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Synthetic Studies of 1,10-Phenanthroline Derivatives as Novel Catalysis Ligands and Their Application in Transition Metals Catalyzed Reactions

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SYNTHETIC STUDIES OF 1,10-PHENANTHROLINE DERIVATIVES AS NOVEL CATALYSIS LIGANDS AND THEIR APPLICATION IN TRANSITION METALS CATALYZED REACTIONS

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The preparation of 1,10-phenanthroline derivatives entailed ring opening reactions of 1,10-phenanthroline epoxide as a key transformation, affording novel bidentate nitrogen ligands with new stereogenic centers in the 5- and 6-position. This research was concerned with [i] the epoxidation of 1,10-phen, [ii] epoxide ring opening reactions, [iii] the formation of *trans*-5,6-disubstituted-1,10-phenanthroline metal complexes, and [iv] application of 1,10-phenanthroline derivatives in metal-catalyze reactions such as palladium-catalyzed allylic substitution and aminohalogenation reactions; Zinc-catalyzed direct aldol reaction, and acetophenone reduction; Nickel-catalyzed Michael addition reaction.

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CHAPTER 1: INTRODUCTION

The concept of "chirality" has been known in chemistry since the 1870's although it would be nearly a hundred years before chemists began using this term. In 1847 Louis Pasteur resolved, for the first time, an enantiomeric pair of tartaric acid salts by mechanical separation based on their difference in crystal shape. Pasteur recognized that the two isomers rotated polarized light in opposite directions. Following Kekule's recognition in 1858 that carbon is tetravalent,[1] van't Hoff and Le Bel independently recognized that when four different groups are attached to carbon, their arrangements can be in two different orientations. Since then, chirality has been recognized as extremely important not only in chemical or biological research, but also to life itself.

What is chirality? Chiral, derived from the Greek word '*cheir*' (hand), refers to the way two otherwise identical molecules (Figure 1.1) can be non-superimposable mirror images of each other just as our hands mirror each other. These molecules are referred to as 'enantiomers' and can react differently with other chiral molecules, such as enzymes. Ultimately, stereoisomers can display drastically different biological activities (*vide infra*).

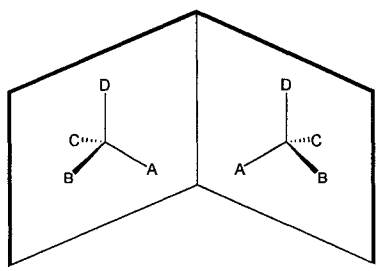


Figure 1.1 Two "chiral" forms (enantiomers)

Many chiral compounds can be found in nature in enantiopure or enantioenriched form. Examples include amino acids, carbohydrates, nucleic acids, and alkaloids. The importance of enantiomerically pure compounds comes from the central role of enantiomer recognition in biological processes. Noyori stated that "*Life depends on chiral recognition, because living systems interact with enantiomers in decisively different manners.*"[2] As a consequence often only one enantiomer of a given drug has the desired effect while the other one may even be harmful. The most well known dramatic example is thalidomide. Its (S) enantiomer exhibits teratogenic activity and the (R) enantiomer acts as a sedative. (Figure 1.2)

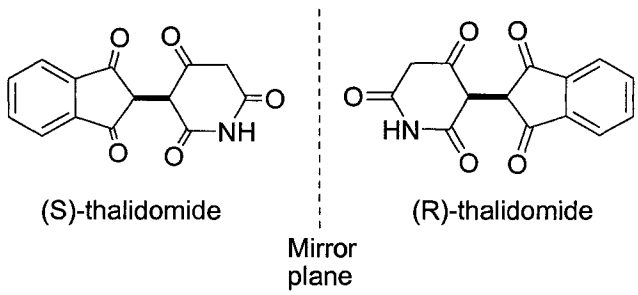


Figure 1.2 (S) and (R)-thalidomide enantiomers

Given the dramatic impact stereochemistry can have on biological activity there is a strong need for enantioselective processes in drug development. Discussed further are some of the reasons why organic chemists have put forward tremendous efforts in the field of asymmetric synthesis during the last few decades. For drug delivery, the potency of an active enantiomer compared with a racemic mixture of active and inactive enantiomer is such that the dose may be reduced. Another reason for the preparation of a

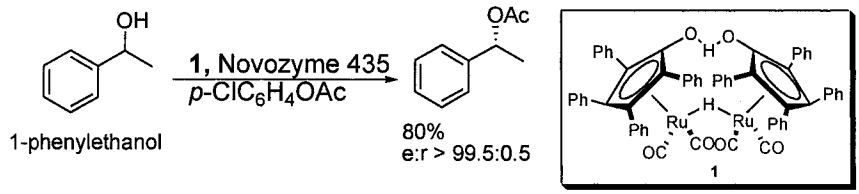
single active stereoisomer is economics, increasing yields of specific enantiomers at low cost and reducing the waste of starting materials and reagents on the inactive isomer.

Stereochemistry also plays an important role in food and agricultural chemistry. Tastes and smells can vary with stereochemistry, for example (R) and (S)-limonene enantiomers are found in oranges and lemons, respectively. Agrochemicals may be easier or harder to degrade depending on which enantiomer of the chemical substance is used. Due to the growing concern about environmental aspects in modern society this branch of industry has an increasing need for enantioselective processes.

1.1 Towards Enantiomerically Pure or Enriched Compounds

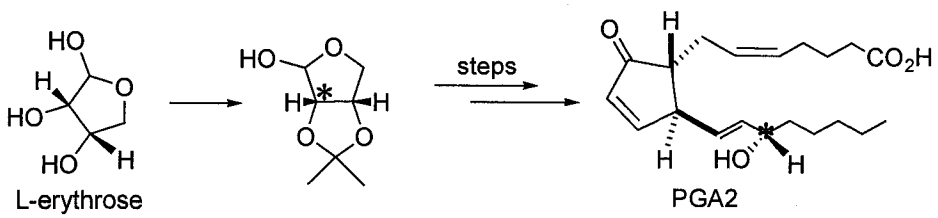
There are three basic approaches to generate enantiomerically pure or enriched compounds.

a) Resolution is the oldest process and is based on the synthesis of the racemic target molecule or intermediate which is then resolved with the help of an enantiomerically pure reagent. Resolution is still important and widely used today, but it has some drawbacks, *i.e.* resolution is often expensive. Also a suitable resolving agent is required and the *unwanted* enantiomer has to be disposed of. The drawback of the *unwanted* enantiomer of the product can sometimes be overcome by recovering/recycling the isomer in a dynamic kinetic resolution process as is done with 1-phenylethanol (Scheme 1.1).[3] The dimeric ruthenium complex **1** catalyzed hydride transfer and was employed in tandem with Novozyme 435 (*Candida Antarctica* lipase B immobilized on resin) to achieve dynamic kinetic resolution.



Scheme 1.1 Resolution of 1-phenylethanol

b) A "chiral pool" approach refers to the synthesis of the target molecule based on commercially available, enantiomerically pure starting materials that contain one or more stereogenic centers. Unfortunately, this method is limited by the availability of suitable starting materials. Costs may also be a problem since unnatural enantiomers, which are man-made, are usually more expensive. A classic example of the "chiral pool" approach is shown in Scheme 1.2; the Stork synthesis of prostaglandin A_2[4] starts with the acetonide derived from L-erythrose.

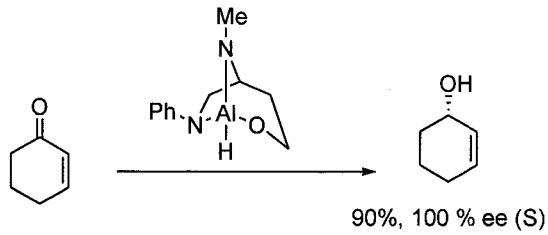


Scheme 1.2 Chiral synthesis of Prostaglandin A_2 starting with commercially available L-erythrose

c) Asymmetric synthesis involves a prochiral substrate that is converted into an enantiomerically pure product in a reaction mediated by a chiral reagent, auxiliary or catalyst, either in stoichiometric or catalytic fashion. Also "asymmetric synthesis" has contributed by making available chiral starting materials to expand the "chiral pool".[5] This enables synthetic chemists to prepare target molecules from chiral starting materials that are unavailable from nature. Due to its importance, asymmetric synthesis and in particular "*asymmetric catalysis*" are discussed in more detail in the following sections.

1.2 Asymmetric Synthesis – Ligands and Metals

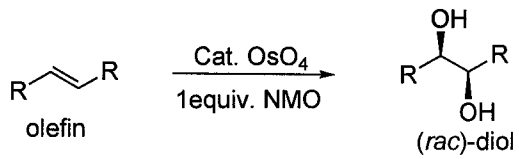
Asymmetric synthesis can also be carried out with the help of chiral reagents [6] which involves the use of at least one equivalent of enantiopure material, as seen for the asymmetric reduction of prochiral ketone with a chiral hydride reagent[7] (Scheme 1.3).



Scheme 1.3 Reduction of 2-cyclohexen-1-one

Because the chiral reagent is usually the most expensive component, a lot of effort has been spent on developing catalytic methods (asymmetric catalysis). When a chiral catalyst is involved, its substoichiometric amount can produce a large amount of enantiomerically enriched or enantiomerically pure product. The catalyst increases the rate of a chemical transformation without itself being consumed. Asymmetric catalysis

can provide a powerful solution to access chiral materials, which are not readily available otherwise. For example, optically active terminal epoxides are not available from nature's "chiral pool", which can now be readily prepared in one step from the corresponding racemates by using the salen [(*R,R*)-*N,N'*-bis(3,5-di-*tert*-butylsalicyldene-1,2-cyclohexane-diaminato(2-)] cobalt (II), catalyzed hydrolytic kinetic resolution (salen = [(*R,R*)-*N,N'*-bis(3,5-di-*tert*-butylsalicyldene-1,2-cyclohexane-diaminato(2-)].[8] Most asymmetric catalysts consist of metal complexes attached to chiral ligands. Metals are known to be extremely efficient catalysts for a wide variety of organic transformations, usually offering high selectivity under mild reaction conditions. One early example of metal catalyzed transformation is the osmium tetraoxide dihydroxylation of olefins using N-methylmorpholine N-oxide (NMO), as co-oxidant.[9] (Scheme 1.4)

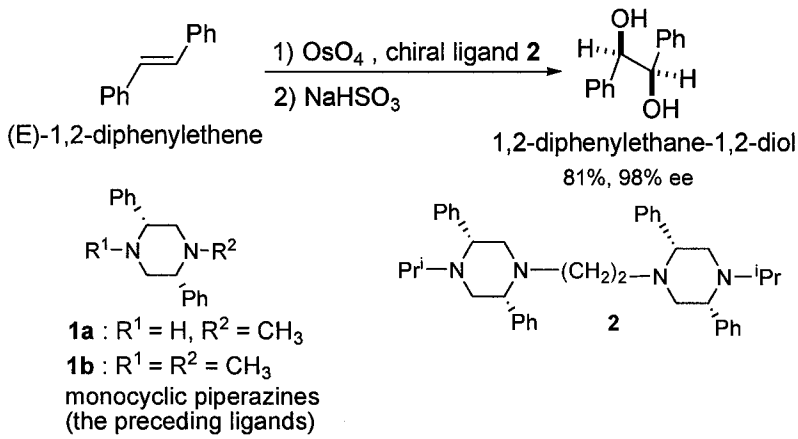


Scheme 1.4 Catalytic dihydroxylation of olefins

There is no universal chiral ligand or catalyst for solving all problems in stereoselective transformations. Changing the chiral ligand will affect the reactivity and selectivity of the metal center.[10] The preparation of new ligands is perhaps the most important step in the development of metal complexes, which exhibit unique properties and novel reactivity. To develop new chiral ligands, a structural template needs to be designed. Consideration of steric, electronic, and conformational properties is necessary

to prepare an effective ligand because they affect metal coordination and thus catalytic activity.

It should be mentioned that the improvement of an existing asymmetric version process is usually a difficult goal to achieve. The improvement may require many years of research before the process can become synthetically useful. An example of this is the asymmetric dihydroxylation of olefins in the presence of *N,N*-dialkyl bispiperazines as chiral ligands (Scheme 1.5).[11] Bispiperazines **2** showed great compared to the preceding ligand.



Scheme 1.5 Dihydroxylation of olefins using *N,N*-dialkylbispiperazines

1.3 Our Hypothesis - Application of 1,10-Phenanthroline Derivatives as Chiral Ligands

Our hypothesis is that the high rigidity of phenanthroline-type ligands improves their catalytic performance. While most literature reports utilize type **I** and **II** templates, we intend to study and optimize type **III** ligands (Figure 1.3).

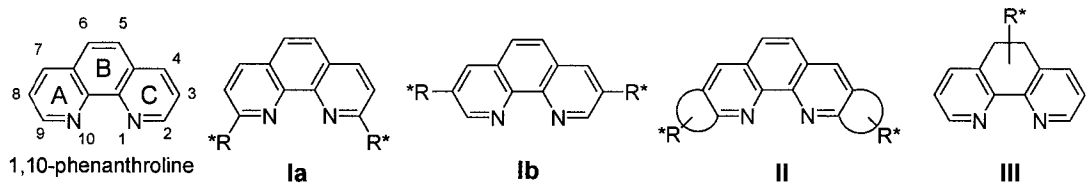
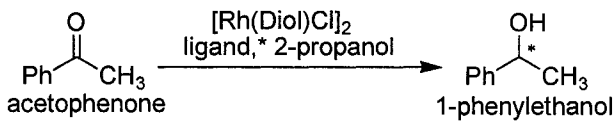


Figure 1.3 1,10-phenanthroline and chiral phenanthroline templates

Phenanthroline ligands and their many complexes find wide application in chemistry.[12-16] The coordination chemistry of 1,10-phenanthroline was discovered in the late nineteenth century.[17] The rigid framework of phenanthroline has given it a superb ability to coordinate with a large number of transition metals. Compared to the more common 2,2'-bipyridine system, 1,10-phenanthroline can form complexes with metal ions more rapidly.[18] The metal-chelating properties of the phenanthroline and its derivatives have been utilized in a range of analytical chemistry such as colorimetric indicators for transition-metal ions,[19, 20] as ion-selective electrochemical sensors,[21, 22] as fluorometric sensors,[23-25] as well as for the development of bio-organic probes.[18, 26]

The bidentate 1,10-phenanthroline template is a strong chelating agent for a variety of transition metals. Therefore, phenanthroline-metal complexes have become attractive templates for which a ligated metal ion can serve as a Lewis acid binding site and catalyst.[27-30] Generally, nitrogen-containing chiral ligands have found wide use in asymmetric catalysis. However, only a few chiral phenanthroline ligands are known. Gladiali *et al.*, in 1986, reported the first optically active 3-substituted phenanthrolines which were used with rhodium for the preparation of chiral secondary alcohols from pro-chiral ketones (Scheme 1.6).[31] In comparison with bipyridines, phenanthrolines have

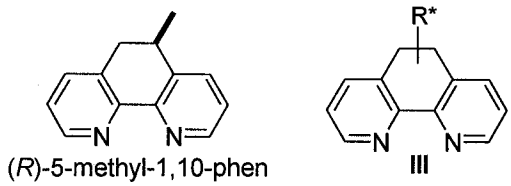
formed more reactive catalyst and shown higher enantioselectivities.[29,30] This supports the hypothesis that the higher rigidity in phenanthroline derivatives stabilizes favorable metal-complexes and translates their chiral information better during catalysis.



Scheme 1.6 Reduction of acetophenone using 3-substituted phenanthrolines

Later, Gladiali and other researchers have reported additional chiral phenanthroline derivatives which can be grouped into two categories: (**I**), the chiral auxiliary is connected to phenanthroline at either the 2- or 3-position or (**II**), the auxiliary is fused to phenanthroline at the 2,3- and 8,9- position (Figure 1.3).[32,33] The chiral domains, when integrated into coordination complexes, may impart stereoselective control to catalytic and molecular recognition processes.

Nevertheless, the ligand system, in which the chiral auxiliary is linked at the B-ring of phenanthroline, is almost unprecedented. In one early work, Chelucci and co-workers synthesized the (*R*)-5,6-dihydro-5-methyl-1,10-phenanthroline as a heterocyclic ligand (Figure 1.4).[34] However, the lengthy synthesis (13 steps) limits the ligand's availability and its catalytic activity has not been tested.



(*R*)-5-methyl-1,10-phen III

Figure 1.4 (*R*)-5,6-dihydro-5-methyl-1,10-phenanthroline and our ligand template with R^* attached to the B-ring

The objectives of this research are to synthesize 5,6-dihydro-1,10-phenanthroline derivatives with chiral centers in the C(5) and C(6) position, and study how stereoselectivity is affected by substituents in the 5- and 6- position during catalytic reactions.

The change in hybridization in the 5- and 6- positions from sp^2 (totally planar 1,10-phenanthroline) to sp^3 causes a twist of the bipyridyl unit, which changes the NCCN dihedral angle (Figure 1.5). By doing so, the steric and/or electronic properties of B-ring substituents can affect metal coordination.

