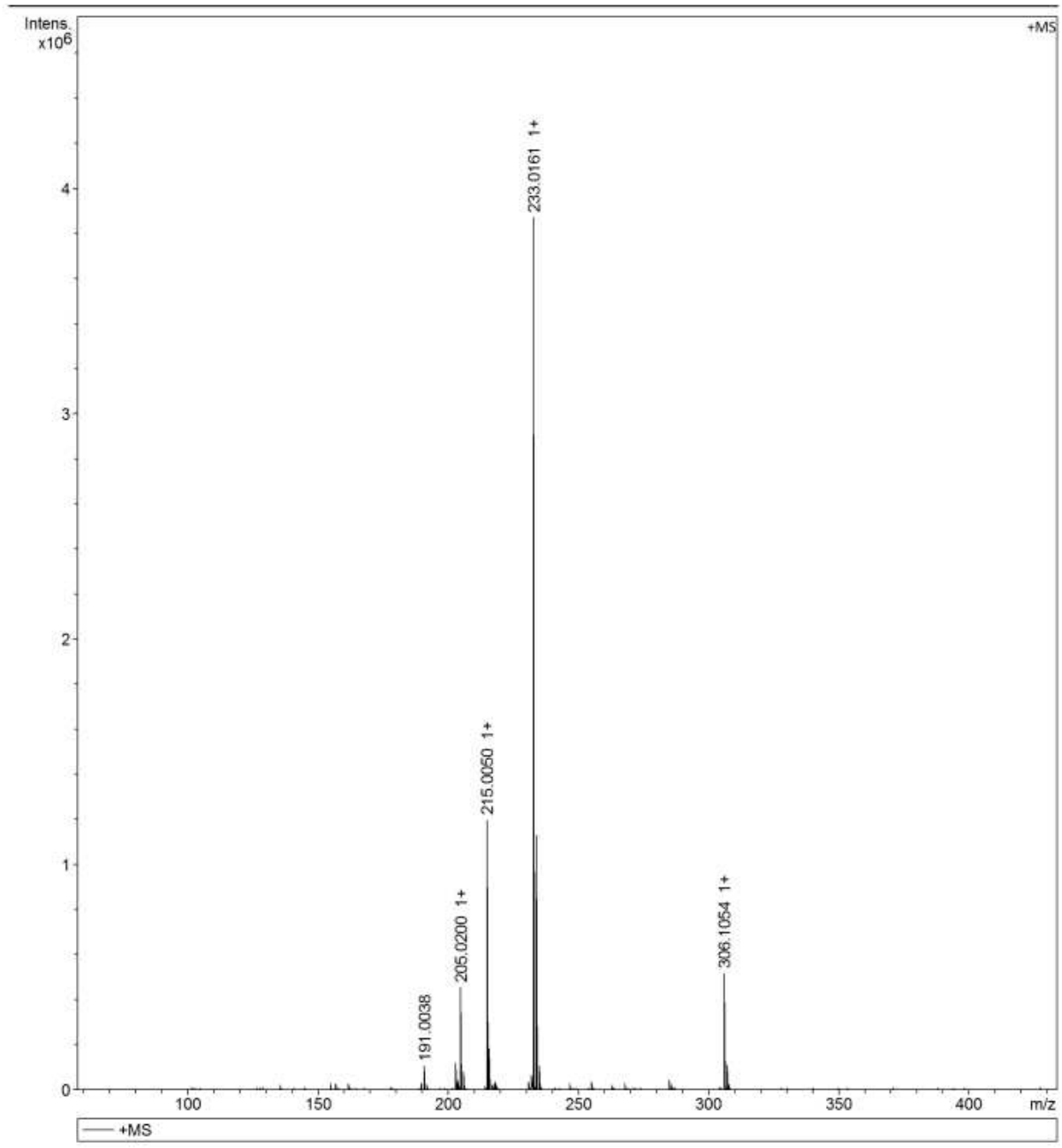
Appendix 57: MS of 3-(α-amino-4-methoxybenzyl-benzenesulfonamide)-2-naphthol compound XXVI