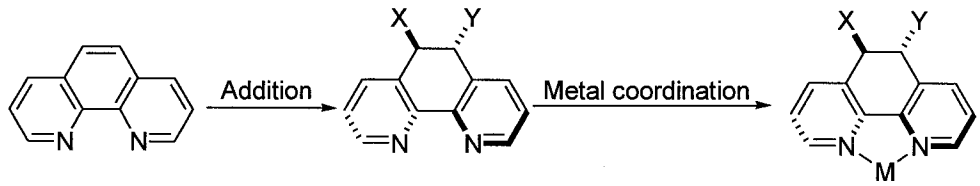


Figure 1.5 Design of 1,10-phenanthroline template

My work on this research project included the synthesis of new enantiopure 1,10-phenanthroline derivatives from 1,10-phenanthroline as starting material, characterization and study of ligand properties toward transition metals, application of the ligand-metal

complexes to transition metal-catalyzed reactions, and learning about asymmetric induction effects as well as the behavior of 1,10-phenanthroline derivatives in asymmetric catalysis.

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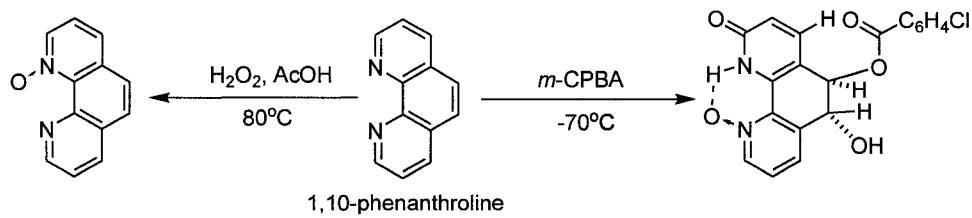
CHAPTER 2: EPOXIDATION

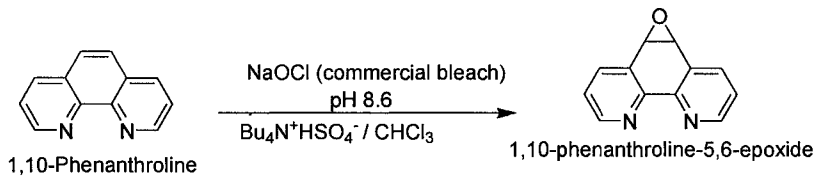
Epoxides are an essential and versatile class of organic compounds. The chemistry of epoxides is particularly attractive since various other functional groups can easily be prepared from them[1] such as alcohols, diols, amino alcohols and others.

In order to introduce chiral centers in the C5 and C6 positions of phenanthroline, the 5,6-dihydro-1,10-phenanthroline epoxide is used as key intermediate in our project. This epoxide can be prepared by oxidation of 1,10-phenanthroline with a suitable oxidizing agent. More traditionally, epoxides are synthesized by the reaction of olefins with hydrogen peroxide in the presence of acetic or formic acid.[2,3] This convenient method involves the *in situ* formation of the corresponding peracid, which serves as the oxidizing agent. However, a downside of this method is potential side reactions of the acid. An example of this is the use of peracid or hydrogen peroxide as oxidant in the oxidation of 1,10-phenanthroline resulting in the formation of a 1,10-phenanthroline-*N*-oxide derivative (Scheme 2.1).[4]



Scheme 2.1 Side reactions during oxidation of 1,10-phenanthroline

A cheap and practical alternative oxidant is aqueous sodium hypochlorite (bleach, NaOCl), which can be used for epoxidation of 1,10-phenanthroline. The synthesis of 1,10-phenathroline epoxide was published in several articles.[4-6] In these reactions, NaOCl was effectively applied as a cheap and convenient chlorine source in the presence of tetrabutylammonium hydrogen sulfate as phase transfer catalyst (PTC, Scheme 2.2).



Scheme 2.2 Epoxidation of 1,10-phenanthroline with NaOCl

The PTC plays an essential role in aqueous-organic two-phase reactions and ensures the transport of inorganic ions into the organic phase. It was also reported that reaction rates for oxidations "become extremely fast provided that the pH of the aqueous NaOCl is lower from 12.7 to about 9.5''.[7]

The B-ring double bond between carbon 5 and 6 of 1,10-phenanthroline is the most reactive site due to the principal canonical forms of aromaticity (Fig. 2.1).[8] There are four of five forms with a 5,6 double-bond, and this bond fixation becomes readily attacked by many reagents.[9, 10]

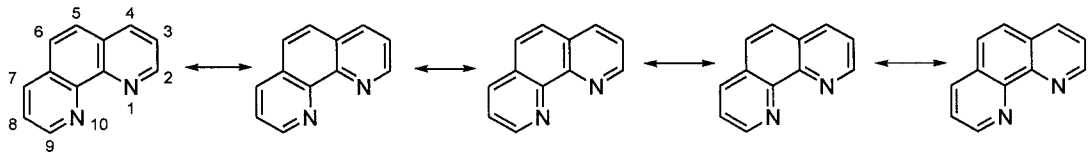
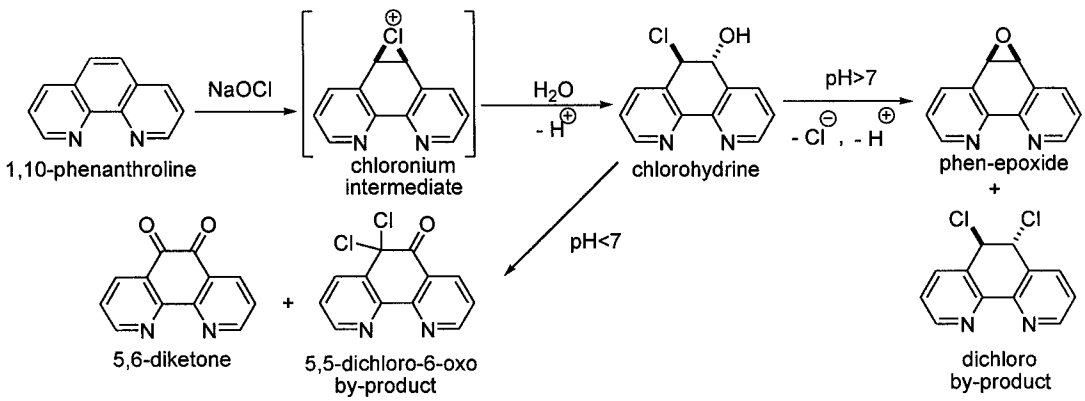


Figure 2.1 Canonical forms of 1,10-phenanthroline

Based on the electrophilic mechanism published by Antkowiak *et al.*,[4] the Cl^+ cation adds to form a 5,6-chloronium intermediate that hydrolyzes to yield the chlorohydrine. The course of the reaction is pH dependent. Under basic conditions (ph>7), chlorohydrine eliminates hydrogen chloride to form the corresponding epoxide, whereas 5,5-dichloro-6-oxo-1,10-phenanthroline and 5,6-dioxo-5,6dihydro-1,10-phenanthroline are formed as products of further oxidation, chlorination, and hydrolysis reactions under acidic conditions (pH<7, Scheme 2.3).



Scheme 2.3 Oxidation pathways of 1,10-phenanthroline at different pH values

We attempted to prepare 1,10-phenanthroline epoxide using various literature procedures,[4-6] however, we were unable to reproduce their results. The epoxidation reaction consumed a large amount of oxidant reagent (industrial bleach), and time to complete (12- 24 hrs). The ratio of epoxide product to by-products varied with different pH values (8.0-9.5). We tested different bleach (4-13% chlorine concentration, in NaOCl) at different pH between 8.0-9.5 which still did not improve the significantly.

Eventually, we modified the method of Lopez *at el.*,[11] and successfully prepared high quality 1,10-phenanthroline epoxide in good yield (70-85%) and less time. 1,10-Phenanthroline epoxide can be obtained by oxidation of 1,10-phenanthroline monohydrate with bleach at pH 8.6 under biphasic ($CHCl_3$/aqueous) conditions while using tetrabutylammonium hydrogen sulfate as phase transfer catalyst. Under our conditions, we used commercial bleach (~6 %) instead of more concentrated solutions (industrial bleach) from Aldrich, which made the reaction less expensive to run. Also, we did not use hydrochloric acid (HCl) to adjust the bleach's pH to avoid the formation of side products (5,6-dichloro and 5,6-chlorhydrin-1,10- phenanthroline). To improve the quality and yield of phenanthroline epoxide, sulfuric acid (6N H_2SO_4) was employed, which reduces the Cl^- concentration that promotes the formation of byproducts. Moreover, 0.5 eq. of PTC provided the best results affording 1,10-phenanthroline epoxide in a short time and good quality. The bleach's quality decreased with time due to self-decomposition (Equation 2.1),[12] which accelerated at decreasing pH values. At the end of the reaction a pH of ~5.0 was typically observed. Because the quality of bleach changed during the reaction time (15 to 30 min.) the yield decreased over time due to side

product formation.[13] Moreover, the epoxidation reaction can be monitored by reverse phase TLC, using MeOH/water (2:1 volume ratio).

$$3NaOCl \rightarrow 2NaCl + NaClO_3$$

Equation 2.1 Self-decomposition of bleach

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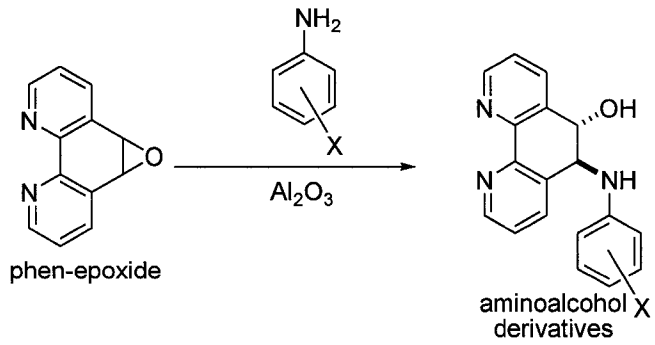
CHAPTER 3: RING OPENING REACTIONS-PREPARATION OF CHIRAL 5,6-*TRANS*- DISUBSTITUTED PHENANTHROLINE DERIVATIVES

Chiral 5,6-dihydro-1,10-phenanthroline derivatives are synthesized by the ring opening reaction of 1,10-phenanthroline epoxide with different amine nucleophiles to functionalize the ligand template. The formation of ensuing amino alcohols proceeds in an *anti*-fashion.

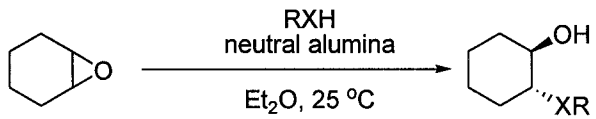
3.1 Epoxide Ring Opening

The ring opening of 1,10-phenanthroline-5,6-epoxide was previously reported by Moody *et al.*,[1] in the preparation of Asciddemin, a natural marine alkaloid, with anticancer properties. They tested various anilines, which were pre-adsorbed on basic alumina, to give the corresponding chiral, racemic aminoalcohol derivatives (Equation 3.1). However, this method could not be extended to the *ortho*-substituted nucleophiles such as 2-cyano and 2-haloanilines. According to the authors, steric congestion on the alumina reaction surface could be a reason for limitation of this method.



Equation 3.1 Conversion of epoxide into aminoalcohol derivatives

The pioneering work of Posner has shown that epoxides could be opened under mild conditions using neutral and basic alumina with a variety of nucleophiles, such as alcohols, thiols, and amines (Equation 3.2).[2-4] He also proposed that alumina catalyzes this reaction by lowering the activation entropy of the epoxide and nucleophile adsorbed close to each other and in the proper orientation for Alumina probably activates the nucleophile by having the Al-O-Al ring on alumina to cleave the heteroatom-H bonds of alcohol, primary and secondary amines.[3]



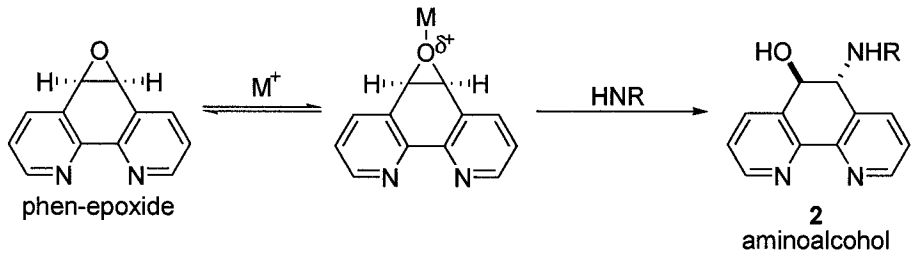
RX = MeO, PhS, *n*-BuNH

Equation 3.2 Epoxide ring opening with alumina catalyst

While looking for practical methods to apply for our substrate, we employed alumina in reactions of 1,10-phenanthroline-5,6-epoxide with known and new nucleophiles (Method A). From experiments we found that the results improved greatly when using activated alumina; Basic Alumina Super I contained less water and worked better than Brockmann I type reagent. In contrast to a previous literature report,[1] we also found that alumina did catalyze reactions with sterically hindered and electron-deficient ortho-substituted anilines (Entry 5, 7, 9, Table 1). However, the use of alumina has some disadvantage including the use of excess nucleophile (3-4 equivalents,) and thorough

quenching and washing with methanol for complete product recovery. Also, the reactions are moisture-sensitive because water deactivates alumina. These reactions often required purification by column chromatography to remove excess amines.

While searching for other methods, we found that magnesium perchlorate[5] ($Mg(ClO_4)_2$) works as an efficient Lewis acid for ring opening of phenanthroline-5,6-epoxide. The magnesium metal assisted aminolysis during the attack of the amine on the metal-coordinated epoxide (Scheme 3.1).



Scheme 3.1 Epoxide ring opening with Lewis acids

In the presence of $Mg(ClO_4)_2$, reactions with 1.0-1.3 equivalents of nitrogen nucleophiles in refluxing acetonitrile cleanly gave the corresponding amino alcohols in very good yields and products could be isolated by a single recrystalization (Method B). Additionally, reactions did not promote any side reactions, (e.g. dehydration) and were suitable for sterically hindered and electrondeficient ortho-substituted anilines (Entries 6, 8, 10, 12, Table 3.1). Furthermore, method B is also applicable to nucleophiles like sodium azide, which could not be used with the alumina method due to poor solubility in dichloromethane.

Table 3.1 Chiral aminoalcohol derivatives (**2a-j**) via epoxide opening

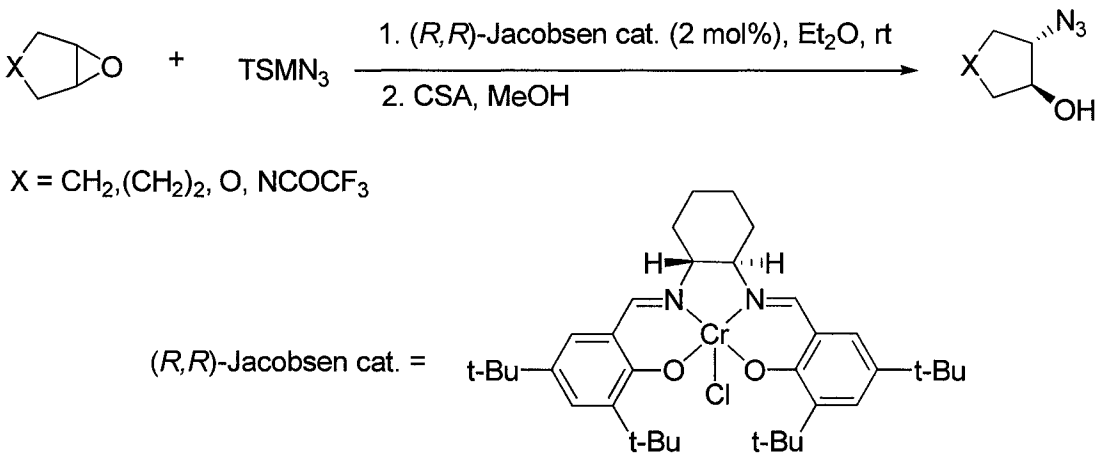
Entry	Nucleophile	Conditions [a]	Product (R =)	Yield % [b]	Melting Points °C
1	Aniline	Method A	**2a** (NH-C_6H_5)	85 (98) [c]	210 (lit. 206)[c]
2		Method B		86	
3	Benzylamine	Method A	**2b** (NH-CH_2-C_6H_5)	85	
4		Method B		87	
5	2-Bromoaniline	Method A	**2c** (NH-2-Br-C_6H_4)	88 (76) [c]	130 (lit. 128)[c]
6		Method B		83	
7	2-Chloroaniline	Method A	**2d** (NH-2-Cl-C_6H_4)	65	155
8		Method B		86	
9	2-Cyanoaniline	Method A	**2e** (NH-2-CN-C_6H_4)	51	149 (lit. 130-131)[c]
10		Method B		73	
11	2-Ethylaniline	Method A	**2f** (NH-2-Et-C_6H_4)	86	146
12		Method B		97	
13	4-ethylaniline	Method A	**2g** (NH-4-Et-C_6H_4)	83	208
14		Method B		78	
15	Sodium azide	Method B	**2h** (N_3)	87 (73) [d]	83 (lit. 99-100)[e]
16	(R)-α-methyl-benzylamine	Method B	**2i** (NH-(R)-(CH_3)-CH-C_6H_5)		
17	4-methoxy-benzylamine	Method B	**2j** (NH-CH_2-4-(CH_3O)-C_6H_4)	62	

[a]Method A: Epoxide (0.255 mmol), nucleophile (3-4 eq.), Al_2O_3 (86 eq.), CH_2Cl_2, 25° C, 24-48 h.
Method B: Epoxide (0.255 mmol), nucleophile (1.0-1.3 eq.), $Mg(ClO_4)_2$ (1.5 eq.), CH_3CN, 80° C, 24-72 h.
[b]Isolated yields after column chromatography or recrystalization. Literature yields are reported in parentheses. All products were characterized by ^1H, ^{13}C NMR, IR and MS spectroscopy.
[c]Reference 1.
[d]Prepared with sodium azide in acetone/water.
[e]Azido alcohol (**2h**) was isolated as hemihydrate.

Due to the symmetric structure of the epoxide, the overall reaction yielded racemic product. In attempts to prepare the corresponding amino alcohols in optically pure form, we used Jacobsen's catalyst; a chiral (salen) chromium complex catalyst that

mediates asymmetric ring opening of epoxides with azidotrimethylsilane ($TMSN_3$) as nucleophile.

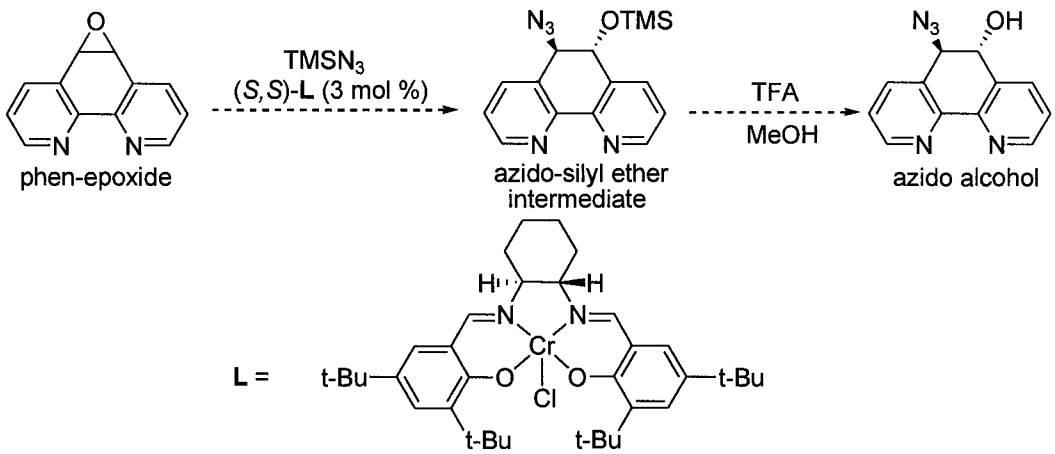
Jacobsen's chiral salen ligand complexes with manganese (III) is a convenient and effective tool for the stereoselective synthesis of the key side chain in the anti-tumor drug Taxol.[6] Replacement of manganese (III) by chromium (III), the (salen) Cr complex served as an effective catalyst for the enantioselective ring-opening of *meso*-epoxides (Scheme 3.2).[7-9]



Scheme 3.2 Asymmetrically epoxide ring opening with Jacobsen catalyst

We tried to apply this catalyst by stirring 1.0 eq. of 1,10-phenanthroline-5,6-epoxide and 1.05 equiv. of $TMSN_3$ with different solvents (CH_2Cl_2, CH_3CN), in the presence of (*S,S*)-Jacobsen's catalyst (3 mol%) at various temperatures (r.t., 35, and 50

°C), followed by the removal of the trimethylsilyl with trifluoroacid in methanol (Scheme 3.3).



Scheme 3.3 Proposed asymmetrically ring opening of 1,10-phenanthroline epoxide with Jacobsen catalyst

Unfortunately, none of our attempted reactions were successful in producing the corresponding azido alcohol. We speculate that the chromium in the Jacobsen catalyst can chelate to the diimine site of the epoxide. Therefore, the phenanthroline derivative can actually compete with the Jacobsen ligand (salen) and interfere with epoxide opening reaction.

3.2 Resolution

We next tried to obtain amino alcohols in enantiomerically pure form via resolution of racemates. Resolution remains a practical, effective and necessary technique to prepare optically pure chiral compounds. Louis Pasteur pioneered this important

approach, which involved the conversion of a mixture of enantiomers into a pair of diastereoisomeric derivatives by reaction with optically pure reagents. Such optically pure reagents are often available from natural sources such as tartaric, malic, and mandelic acids, and alkaloids include brucine, strychnine, morphine and quinine.

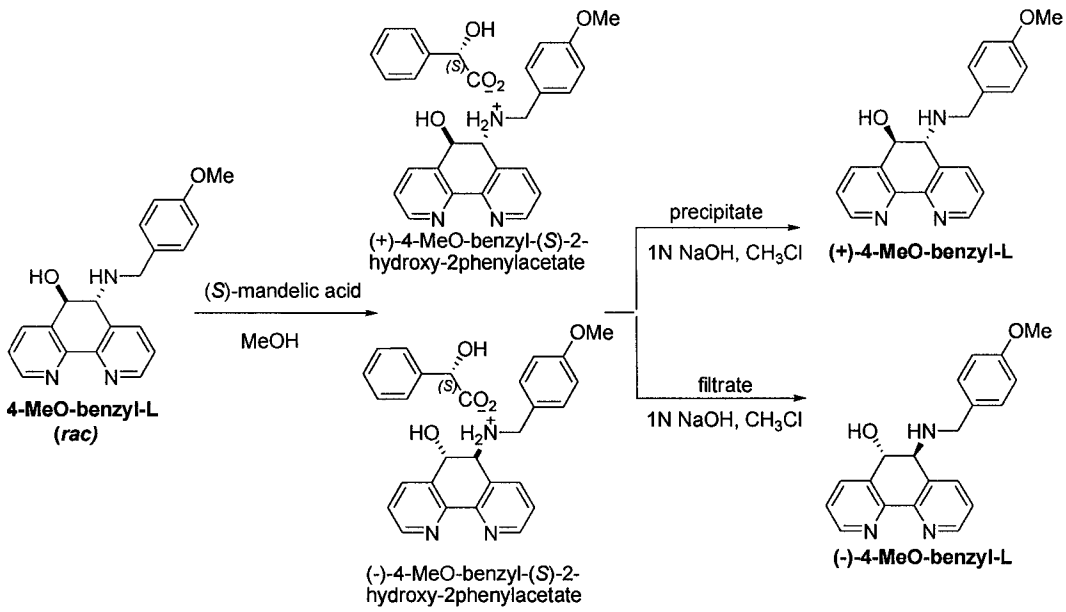
$$R/S \text{ (enantiomers)} + R^* \rightarrow RR^* + SR^* \text{ (diastereomers)}$$

The diastereomers RR^* and SR^* have physical properties (e.g. solubility, boiling point, chromatographic behavior, etc.) which are often significantly different. Often, enantiomers are separated because their diastereomeric salts differ in solubility and allow for fractional crystallization.

Several resolution methods have been reported in the literature that use mandelic acid[10], dibenzoyl tartaric acid[11-13], and oxalic acid.[14] Recently chiral 1,1'-bi-2-naphthol with inexpensive boric acid in acetonitrile and methanol have been employed for chiral separation.[15] We focused on the formation and separation of diastereomeric salts between racemic amino alcohols by using chiral acids such as S-mandelic, S-tartaric, D-camphoric acid, which are commercially available.

Resolution of *trans*-5,6-dihydro-6-N-(4-methoxybenzyl)-1,10-phenanthroline-5-ol (**4-MeO-benzyl-L**) was achieved by reaction of racemic **4-MeO-benzyl-L** with 1.2 equiv of S-mandelic acid in methanol while heating. The mixture was then allowed to stand and the less soluble diastereomeric salt, (+)-4-MeO-benzyl-(*S*)-2-hydroxy-2-phenylacetate, precipitated or crystallized out (Scheme 3.4) was separated from the (-)-4-MeO-benzyl-

(*S*)-2-hydroxy-2-phenylacetate was isolated after filtering and washing with cold-methanol.



Scheme 3.4 Resolution of 4-MeO-benzyl adduct with S-mandelic acid

^{1}H NMR determined the efficiency for separation of diastereomeric salts (Figure 3.1). The (+)- and (-)-4-MeO-benzyl-(*S*)-2-hydroxy-2-phenylacetate salts yielded singly pure amino alcohol products following base extraction. The $[\alpha]_D$ in methanol at 20°C for (+)- and (-)-4-MeO-benzyl adducts are +12.1° and –13.4°, respectively.

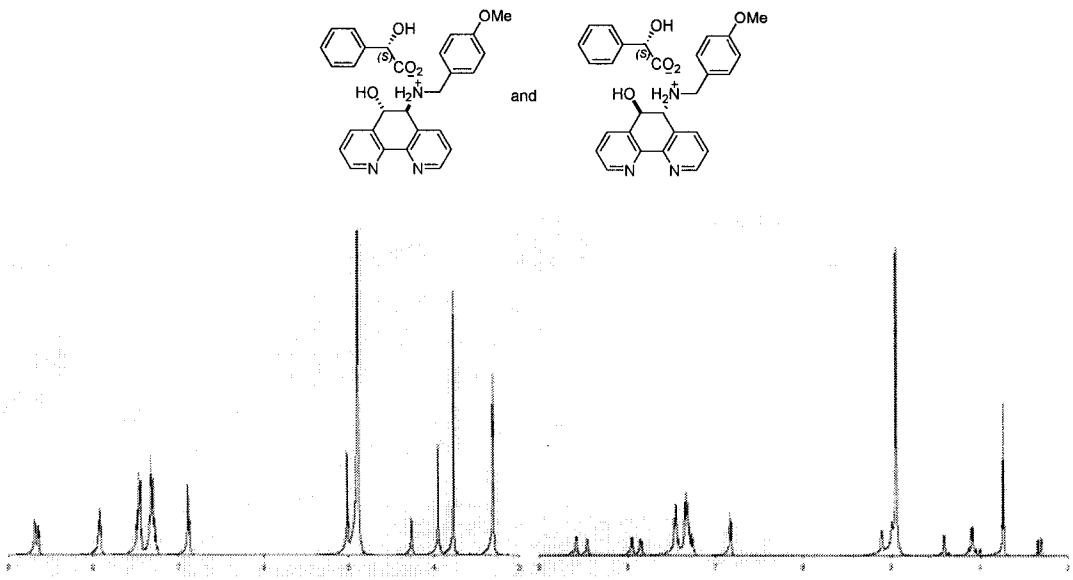
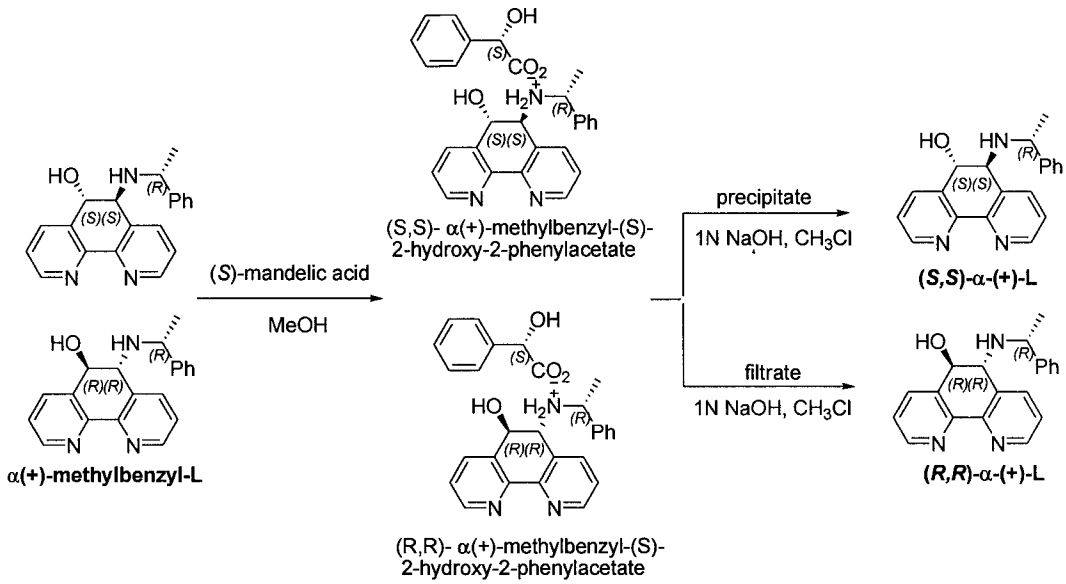


Figure 3.1 ^{1}H NMR spectra of 4-MeO-benzyl-(*S*)-2-hydroxy-2-phenylacetate diastereomeric salts; absolute stereochemistry has not been established

A similar method was applied to separate diastereomeric *trans*-5,6-dihydro-6-*N*-α(+)-methylbenzyl-1,10-phenanthroline-5-ol isomers (**α(+)-methylbenzyl-L**) which could not be separated by simple column chromatography or recrystallization. The white crystal (*S,S*)- α(+)-methylbenzyl-(*S*)- 2-hydroxy-2-phenylacetate complex salt was separated from (*R,R*)- α(+)-methylbenzyl-(*S*)- 2-hydroxy-2-phenylacetate complex salt by filtering and methanol washing. Neutralization of the salts with base afforded enantiopure amino alcohols (Scheme 3.5). Proton NMR spectra showed the **(*S,S*)-** and **(*R,R*)-α(+)-L** were obtained with >99% purity. The $[\alpha]_D$ at 20°C for (*S,S*)- and (*R,R*)-α(+)-adducts are +29.8° and –5.3°, respectively.



Scheme 3.5 Resolution of α(+)-methylbenzyl-L with S-mandelic acid

3.3 5,6-Oxazolidinone-1,10-Phenanthroline Derivatives

In order to avoid side reactions of the hydroxyl group (-OH) and the formation of competing diastereomeric conformers, we linked the functional groups in the 5- and 6-positions (Figure 3.2) in the form of its *oxazolidinone*. Its conformer is locked in the pseudodiequatorial position.

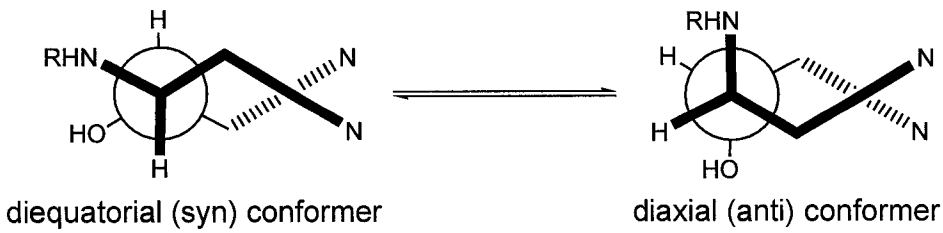
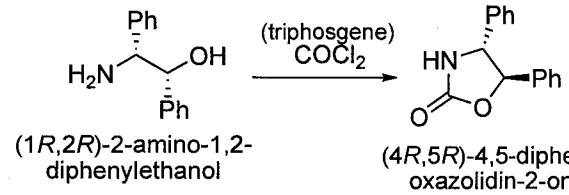


Figure 3.2 Side view of diastereomeric conformers

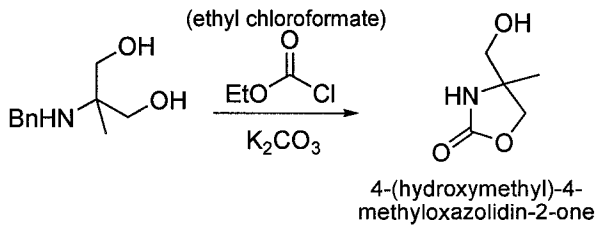
Oxazolidinones are a well-known class of compounds in medicinal chemistry. In 1978, 3-(p-alkylsulfonylphenyl)oxazolidinone derivatives were first shown to be active against plant diseases,[16] and their antibacterial properties were discovered six years later. Besides that, oxazolidinone chiral auxiliaries are often used for diastereoselective Michael additions,[17] alkylations,[18] aldol condensation, Diels-Alder, and other reactions.