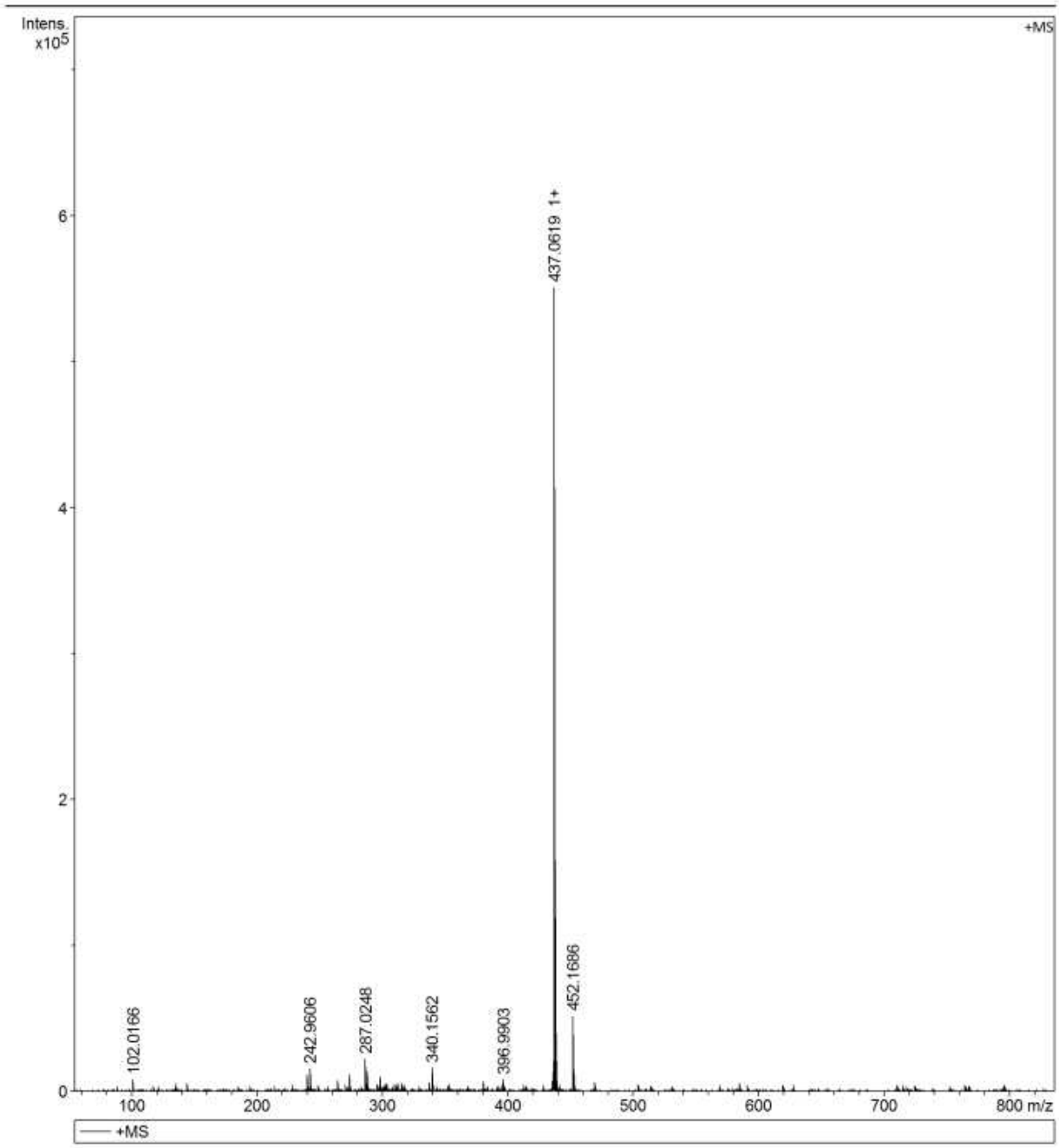
Appendix 58: MS of 3-(α-amino-2-nitrobenzyl-benzenesulfonamide)-2-naphthol XXVII