Oxazolidinones can be formed via reactions between aminoalcohols and a number of reagents. The use of phosgene or diethyl carbonate provided the most direct route to oxazolidinones as outlined in Scheme 3.6.[19-21]



Scheme 3.6 Preparation of 4,5-diphenyloxazolidin-2-one with phosgene

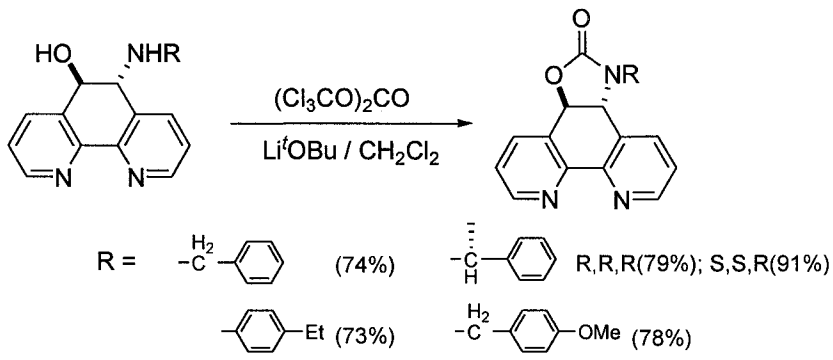
Ethyl chloroformate can also be employed; it first reacted with the amine of amino alcohols and the resultant carbamate can then be cyclized in the presence of base to afford the corresponding oxazolidinone (Scheme 3.7).[22]



Scheme 3.7 Preparation of 4-(hydroxymethyl)-4-methyloxazolidin-2-one with ethyl chlorofomate

We employed the same method to convert *trans*-5,6-aminoalcohol adducts into their oxazolidinone derivatives. The 5,6-dihydro-aminoalcohol-1,10-phenanthrolines reacted with ethyl chloroformate in the presence of different bases (Et_3N, NaH), and solvents (THF, MeCN), at 0 °C to room temperature under argon atmosphere. The desired products were obtained with low to moderate yield (17-45%) after purification. More side products were produced when we used NaH as base in THF or MeCN as solvent.

To improve the yield for this reaction, other reagents (triphosgene, N,N-carbonyldi-imidazole) and bases (Li^t-OBu, $NaOCH_3$) were tested. We found that oxazolidinone derivatives can be prepared in good yield with the use of triphosgene (1.0 equiv), a safer phosgene replacement, and Li^{t}OBu (3.0 eq.) in anhydrous CH_2Cl_2 at 0 °C to room temperature under argon atmosphere (Scheme 3.8). After purification via silica gel chromatography, the desired products were isolated in good yields (73-91%).



Scheme 3.8 Preparation of 5,6-oxazolidinone-1,10-phenanthroline derivatives with triphosgene

However, the carbonylation was unsuccessful with *o*-substituted aniline derivatives. This may be due to the hindering effect of the substituent in the *ortho* position, which prevents amine unit to react with triphosgene.

3.4 NMR Studies

The 5-hydroxy (OH) and 6-amine (NHR) substituents on the phenanthroline ligands can interconvert between pseudoaxial and equatorial position. This alters the ligand twist for equilibrating diastereomeric conformers that affects the ligand chelation site (NCCN, Figure 3.2).

Metal-ligand complexes play an important role in asymmetric catalysis by creating chiral steric barriers and controlling torsional twists. To optimize our ligands we studied *vicinal coupling constants* to determine the syn and anti ratio of conformers.

In hydrocarbons, the spin of the hydrogen nucleus in one C-H bond is coupled to the spin of those hydrogens in adjacent C atoms. This H-C-C-H interaction (Figure 3.3-A) is expressed through its **vicinal coupling constant**, ^3J. The spin-spin splitting patterns follow the $n + 1$ rule (Figure 3.3-B). ^3J measures the magnitude of the splitting, and the actual magnitude of ^3J between two adjacent C-H bonds is depended on the dihedral angle α connecting these two bonds (Figure 3.3-C).[23]

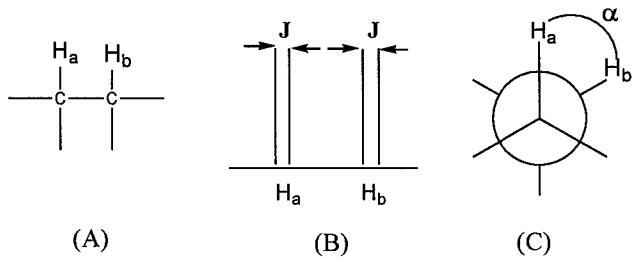


Figure 3.3 Spin-spin splitting and dihedral angle of vicinal protons

Due to the asymmetric structure of *trans*-5,6-di-substituted-1,10-phenanthrolines, H(5) and H(6) are non-equivalent and couple to each other. Their spin-spin splitting appears as two doublets in the proton spectrum. ^{1}H NMR coupling constants were studied for various ligands and results compared to calculated values for ***trans*-4-MeO-benzyl-L** (A, Figure 3.4) and 3-(4-methoxybenzyl)-3,3a-dihydro-oxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one (**oxa-4-MeO**, (B) Figure 3.4) as summarized in Table 2.

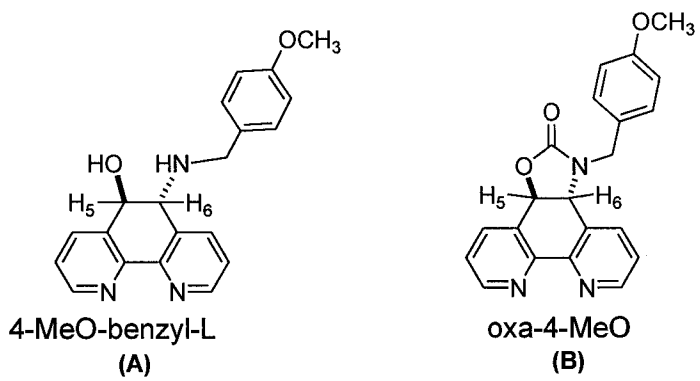


Figure 3.4 Vicinal protons (H_5 and H_6) in 4-MeO-benzyl-L and oxa-4-MeO

Table 3.2 Comparison of calculated and experimental data

	^{1}H NMR, $J_{5,6}$ [Hz] (observed)	^{1}H NMR, $J_{5,6}$ [Hz] for ***anti*** conformer (calculated)	^{1}H NMR, $J_{5,6}$ [Hz] for ***syn*** conformer (calculated)
4-MeO-benzyl-L	9.5,[a] 5.9[b]	1.7	13.0
4-MeO-benzyl-L·H$^+$	4.4,[b] 3.7[c]	1.7	12.7
oxa-4-MeO	13.9[a]		14.2

[a] Recorded in $CDCl_3$, [b] Recorded in MeOD, [c] Recorded in D_2O

The computational studies for $J_{5,6}$ of ligands (**A**) and (**B**) were done by Professor John Miller at WMU which helped to determine preferred conformations in conjunction with ^{1}H NMR experiments. For ***trans*-4-MeO-benzyl-L** (**A**), the $J_{5,6}$ for H(5) and H(6) were 9.5 Hz (*syn* preferred) and 5.9 Hz (*anti* preferred) in $CDCl_3$ and MeOD, respectively. Changing from an aprotic solvent to a protic one caused a reverse in the anti/syn ratio from 31/69 to 63/37, (Boltzman distribution ratio). The protic solvent perhaps breaks up the intramolecular H-bonding between the amino and alcohol group in the pseudodiequatorial conformer forming very bulky sovation shells that prefer a pseudodiaxial arrangement to avoid allylic strain. A similar switching helicity was made when (**A**) was protonated with HCl gas, shifting the equilibrium further toward the anti isomer **A·H** (4.4 Hz, 75% in MeOD and 3.7 Hz, 82 % in D_2O).

Cyclization of (**A**) through carbonylation with triphosgene yielded oxazolidinone (**B**), which permanently locked the 5- and 6-sustituents in the syn conformation. The experimental value of $J_{5,6}$ (13.9 Hz) was very close to the calculated value (14.2 Hz).

Figure 3.5 shows the change in chemical shift and coupling constants for methine and benzyl protons.

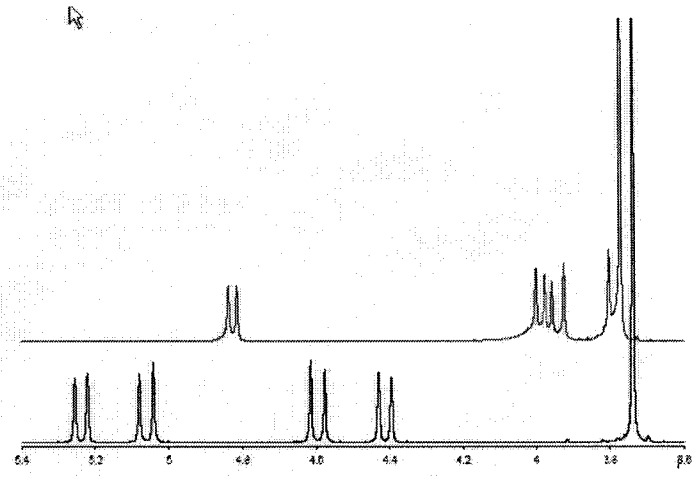


Figure 3.5 ^{1}H NMR spectra of **A** (above) and **B** (below) in $CDCl_3$

Oxazolidinone derivatives (**(*S,S*)** and **(*R,R*)-oxa-α(+)**, **oxa-benzyl**, and **oxa-4-Et-anilyl**) showed identical $J_{5,6}$ values (13.9 Hz) in ^{1}H NMR experiments.

Ligands (**A**) and (**B**) were also studied with solid-state data from X-ray diffraction, carried out by Professor Marc Perkovic at WMU. Amino alcohol (**A**) preferred a syn arrangement with a dihedral angle (NCCN) of 21°, which was close to the calculated value 19.6°, and 23° for oxazolidinone (**B**) where the calculated value was 21.8° (Figure 3.6).

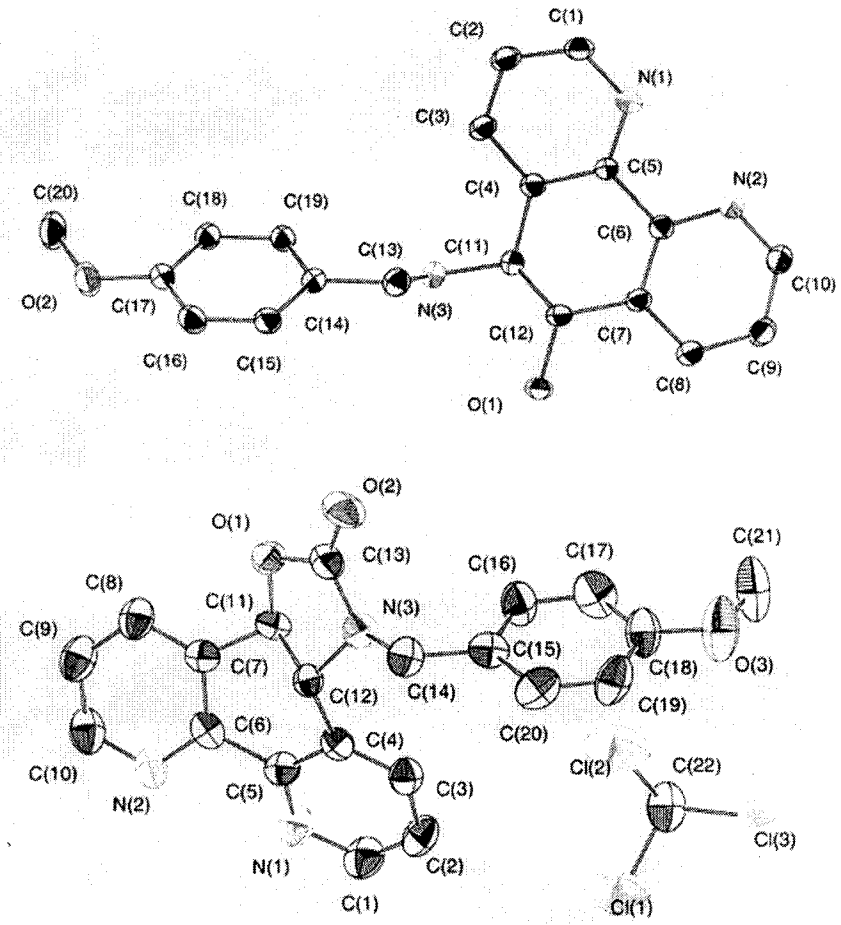
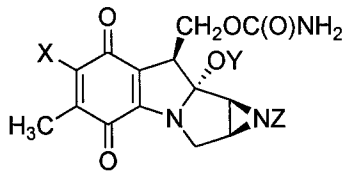


Figure 3.6 Molecular structure (ORTEP view) of 4-MeO-benzyl-L (above) and oxa-4-MeO (below)

3.5 C_2-Symmetric Ligand

Among the vast number of chiral ligands that have been prepared so far, nevertheless a relatively small number of them stand out because of their broad applicability. Ligands are capable of exerting a high level of enantiocontrol in many different metal-catlyzed reactions. Often C_2 symmetry can beneficially affect enantioselectivities.

Similarly to epoxides, aziridines are valuable synthetic intermediates because the strained three-membered ring can be opened by a variety of nucleophiles. Aziridines can be found in natural products such as mitomycin, porfiromycin, and mitiromycin, which are potent antitumor and antibiotic agents (Figure 3.7).[24, 25]

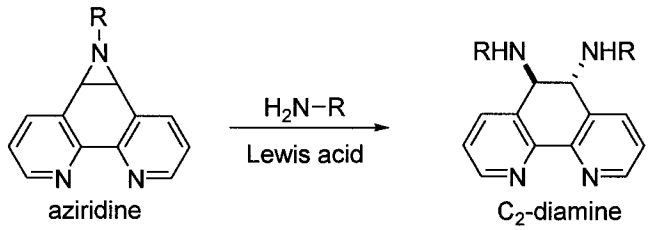


Mitomycin A: X = OMe, Y = Me, Z = H
Mitomycin B: X = OMe, Y = H, Z = Me
Mitomycin C: X = NH_2, Y = Me, Z = H
Porfiromycin: X = NH_2, Y = Me, Z = Me

Figure 3.7 Mitomycins, aziridine containing, antitumor and antibiotic agents

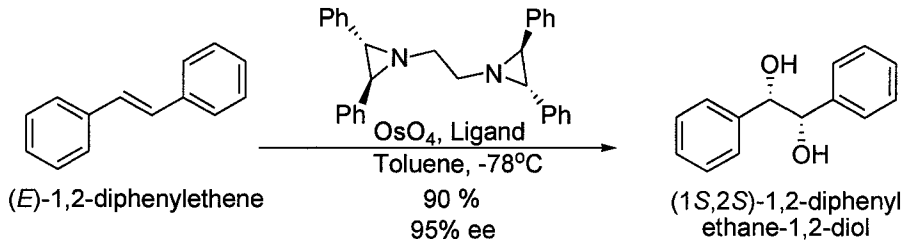
Because aziridine structures are closely related to epoxides; the approaches to their syntheses are very similar. The simplest preparation of aziridines is the ring closure of a β-functional ethylamine and the required precursors for this route to aziridines is usually a 1,2-amino alcohols.

To apply the concept of C_2 symmetry to our phenanthroline ligand template, we introduced identical substituents in the 5- and 6-positions. Similar to the preparation of *trans*-5,6-dihydro-aminoalcohol-1,10-phenanthroline, the C_2-*trans*-5,6-dihydro-diamine-1,10-phenanthroline was synthesized by aminolysis of 5,6-dihydro-aziridine-1,10-phenanthroline intermediate using a Lewis acid catalyst (Scheme 3.9).



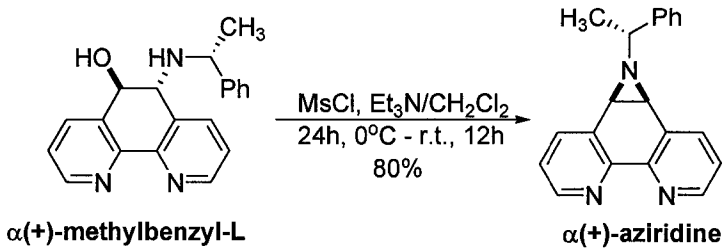
Scheme 3.9 Acid salt's metal catalyzes aziridine ring opening

Aziridines can also be utilized as ligands in asymmetric catalysis as outlined in Scheme 3.10.[26]



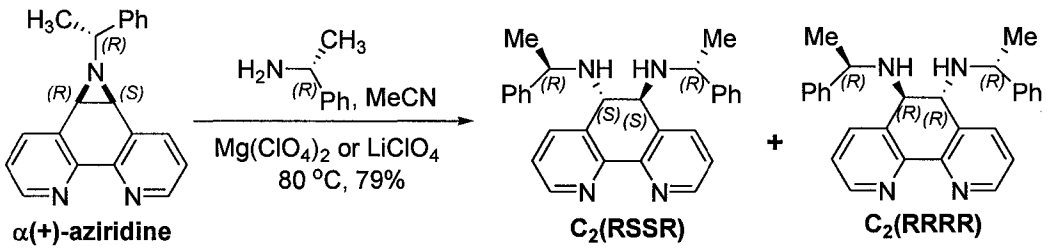
Scheme 3.10 Asymmetric dihydroxylation using an aziridine containing ligand

The preparation of 1a,9b-dihydro-1-((R)-1-phenylethyl)-1H-azirino[2,3-f][1,10] phenanthroline (**α(+)-aziridine**, Scheme 3.11) was accomplished by mesylation of a diastereoisomeric mixture of (5*R*,6*R*) and (5*S*,6*S*) of 6-((R)-1-phenylethylamino)-5,6-dihydro-1,10-phenanthrolin-5-ol according to the literature procedure.[27] The aziridine product was generated via spontaneous intramolecular mesylate displacement in 80% yield.



Scheme 3.11 The preparation of α(+)-aziridine derivative

Ring opening of **α(+)-aziridine** was carried out with (*R*)-α-phenylethylamine in the presence of lithium or magnesium perchlorate, the diastereomeric ((1'*R*,5*R*,6*R*,1'*R*) and (1'*R*,5*S*,6*S*,1'*R*)) of *trans*-5,6-dihydro-N5,N6-bis((R)-1-phenylethyl)-1,10-phenanthro-line-5,6-diamine (**C_2(RRRR), C_2(RSSR)**) product were separated by column chromatography using SiO_2, $CHCl_3$/3% MeOH (Scheme 3.12) and thus isolated in enantiopure form in 79 % yield.



Scheme 3.12 Preparation of C_2(RRRR) and C_2(RSSR) diamine derivatives

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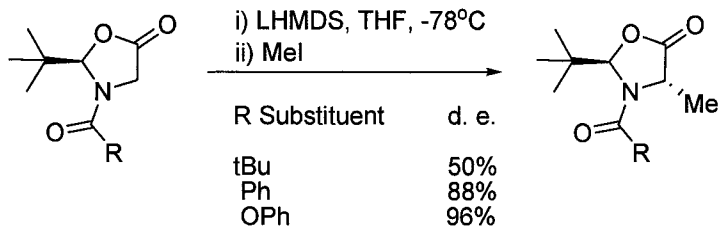
Chapter 4: Metal Complexes of 5,6-Disubstituted 1,10-Phenanthrolines

Many ions and organic functional groups can form complexes with metals. The concept of a metal complex originated in the work of Alfred Werner, who, in 1913, was awarded the first Nobel Prize in inorganic chemistry. The formation or presence of bonds between two or more separate binding sites within the same ligand and a single atom is described as *chelation.* The word *chelate* was first applied in 1920 by Morgan and Dew,[1] who stated: "The adjective chelate, derived from the great claw or **chela (chely- Greek)** of the lobster or other crustaceans, is suggested for the caliper like groups which function as two associating units and fasten to the central atom so as to produce heterocyclic rings." Metal complexation is of widespread interest. Many scientific disciplines study it, especially organic chemistry where transition metal-catalyzed reactions are becoming increasingly important tools. Various metals, combined with suitable organic ligands, form catalysts that can be efficiently used for the formation of C-C, C-N and C-O bonds in functionalized organic molecules.

In asymmetric synthesis, the metal complexes (chiral catalysts) often consist of transition metals and chiral ligands. Most chiral ligands are small heterocyclic compounds that rely on sterically demanding functional groups to control the conformation of their ring system. Under ideal circumstances, the conformation of a chiral catalyst should be constrained to ensure that its prochiral center reacts with a reagent via diastereoisomeric transition states, and are sufficiently different in energy to ensure that only a single diastereoisomer is formed as product. The complex interplay within the catalyst is often subtle, and many examples exist where small changes in bond

angles, or heteroatom hybridization can result in large changes in diastereoselectivities. For example, asymmetric induction during α-substitution in Scheme 4.1[2] was depended upon the nitrogen protecting group.



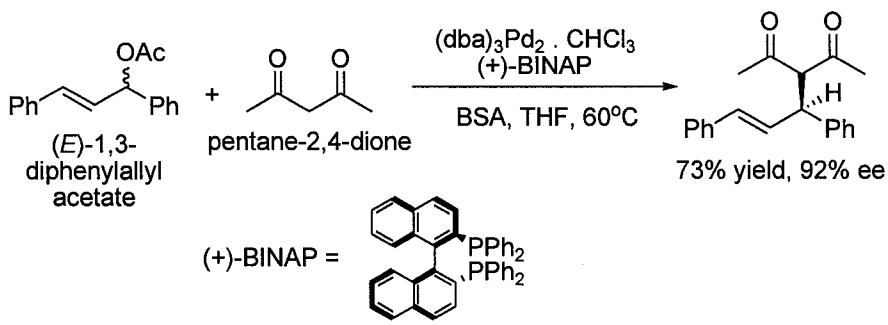
Scheme 4.1 Nitrogen protecting group affects diastereoselectivity

1,10-Phenanthroline can form many different metal complexes. This property has been exploited for the detection of metal ions since 1930's and similar coordination chemistry can be achieved in 5,6-dihydrophenanthroline derivatives. The change of hybridization in the 5- and 6- positions from sp^2 to sp^3 causes a change of the N-C-C-N dihedral angle and it affects the diimine chelating site. To investigate how this modification of ligands will affect the catalytic function before and after metal coordination, we prepared 1,10-phenanthroline complexes with several transition metals such as Pd, Ni, Zn, and Ru. Additionally, we studied chiral ligand structures through solid state analyses to better understand the effect of ligand modification.

4.1 Palladium-1,10-Phenanthroline Complexes

4.1.1 Dichloropalladium-1,10-Phenanthroline Complexes

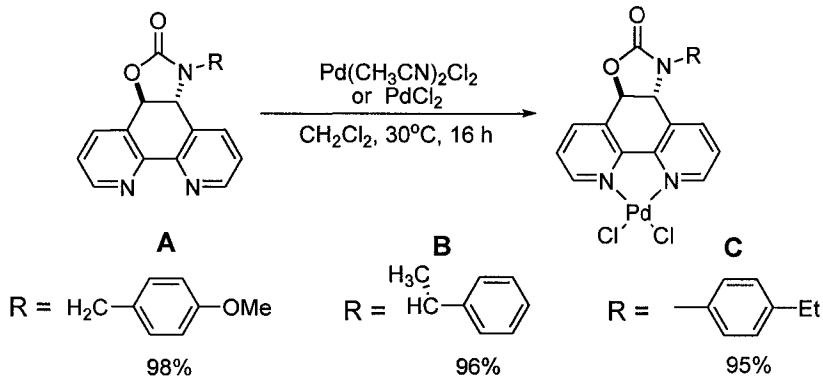
Palladium (Pd) is a rare silver-white transition metal of the platinum group. It is primarily used as an industrial catalyst, i.e. to speed up hydrogenation or dehydrogenation reactions as well as petroleum cracking. Pd-based catalysts play an indispensable role in synthetic organic chemistry. Particularly for asymmetric C-C bonds formation, the catalyzed-asymmetric allylic reaction is now a widely used process in organic chemistry (Scheme 4.2).[3-5]



Scheme 4.2 Pd-catalyzed allylic alkylation[4]

A dichloropalladium (II) complex with a bidentate donor ligand is found in the basic metal complex structure, a square planar metal arrangement. Its structure contains a Pd metal atom coordinated with two chlorine atoms and a ligand that has two binding sites to Pd. We reacted our ligands with dichloropalladium (II) to study the corresponding complexes.

The dichloropalladium-1,10-phenanthroline complexes (**A-C**) were prepared by modified literature procedures (Scheme 4.3).[6,7] 5,6-Oxazolidinone-1,10-phenanthroline derivatives were mixed with bis(acetonitrile) palladium chloride, $Pd(CH_3CN)_2Cl_2$, or palladium(II) chloride, $PdCl_2$, in CH_2Cl_2 heated at 30°C for 12hrs, affording very good to nearly quantitative yields of the corresponding metal-complexes.



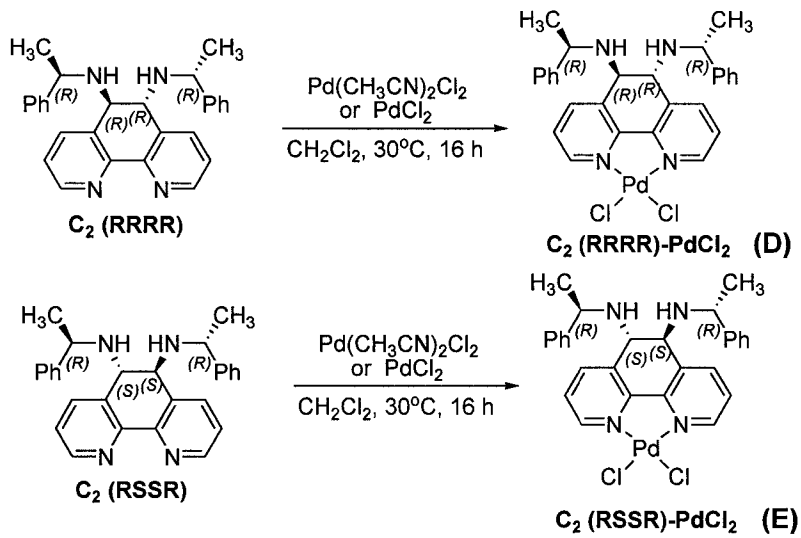
Scheme 4.3 Palladium-1,10-phenanthroline complexes

From ^1H NMR spectra in DMSO-d_6, the $J_{5,6}$ of (**A**, **C**) free ligands were compared to those of metal complexes. Coupling constants changed from 13.91 Hz to 14.65 Hz in both cases. Using the Karplus correlation, the increase of the $J_{5,6}$ value suggests that the dihedral angle NCCN has changed to a larger angle after complexation.[8] The final proof for this will only be available through solid-state analysis.

Unfortunately, attempted re-crystallizations of ligands **A** and **C** with various solvent systems (DMSO, DMSO/water, DMF), at different temperatures and techniques

(solvent evaporation, solvent liquid/vapor diffusion, cooling, gradual cooling under vacuum) were unsuccessful. The complexes (**A** & **C**) were characterized by ^{1}H, ^{13}C NMR, and melting point. The study of complex **B**, due to its insolubility in most organic solvents, even in hot DMSO was limited.

The C_2-symmetrical ligands, **C_2 (RRRR)** and **C_2 (RSSR)**, were also complexed to dichloropalladium, following similar procedures (Scheme 4.4).



Scheme 4.4 Palladium-diamine-1,10-phenanthroline complexes

^{1}H NMR confirmed palladium coordination with C_2 ligands at the diimine site instead of the diamine moiety. In the **C_2 (RRRR)-$PdCl_2$ (D)** complex, we observed heteroaromatic proton resonance shifts downfield as follows: δ 8.59 → 8.82 ppm for H's at 2- and 9- position, (7.35-7.40) → 7.61ppm and 7.80 ppm for H's at the 3,8-, and the 4,7- position, respectively (Figure 4.1). Moreover, the strong complexation capability of

the diimine functionality was evident in the solid state. The crystal structure of **C_2 (RRRR)** showed that a $CHCl_3$ molecule was chelated at the diimine site (Figure 4.2). Similar effects were seen for the proton resonance of the **C_2 (RSSR)-$PdCl_2$** complex.

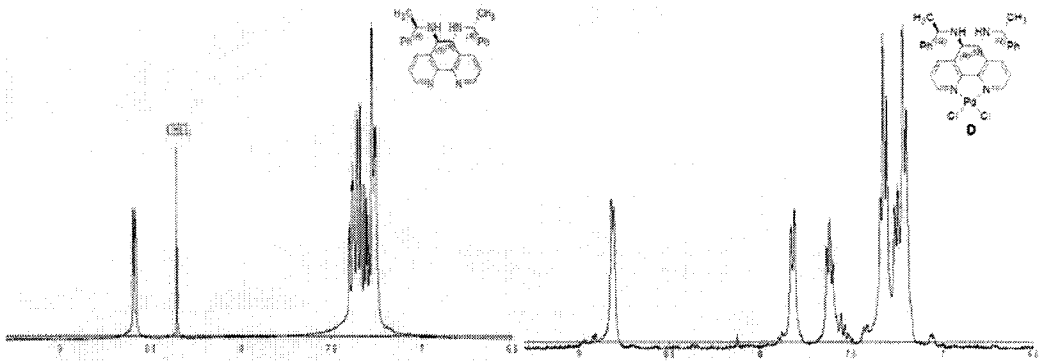


Figure 4.1 Comparison of C_2 diamine ligand with its palladium complex

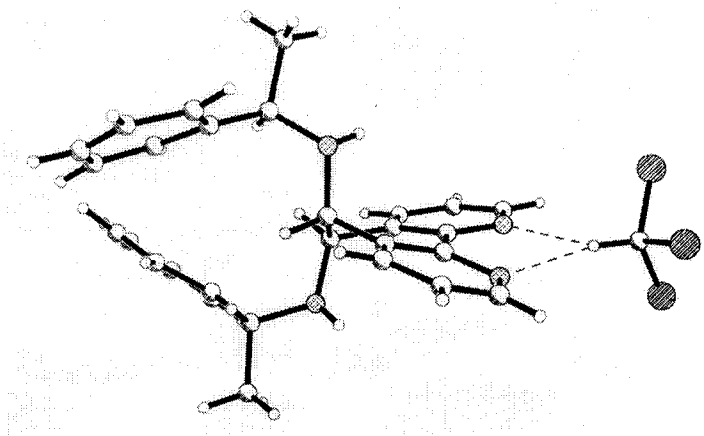
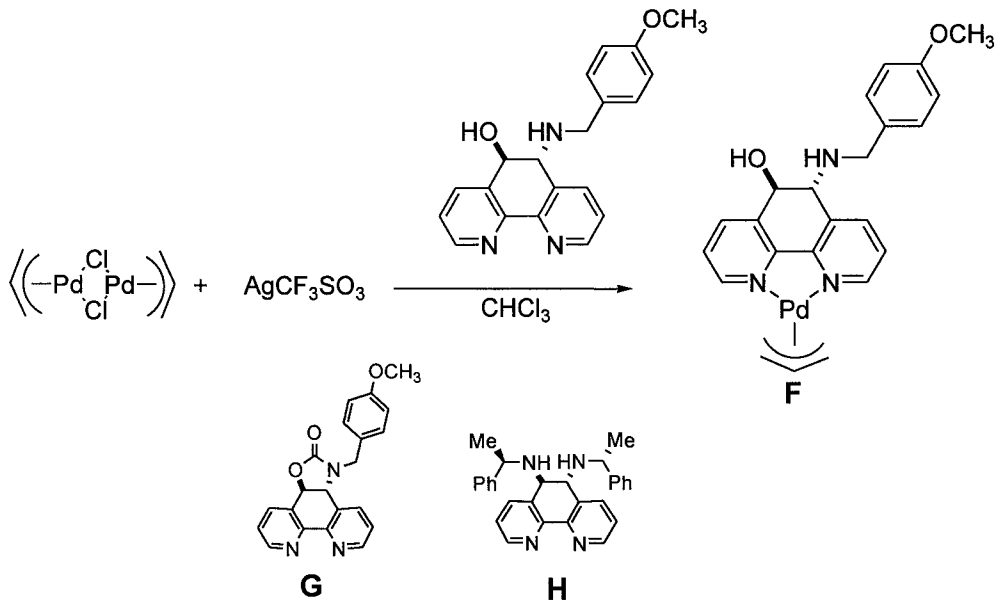


Figure 4.2 Crystal structure of C_2 (RRRR) chelated to $CHCl_3$

4.1.2 (π-Allyl)Palladium 1,10-Phenanthroline Complexes

Metal π-complexes are organometallic compounds, containing a bond between carbon and a delocalized π-electron system and may therefore be considered to be bonded to two or more contiguous ligands atoms. π-Allyl complexes are of significant utility in organic chemistry. Amongst the most noteworthy and commonly used are allylpalladium(II) complexes which react with nucleophiles, allylstannanes and allylboranes.

We employed (π-allyl)palladium chloride dimer to synthesize (π-allyl)palladium-1,10-phenanthroline complexes. 5,6-Dihydro-6-(4-methoxybenzylamino)-1,10-phenanthrolin-5-ol (1,3-η^3-propenyl)palladium trifluoro-methanesulfonate (**4-MeO-benzyl-Pd-OTf, F**) was prepared using a known procedure.[9-11] The method initially involved a reaction of the allylpalladium chloride dimer with the silver salt, $AgCF_3SO_3$, through ligand and metal exchange. Formation of the complex occurs upon addition of the 5,6-dihydro-6-(4-methoxybenzylamino)-1,10-phenanthrolin-5-ol ligand (Scheme 4.5).



Scheme 4.5 (π-Allyl) palladium complexes with 1,10-phenanthroline derivatives

To understand the change of the NCCN dihedral angle after complexation, it was important to obtain structural information for these (π-allyl)palladium complexes. The structure of complex **F** was determined by X-ray analysis and NMR spectroscopy and compared to computational calculations.

The crystallization of metal complexes was achieved at -10^{o}C by a solvent diffusion technique under approximately stoichiometric conditions. An ORTEP representation of the ligand complex is shown in Figure 4.3. The geometry of the complex shows that the Pd is coordinated to two nitrogen atoms at the chelated site of the ligand yielding a N-C-C-N dihedral angle of -8.6^{o}; the free ligand has an angle of 21^{o}.