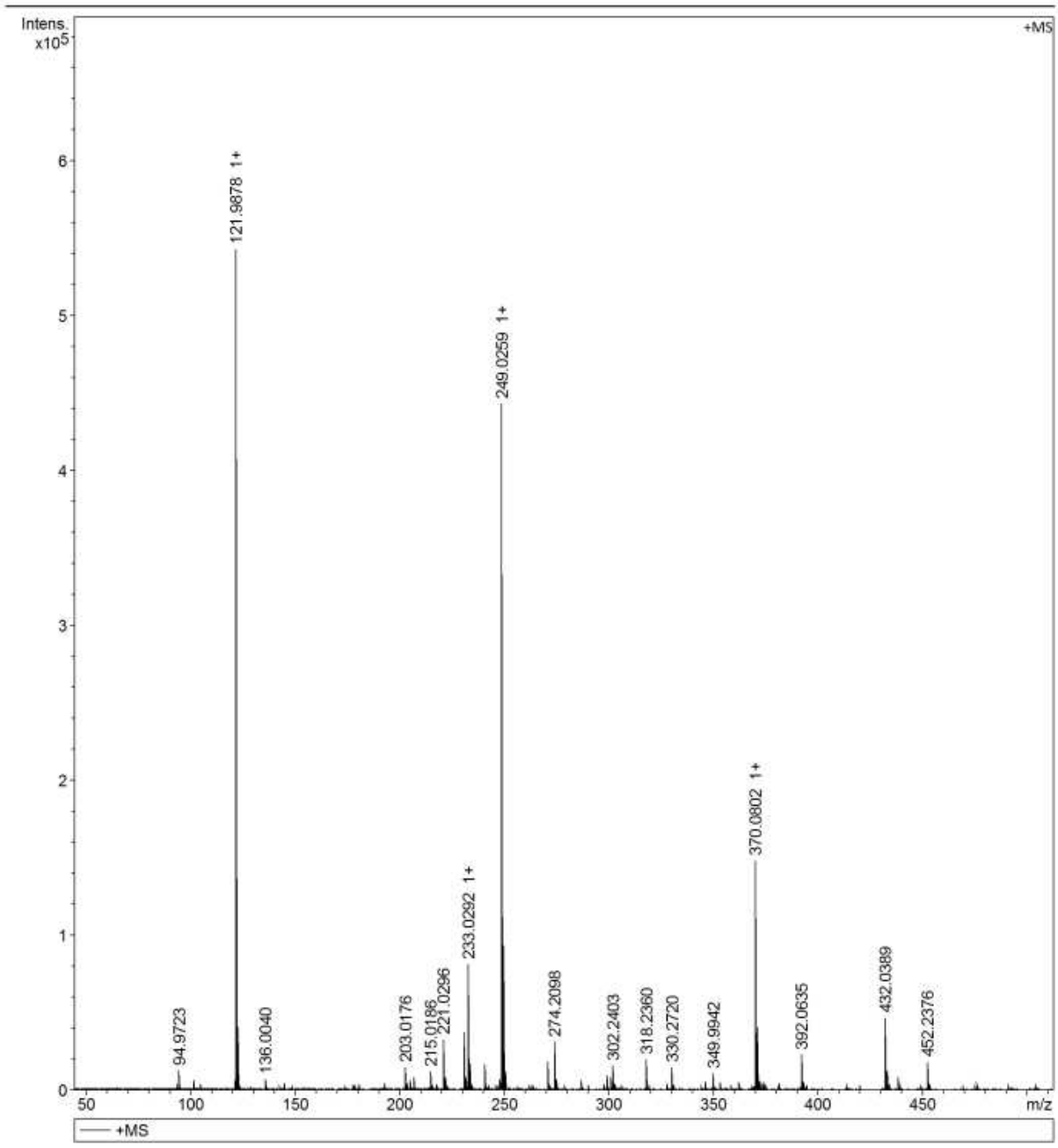
Appendix 59: MS of 1-(α-diethylaminophenyl)-2-naphthol XXIX



Appendix 60: MS of 1-(α-butylaminophenyl)-2-naphthol XXXI



Appendix 61: MS of 1-(butylamino-3-hydroxynaphthol)-diazoniumacetophenone compound XXXIV



Appendix 62: MS 4-((4-(amino(4-methoxyphenyl)methyl)-3-hydroxynaphthalen-2-ol)diazenyl) benzene sulfonamide XXXVI