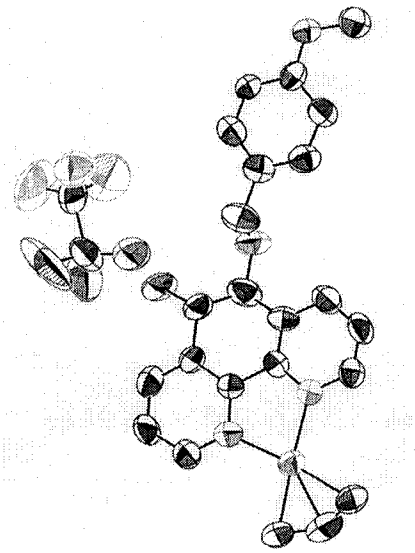


Figure 4.3 Molecular structure (ORTEP view) of the complex **F**

Computational chemistry DFT studies using B3LYP method, mixed basis sets (LANL2DZ, in the pseudopotential mode for Pd, and 6-31G* for O, H, C, N) have been performed to visualize the geometry and electronic structure of complex **F** in the ground state. The optimized structure revealed a NCCN dihedral angle of 12.6° (Figure 4.4).

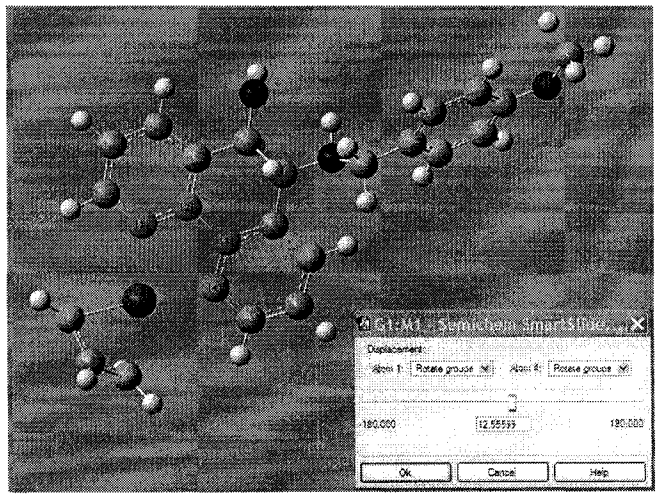


Figure 4.4 Gaussian view window showing the N-C-C-N dihedral angle value

Complex **F** formation can be followed by ^{1}H NMR in DMSO-d$_6$. The chemical shift of the terminal π-allyl protons changes significantly for several protons (δ 5.85→6.05 ppm for H-2; 4.24→4.51 ppm for H_{syn}; 3.39→3.55 ppm for H_{anti}), and heterocyclic protons (δ 8.64→8.89 ppm for H's at the 2- and 9- position; 7.86→8.27, 7.82→8.21 for H's at the 4- and 7- position; and 7.40→7.79 for H's at 3- and 8- position). The $J_{5,6}$ value was not change (4.76 Hz).

The 5,6-oxazolidinone-6-(4-methoxybenzylamino)-1,10-phenanthroline(1,3-η^3-propenyl)palladium trifluoromethanesulfonate (**oxa-4-MeO-Pd-OTf**, **G**) and (5*R*,6*R*)-5,6-dihydro-N5,N6-bis((*R*)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine η^3-propenyl) palladium trifluoromethanesulfonate (**C_2 (RRRR)-Pd-OTf**, **H**) complexes were prepared in the same way as complex **F**.

The formation of complex **G** was confirmed by comparing ^{1}H and ^{13}C NMR spectra in $CDCl_3$, both before and after complexation with the Pd dimer. The splitting and chemical shifts of the heterocyclic protons changed from "triplet" to "doublet-doublet" (δ 8.82→8.78 ppm.), (δ 7.86→8.21 ppm) for protons at the 2-, 9-, and 4-, 7- position, respectively and "doublet-doublet" to "doublet-doublet-doublet" (δ 7.38→7.76 ppm). There were two additional resonance peaks of sp^2 carbon and one more of sp^3 for the π-allyl carbons in the decoupled carbon NMR spectrum. Furthermore, comparison between complex **G** and the π-allyl-Pd dichloride dimer in $CDCl_3$ also confirmed complexation. The π-allyl resonance in complex **G** shifted downfield (δ 5.46→5.92 ppm for H-2;

4.11→4.40 ppm for H_{syn}; 3.04→3.55 ppm for H_{anti}). The $J_{5,6}$ value in **G** also increased from 13.91 to 14.65 Hz (Figure 4.5).

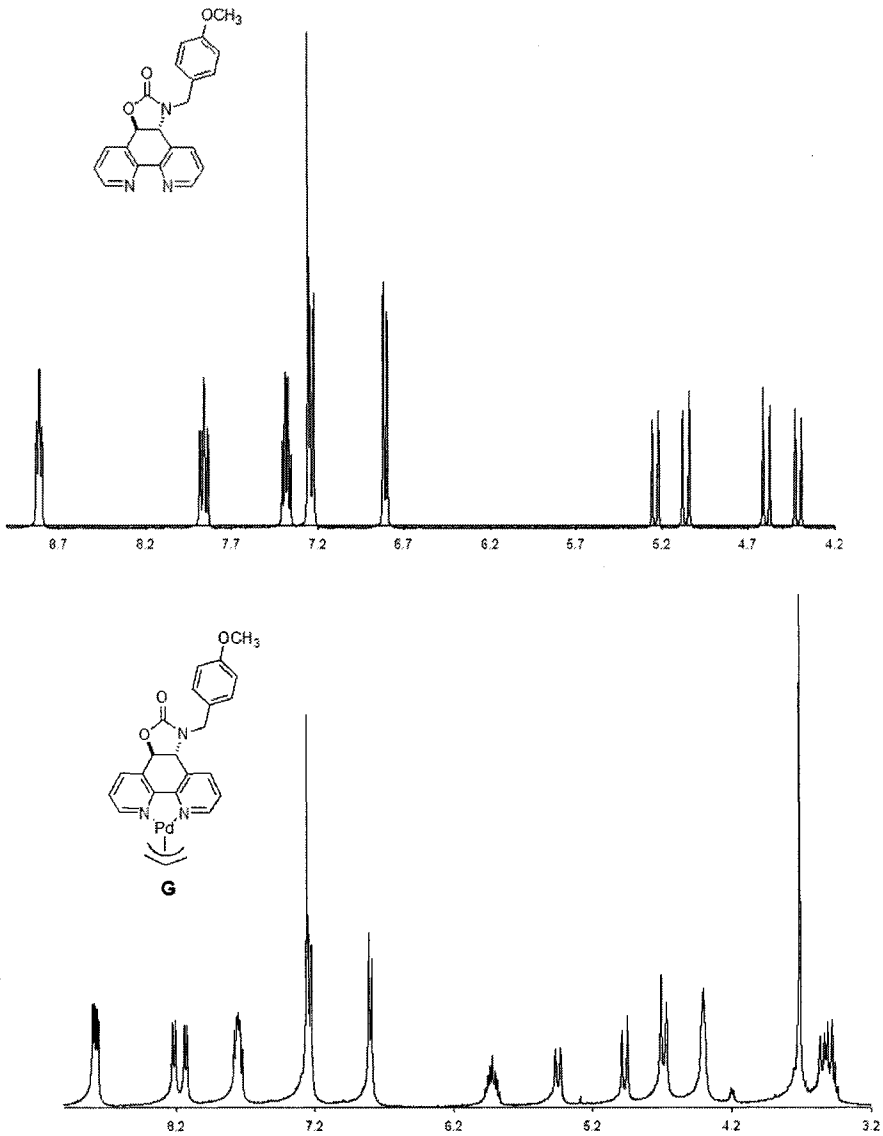


Figure 4.5 ^{1}H NMR spectra of 4-oxa-MeO (above) and its (π-allyl) palladium complex (below)

The crystallization of the **C_2 (RRRR)-Pd-OTf (H)** complex was performed in the same way as for **F** and yielded tiny yellow-needline crystals. Unfortunately, the complex

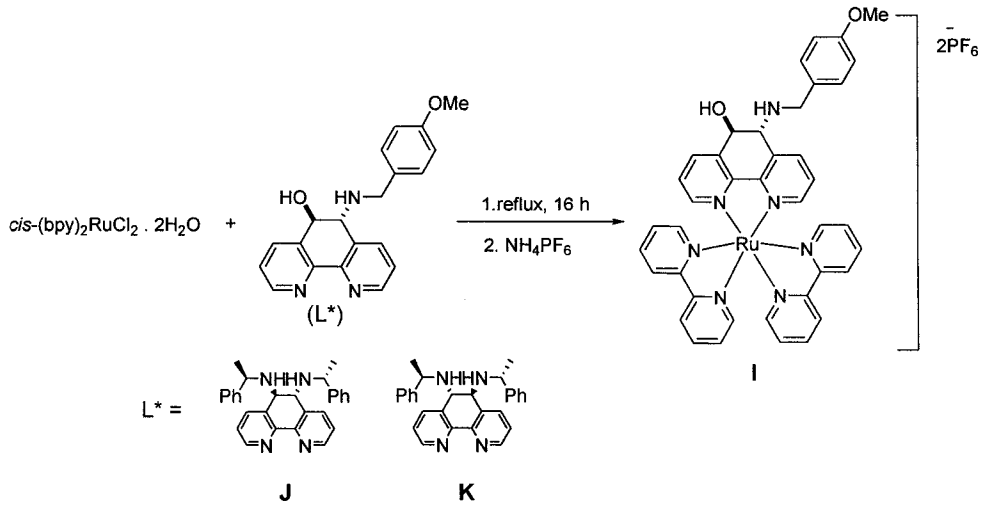
structure cannot be examined by X-Ray analysis due to its labile physical property; however, the formation of its (π-allyl)palladium complex was verified by ^{1}H NMR.

4.2 Ruthenium – 1,10-Phenanthroline Complexes

Ruthenium is an element with the widest range of oxidation states in the periodic table (from –2 to +8). The metal-complexes of each oxidation state can assume several coordination geometries. The wide range of oxidation states, coordination geometries, and tunable properties result in the ability of ruthenium complexes to catalyze a significant range of chemical transformation such as ring-closing metathesis,[12] hydrogenation,[13] cyclopropanation,[14] and many more. In addition, ruthenium complexes have been used as chiral building blocks for supramolecular chemistry,[15] or as chiral probes for biological molecules (DNA, polynucleotides).[16] The majority of the ruthenium complexes used are in the +2 oxidation state. Octahedral hexacoordinated ruthenium(II) complexes bearing 2,2'-bipyridine ligands (bpy) have been used extensively as visible light-active photosensitizers because they exhibit metal-to-ligand charge transfer (MLCT) excited states.[17-19]

In order to broaden the scope of metal-1,10-phenanthroline complexes we focused on complexation with Ru(II). The *cis*-$(bpy)_2RuCl_2{\cdot}2H_2O$ was prepared in 68-70% yield following a literature procedure,[20] and used as ruthenium metal source. The *cis*-$(bpy)_2RuCl_2.2H_2O$ was confirmed by measuring UV absorption (547 and 368 nm) and comparison with literature values (550 and 375 nm).[21] The $[Ru(bpy)_2(phen)](PF_6)_2$

complexes were obtained after refluxing *cis*-$(bpy)_2RuCl_2.2H_2O$ and the ligands in aqueous methanol, followed by addition of NH_4PF_6 (Scheme 4.6).



Scheme 4.6 $[Ru(bpy)_2(L^*)](PF_6)_2$ complexes

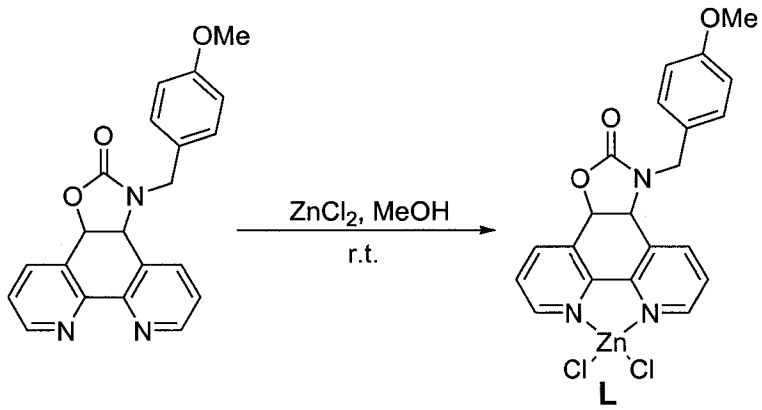
Attempted recrystalization of complexes **I**, **J**, and **K** in different solvent mixtures (DCM/Hexanes, acetone/ether, DMSO/water), and subsequent ion exchange with $^-ClO_4$, OTf were unsuccessful. Materials were characterized by ^1H, ^{13}C NMR and melting point.

4.3 Zinc and Nickel-1,10-Phenanthroline Complexes

Zinc and Nickel complexes of 1,10-phenanthroline ligands were prepared using the same literature procedure.[22] The authors reported a method for dichloro(1,10-phenanthroline-2,9-dicarbaldehyde dioxime)zinc as well as (dichloro)(DMSO)-(1,10-phenanthroline-2,9-dicarbaldehyde dioxime)nickel for the purpose of X-ray diffraction study.

4.3.1 Zinc-1,10-Phenanthroline Complex

In our lab we used 5,6-oxazolidinone-6-(4-methoxybenzylamino)-1,10-phenanthroline as ligand to prepare dichloro(5,6-oxazolidinone-6-(4-methoxybenzylamino)-1,10-phenanthroline)zinc and nickel complexes; $ZnCl_2$, and NiBr were used as metal sources. The ligand reacted with metal salt under (1:1) metal/ligand ratio in DMSO, and was followed by vapor diffusion of DCM (Scheme 4.7), no solid formed. Additional unsuccessful crystallization attempts were carried out at room temperature.



Scheme 4.7 Dichloro-1,10-phenanthroline-zinc complex

After the ligand reacted with $ZnCl_2$ in MeOH overnight at room temperature the formation of dichloro[5,6-oxazolidinone-6-(4-methoxy-benzyl-amino)-1,10-phenanthroline]zinc (**L**) was corroborated by ^1H NMR analysis. The proton resonance peaks in the 2- and 9- position (δ 8.83 ppm) changed from "triplet" to "doublet" after complexation; same as for H's in the 4-, 7- and 3-, 8- position, the resonance peaks changed from "triplet" to "doublet-doublet" and from "doublet-doublet" to "doublet-doublet-doublet", and shifted downfield (δ 7.86 → 8.21 ppm), (δ 7.39 → 7.82 ppm), respectively. The

methine protons in the 5-, 6- position were also shifted downfield (Figure 4.6). The $J_{5,6}$ value changed from 13.91 to 14.28 Hz after complexation.

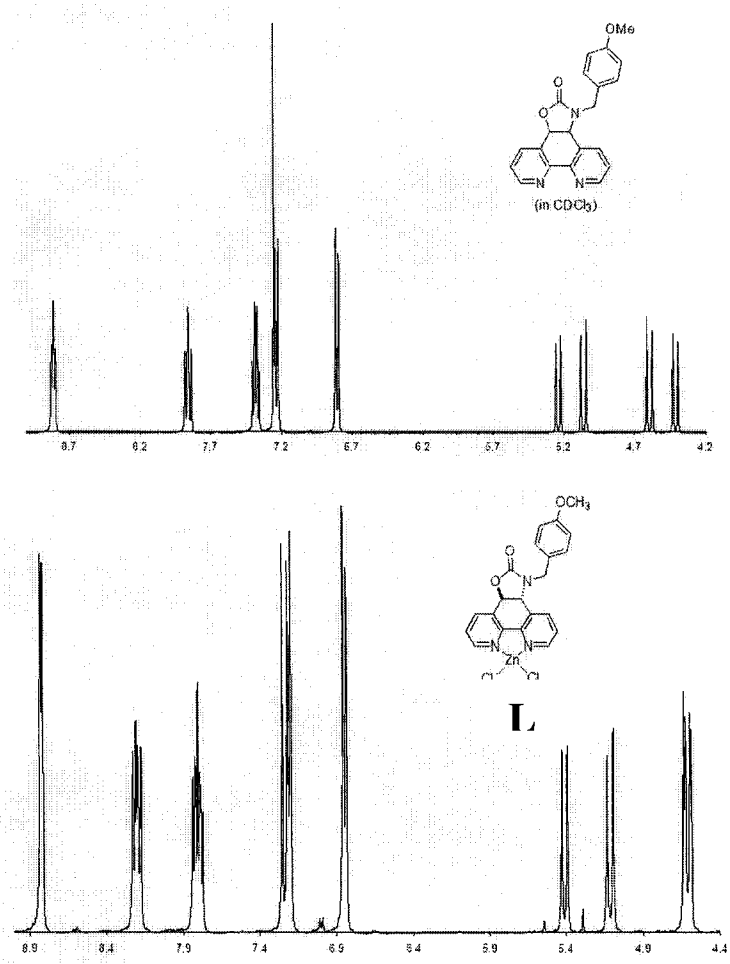


Figure 4.6 ^{1}H NMR spectra of 4-oxa-MeO (above) and 4-oxa-MeO-$ZnCl_2$ (below)

4.3.2 Nickel-1,10-Phenanthroline Complex

The dibroro[5,6-oxazolidinone-6-(4-methoxy-benzyl-amino)-1,10-phenanthroline]nickel complex was prepared using $NiBr_2$ instead of $ZnCl_2$. No crystals or precipitate formed after different recrystalization methods were explored. Unfortunately, nickel

complexes could not be characterized by NMR spectroscopy due to their paramagnetic properties.

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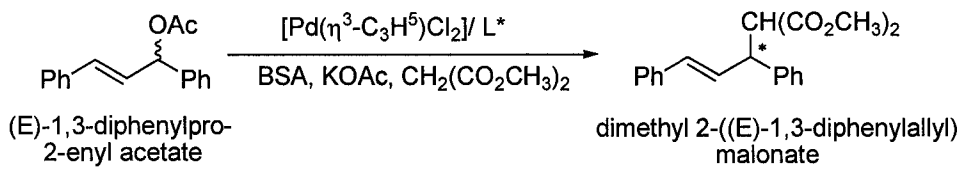
CHAPTER 5: PALLADIUM CATALYZED ASYMMETRIC ALLYLIC ALKYLATION

The palladium-catalyzed substitution reaction of allylic substrates has been examined thoroughly during the last four decades, beginning with Tsuij's pioneering work in 1965.[1] The first allylic substitution reaction in the presence of palladium catalyst was reported in 1970,[2,3] and in 1973 Trost published the first asymmetric version.[4] Palladium-catalyzed asymmetric allylic alkylation reactions are widely used in organic chemistry, particularly for asymmetric carbon-carbon bond forming reactions.[5-8] It also has become the standard test reaction to determine the effectiveness of new ligands. Specifically, (*E*)-1,3-diphenylpro-2-enyl acetate has been used as the substrate and many ligands have been applied to this enantioselective alkylation of this compound (Scheme 5.1).[8]



Scheme 5.1 Allylation of (*E*)-1,3-diphenyl-2-propenyl acetate

5.1 Mechanism and Catalytic Cycle with Palladium

To obtain good stereoselectivity the incoming nucleophile needs to discriminate enantiotopic faces of the π-allyl complex of (*E*)-1,3-diphenylpro-2-enyl acetate (Figure 5. 1).[7] Nucleophilic attack usually occurs from the face opposite the metal and an overall

retention of stereochemistry is achieved. The induction at the π-allyl depends upon the nature of the allyl moiety with respect to the chiral space about the ligands.

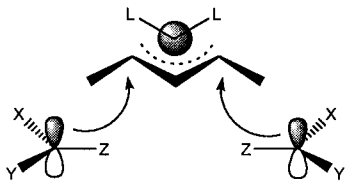
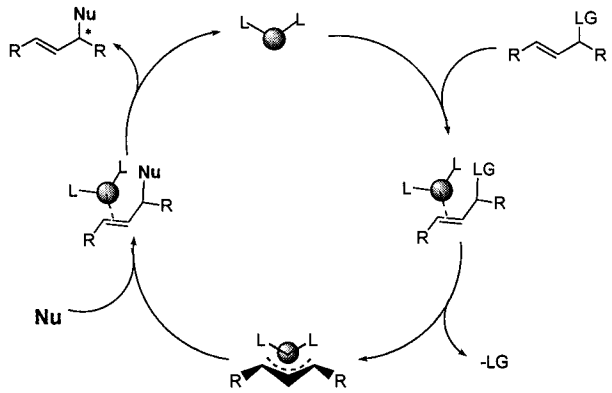


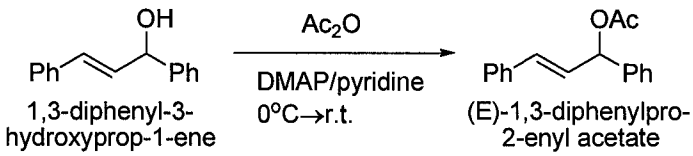
Figure 5.1 Nucleophile attacking on π-allyl complex

According to the widely accepted mechanism of Pd-catalysis asymmetric allylic substitution proposed in "*Catalytic Asymmetric Synthesis*" by Trost and Lee,[9] the catalytic cycle begins with the formation of an η^2 -Pd^0 complex and subsequent dissociation of the leaving group which provides the η^3 -Pd^{+2} complex. A nucleophile moves toward displacing the Pd with inversion at either the proximal or distal terminus of the allyl moiety to generate the η^2 -Pd^0 complex. Decomplexation of Pd regenerates the catalyst and the product is released (Scheme 5.2).



Scheme 5.2 Catalytic cycle with palladium

In order to investigate the performance of our new ligands in asymmetric catalysis and particularly in asymmetric alkylation of (*E*)-1,3-diphenylpro-2-enyl acetate, we tested the reaction shown in Scheme 5.1. (*E*)-1,3-Diphenylpro-2-enyl acetate was prepared according to the literature procedure,[10] by reacting 1,3-diphenyl-3-hydroxyprop-1-ene with acetic anhyride in the presence of DMAP as catalyst. After purification (*E*)-1,3-diphenylpro-2-enyl acetate was isolated in good yield (80%, Scheme 5.3), which was confirmed by NMR (^{1}H, ^{13}C).



Scheme 5.3 Preparation of (*E*)-1,3-Diphenyl-2-propenyl acetate

The Pd-catalyzed alkylation of the allylic acetate was carried out in the presence of a (π-allyl)-palladium-ligand complex, generated *in situ* from 2.5 mol% $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ and 10 mol% of our ligand. Dry dichloromethane was chosen as solvent based on the literature discussion,[10] stating that solvent polarity does affect the reaction. For example, DMSO gives shorter reaction time but lower enantioselectivities. Dichloromethane alone was impracticable due to the low solubility of the sodium salt of dimethyl malonate. However, the use of *N*, *O* – bis (trimethylsilyl) – acetamide (BSA) and sodium acetate (NaOAc) as bases to deprotonate dimethyl malonate avoided these difficulties and provided the product. The transformation was complete after 24 h and our preliminary results are summarized in Table 5.1.

Table 5.1 Allylic alkylation's result data

Entry	Nucleophile	Ligand	Isolated Yield (%)	E. e. (%)
1	$NaCH(CO_2CH_3)_2$	**(*rac*)-oxa-4-MeO**	81	0[a,b]
2	$NaCH(CO_2CH_3)_2$	**(+)-oxa-4-MeO**	80	0[a,b]
3	$NaCH(CO_2CH_3)_2$	**(*S,S*)-oxa-α(+)**	86	1[a], 0[b]
4	$NaCH(CO_2CH_3)_2$	**C_2 (RRRR)**	86	14[a], 0[b]
5	$NaCH(CO_2CH_3)_2$	**C_2 (RSSR)**	81	3[a], 0[b]

[a] The enantiomeric excess be determined by ^1H NMR with (+)-Eu(hpc)$_3$
[b] The enantiomeric excess be determined by Daicel OD-H 25x0.46 cm (L x I.D.) at λ = 254 nm; flow rate 0.5 mL/min; eluent : Hexanes/IPA (200:1), t_R = 23.5 t_S=25.0 min.

The product was analyzed with chiral shift reagent, (+)-Eu(hpc)$_3$ and chiral HPLC methods to determine the enantiomeric excess of product.

5.2 NMR With Shift Reagents

Enantiomers cannot be differentiated in the NMR spectrum because the probe is isotropic. However, diastereomers display different chemical shifts. Diastereoisomeric complexes are formed by mixing the chiral shift reagent (+)-Eu(hpc)$_3$ with racemic dimethyl 2-((*E*)-1,3-diphenylallyl)malonate product. (+)-Eu(hpc)$_3$ is a Lewis acid and Eu^{3+}coordinates with one or two oxygen atoms in carbonyl groups (Figure 5.2).

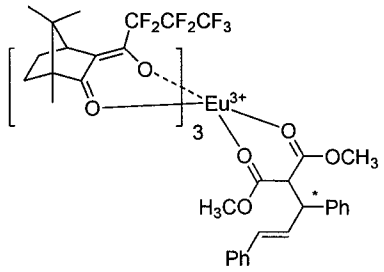


Figure 5.2 Interaction of (+)-Eu(hpc)$_3$ with malonate product

The proton resonance from the malonate methyl groups of diastereoisomers complexes showed 2 singlets and a doublet at 4 ppm. region, in which the singlets were from different enantiomers (Figure 5.3). The singlet with the highest chemical shift ppm corresponds to the (*R*)-enantiomer.[10]

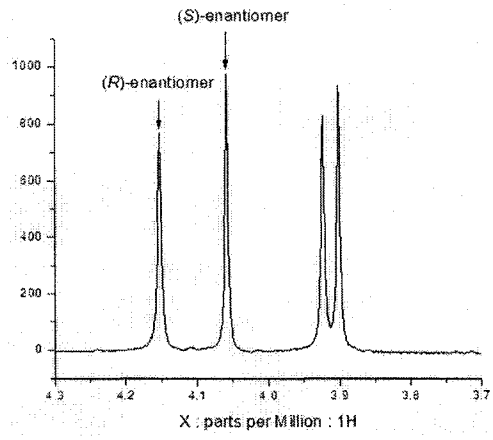


Figure 5.3 Chemical shift of methyl protons in malonate enantiomers

5.3 Chiral HPLC

A chiral column (Daicel, Chiralcel OD-H) was used to determine the ee % of the product by HPLC. The chiral column is commercially available and made by

immobilizing a single enantiomer, cellulose tris(3,5-dimethylphenyl carbamate), onto the stationary phase (Figure 5.4). The separation of allylic substitution enantiomers is based on the interaction of each enantiomer with the cellulose tris(3,5-dimethylphenyl carbamate) in the stationary phase in which one enantiomer will be retained in the column longer than the other.

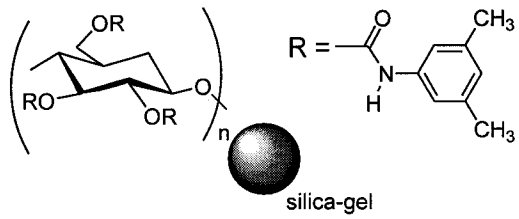


Figure 5.4 Cellulose tris (3,5-dimethylphenyl-carbamate) coated on silica-gel

The palladium complexes of ligands **(*S,S*)-oxa-α(+)**, **(*rac*)-oxa-4-MeO**, **(+)-oxa-4-MeO**, **C_2 (RRRR)**, and **C_2 (RSSR)** catalyzed allylic substitution reactions. The products were isolated in good yield (80-86%); however, there was no enantioselectivity. No asymmetric induction was relayed through the palladium-ligand complex to afford the stereoselective substitution. The difference ee% analysis's results between shift reagent and HPLC method (Table 5.1, entry 3-5), which could be explained that the substitution product NMR sample was contaminated with some impurities that might affect the methyl's proton peaks. Additionally, it could be error from integration in NMR spectrum. Comparison X-Ray analysis of **4-MeO-benzyl-L** and **4-MeO-benzyl-Pd-OTf** showed the dihedral angle (N-C-C-N) was changed to smaller angle (8.6^0), therefore ligand could not created steric hindrance or electronic effect at the catalytic site to cause asymmetric induction affect (Figure 5.5).

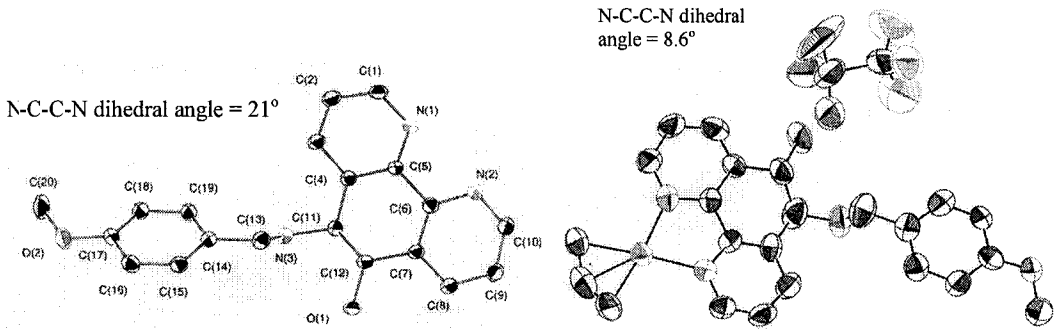
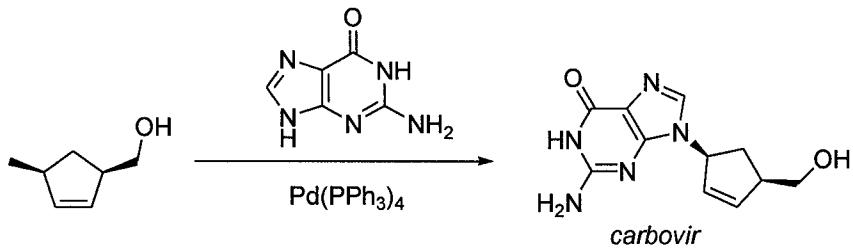


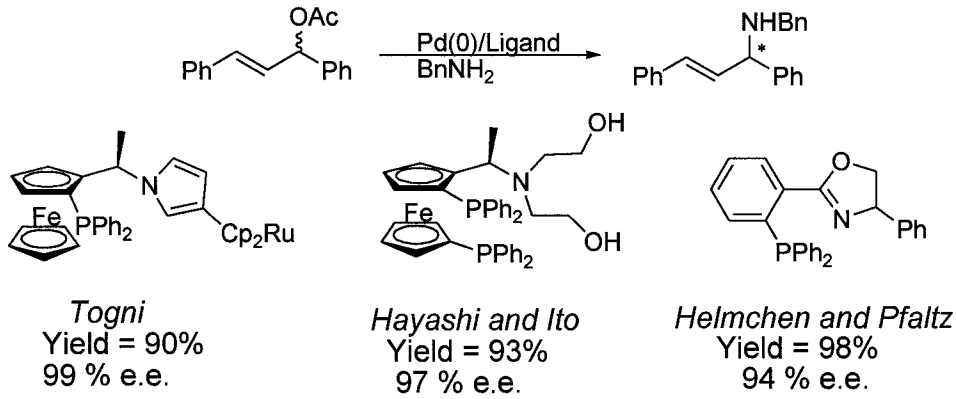
Figure 5.5 ORTEP representation of 4-MeO-benzyl L (left) and 4-MeO-benzyl-Pd-OTf (right)

As an extension of this investigation, asymmetric allylic amination of 1,3-diphenylprop-3-en-1-yl acetate with benzylamine was also carried out. Allylic amination with allylic acetates has been used in the synthesis of carbocyclic nucleoside such as *carbovir*, an *in vitro* inhibitor of the HIV virus (Scheme 5.4),[11] using $Pd(PPh_3)_4$ as metal source.



Scheme 5.4 Palladium-mediated reactions used in the synthesis of *Carbovir*

During the past decades many studies have focused on efficient chiral catalysts. Among them, the ligand developed by Togni,[12] Hayashi and Ito,[13] and Helmchen and Pfaltz[14] has proven to be very effective in allylic amination reactions (Scheme 5.5).



Scheme 5.5 Ligands for allylic amination reactions

We applied phenanthroline ligands to the palladium-catalyzed allylic amination of (*E*)-1,3-diphenylpro-2-enyl acetate with benzylamine in tetrahydrofuran (THF). The catalyst was prepared *in situ* by mixing 2.5 mol% $Pd(dba)_3$ and 5 mol% ligands (***rac*)-oxa-4-MeO, 4-Et-anilyl, benzyl L,** and (***rac*)-α(+) L** under an argon atmosphere. Unfortunately, conversions were low (< 10%).

Based on the results reported above, there is a possibility that these ligands will find future applications. Catalysis results may be improved by modifying the 2- or/and 9-position, which would possibly amplify the helical twist. This amplification may be necessary to better relay stereochemical information from the B-ring.

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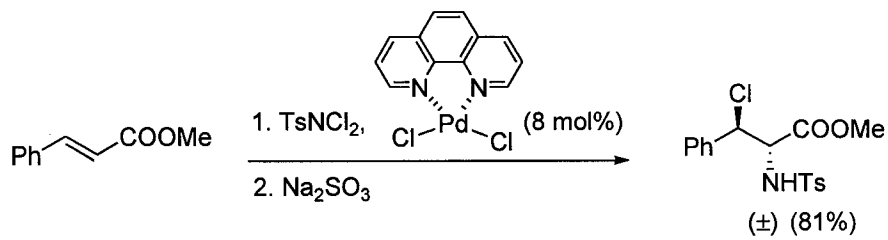
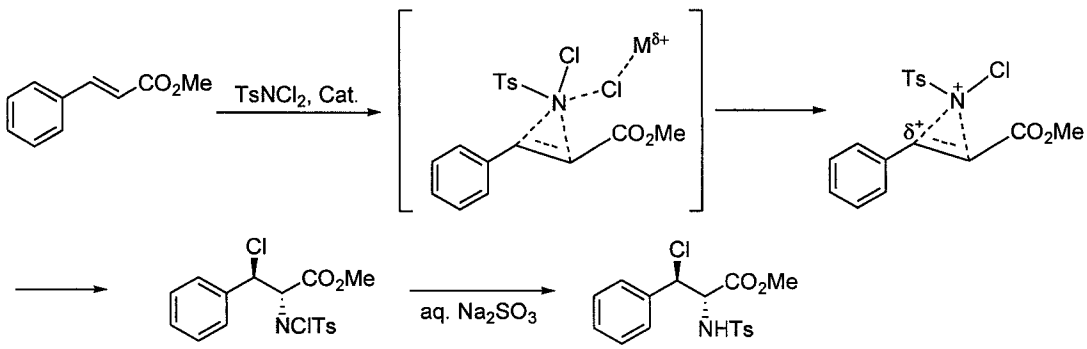
CHAPTER 6: PALLADIUM CATALYZED AMINOHALOGENATION

Vicinal haloamine compounds are very important intermediates for organic and medicinal chemistry. They can be transformed into aziridines or β-substituted amino acids.[1, 2] Recently, Guigen Li's group has done several studies of the heterolytic additions of nitrogen and halogen atom to olefins,[3-9] and transition metal-catalyzed aminohalogenation of cinnamic esters is one methodology that interested us. Li[6] reported the use of metal-ligand complexes as the catalysts in the aminohalogenation of α,β-unsaturated carboxylic esters. Out of eight different metal complexes Li found dichloro-1,10-phenanthroline-palladium(II) was the only metal complex that carried out the reaction to completion in 81% yield. The reactions were performed by simply combining of cinnamic esters (olefin substrates), N,N-dichloro-IpI-toluenesulfonamide ($TsNCl_2$, or dicholoramine T) as nitrogen and chlorine sources, and dichloro-1,10-phenanthroline-palladium(II) in acetonitrile at ambient atmosphere (Scheme 6.1).



Scheme 6.1 Aminochlorination of cinnamic ester with Pd-1,10-phenanthroline complex[6]

Li's aminohalogenation reactions were reported with > 95% regio- and stereoselectivity in most case. *N*-*N*-Dichlorosulfonamide reacts with the olefin to form an *N*-chloroaziridinium intermediate and the palladium metal center of metal complex coordinates to the chlorine atom of $TsNCl_2$ which weakens the N-Cl bond and Cl^- leaves to form the "Ts-$N^{\delta+}$-Cl" species. The Pd-associated chlorine anion then acts as nucleophile to open the *N*-tosyl-*N*-chloro aziridium intermediate.[3, 4, 6]The S_N2 mechanism of aziridinium ring opening is accountable for the *anti* seteroselectivity. And because the stabilization effect of the phenyl ring, the β-carbon of the aziridinium ring has a more positive charge than the α-carbon, therefore controlling the regioselectivity of the reaction (Scheme 6.2).



Scheme 6.2 Proposed mechanism of aminohalogenation reaction

The regioisomers were distinguished by their ^1H NMR spectra in which the coupling constants and correlation patterns in the HMBC spectrum (Heteronuclear Multiple Bond Correlation) clearly showed their structural differences. Sudalai reported[10] α proton resonance for aminobromination reactions that help explain the regiochemistry.

In general, the α proton appears more upfield in comparison to the β proton. Moreover, the multiplicity of each methine proton changes depending on the adjacent substituent (Figure 6.1). For ethyl ester **4a**, the α proton is adjacent to the bromine and gives a doublet peak. However, in methyl ester **3a**, the α proton is attached to the carbon with the *p*-toluenesulfonamido group and couples with the NH, thus yielding a doublet of doublet peak.

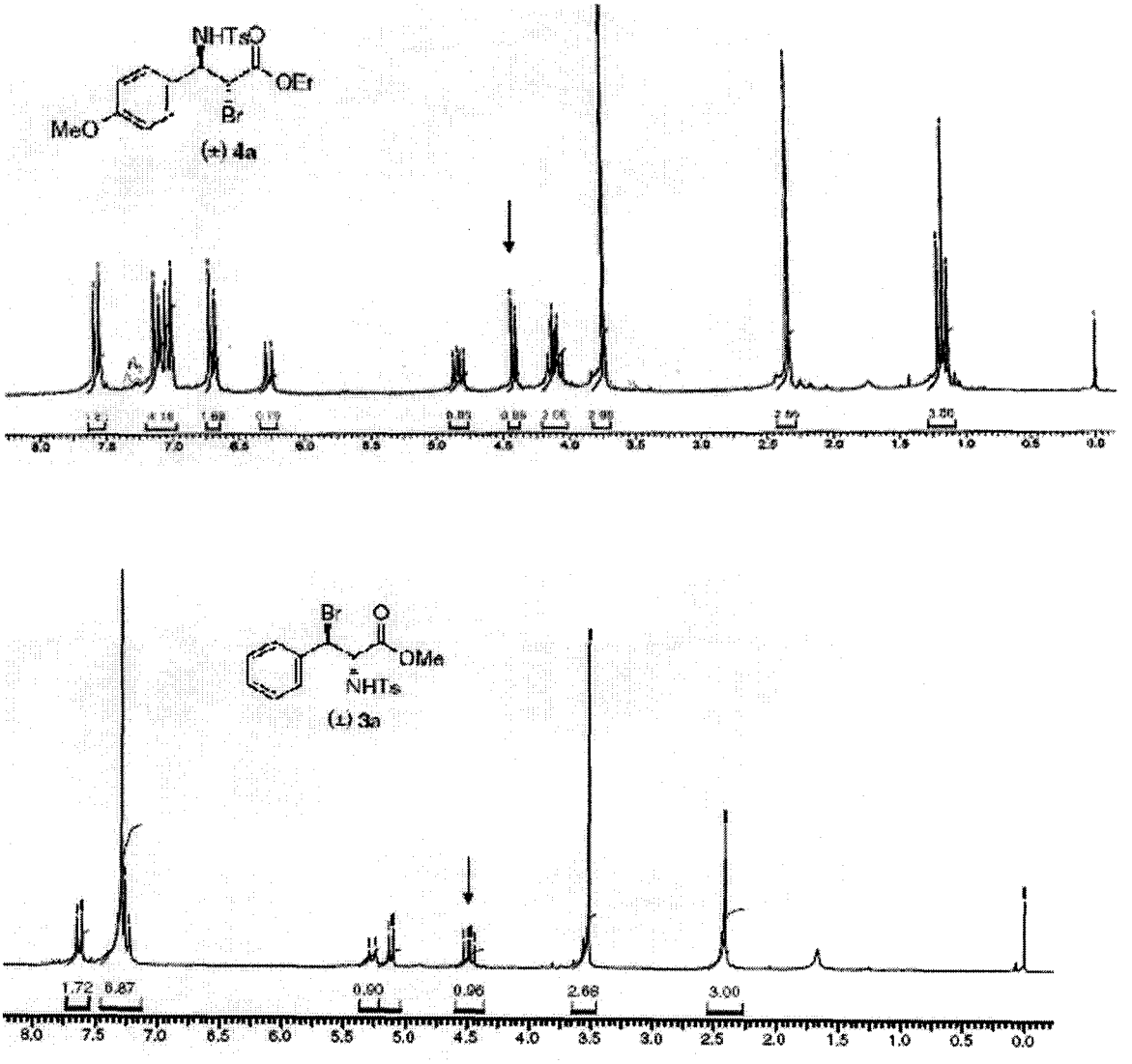
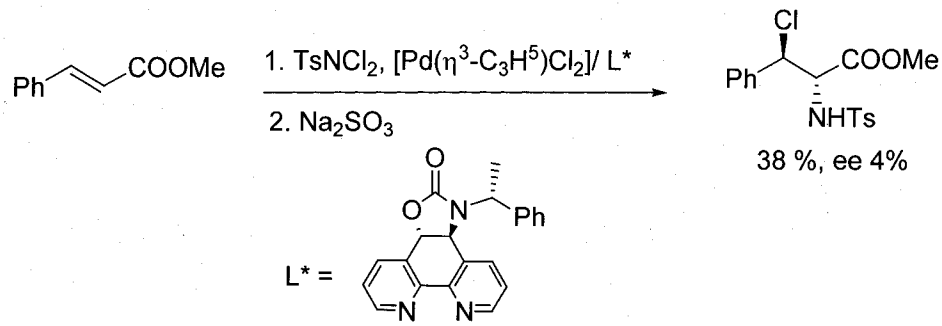


Figure 6.1 ^{1}H NMR spectra of aminobromination products reported by Sudalai[10]

To investigate whether our ligands could catalyze in aminohalogenation reactions, we applied (rac)-oxa-4-Et-anilyl-$PdCl_2$, (*rac*) and (+)-oxa-4-MeO-$PdCl_2$, and (*S,S*)-oxa-α(+)-$PdCl_2$ complexes as catalyst. Following the literature procedure as shown in Scheme 6.1,[6] the methyl cinnamate (1.0 equiv) reacted with $TsNCl_2$ (1.2 equiv) in acetonitrile in the presence of ligand-palladium complexes (8 mol%). Upon completed conversion, the crude mixture was reduced with a Na_2SO_3 solution. After regular workup and purification with SiO_2 chromatography, we obtained an unknown major product (30-38% yield), which is likely analogous to the aminohalogenation product reported by Li, *trans*-methyl 3-chloro-3-phenyl-2-(tosylamino)propanoate. We speculate that the unknown could be one of the *syn*- aminohalogenated product based on comparison with ^1H NMR spectra ($J_{vicinal}$); vicinal protons decreased from 10.3 to 2.93 Hz. The ^{13}C NMR spectrum showed 4 sp^3 and 13 sp^2 carbons; the GCMS showed the molecular mass of M+1 (369). We also obtained an inseparable mixture of vicinal haloamine derivatives.

Under modified reaction conditions, the methyl cinnamate (1.0 equiv) reacted with $TsNCl_2$ (1.2 equiv) in the presence of the (*S,S*)-oxa-α(+)-palladium complex, which was generated *in situ* from (*S,S*)-oxa-α(+) ligand (10 mol%) and allylpalladium chloride dimer (2.5 mol%). The reaction successfully produced the *trans*-methyl 3-chloro-3-phenyl-2-(tosylamino) propanoate product in good regio- and stereoselectivity (19:1) in dry DCM as solvent (Scheme 3). Contrary to Li's report there was no control in regio- and stereoselectivity when MeCN was employed. The enantiomeric excess of *trans*-

methyl 3-chloro-3-phenyl-2-(tosylamino)propanoate was determined to be 4% by chiral HPLC analysis on a Chiralcel OD-H column.



Scheme 6.3 (*S,S*)-oxa-α(+)-Pd-catalyzed aminochlorination of methyl cinnamate

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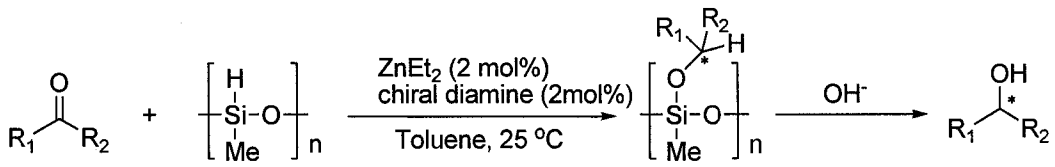
CHAPTER 7: REDUCTION OF ACETOPHENONE WITH TRI-ETHOXY-SILANE, $(EtO)_3SiH$

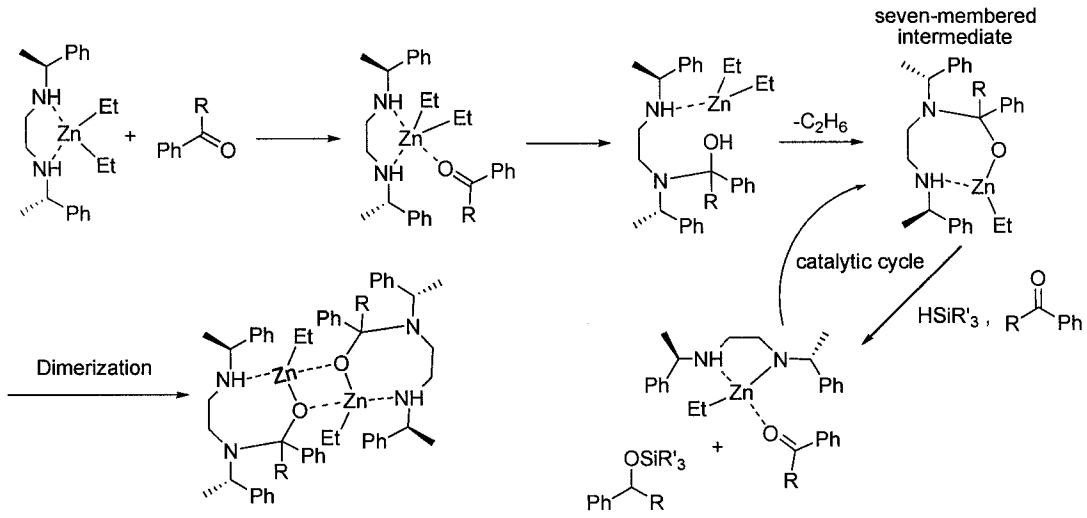
The enantioselective reduction of prochiral ketones to optically active secondary alcohols remains a pivotal transformation in organic synthesis and the use of chiral metal complexes as catalysts is an ideal method. Asymmetric hydrosilylation has been known since the early 1970s by using nickel-coordinated chiral phosphines,[1] and later the most efficient catalyst was developed with ruthenium catalysts coordinated to chiral diamines.[2,3] Mimoun and co-workers[4] have recently accomplished the enantioselective hydrosilylation of ketones in the presence of a chiral diamine zinc catalyst and polymethylhydrosiloxane (PMHS) as hydrosilylating reagent. Subsequently hydrolysis of the silyl ether product gave the desired secondary alcohols (Scheme 7.1).



Scheme 7.1 $ZnEt_2$ mediated reduction of carbonyl compounds

According to Mimoun,[4] catalytic activity can only be achieved when both a chiral diamine and $ZnEt_2$ are employed. $ZnEt_2$ coordinates ligands such as diamines and forms monomeric tetrahedral complexes. The author proposed a mechanism (Scheme 7.2) in

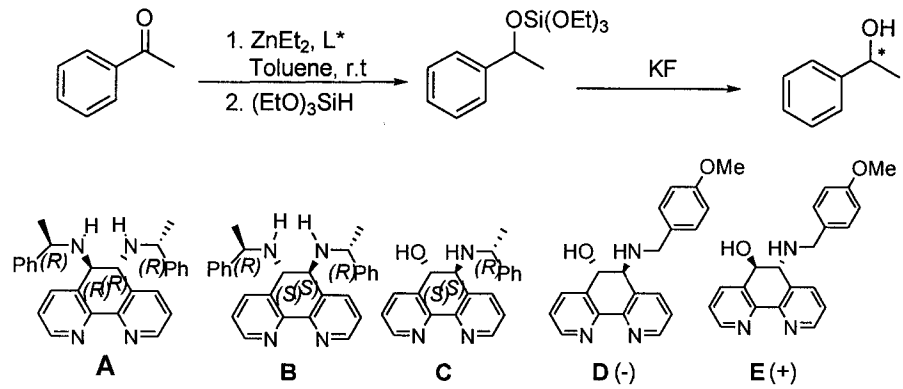
which the $ZnEt_2$-diamine complex reacts with the carbonyl compound to form the seven-membered intermediate during the reduction with PMHS to give silyl ether.



Scheme 7.2 Reduction of carbonyl compounds by chiral diamines and $ZnEt_2$

In order to explore application for our novel C_2 diamines, we employed (5*S*,6*S*)- and (5*R*,6*R*)-5,6-dihydro-N5,N6-bis((*R*)-1-phenylethyl)-1,10-phenan-throline-5,6-diamines in the enantioselective reduction of acetophenone with tri-ethoxy-silane and Zn(II). Following the literature procedure.[5] Acetophenone was treated with 5 mol% of diethylzinc (1.0M in hexanes), and 5 mol% of the chiral ligand in freshly distilled toluene at ambient temperature in the presence of 1.2-1.5 eq. of $(EtO)_3SiH$ for 18 h. The reaction was monitored by TLC, the silyl ether product purified by column chromatography on silica gel and subsequently hydrolyzed with aqueous KF solution in methanol to give the desired alcohol, 1-phenyl-1-ethanol (Scheme 7.3). The product was characterized by ^1H, ^{13}C NMR spectroscopy, and the enantiomeric purity of 1-phenyl-1-ethanol was assessed by HPLC on a chiralcel OD-H column. The HPLC spectra's area peaks for each alcohol

enantiomer were used to calculate enantiomeric excess. The pure commercial (R)-(+)-1-phenyl-1-ethanol alcohol was injected in the HPLC system to use as a reference standard and to assign the product configuration. The results are summarized in Table 7.1.



Scheme 7.3 1,10-phenanthroline ligands and $ZnEt_2$ catalyzed reduction of acetophenone with $(EtO)_3SiH$

Chiral amino alcohol ligands were also tested for this reaction. Similar to C_2 diamines, amino alcohol ligands complexed with $ZnEt_2$ upon addition of acetophenone and $(EtO)_3SiH$ (Scheme 7.3) but with only low stereoselectivity (Table 7.1).

Table 7.1 Enantioselective reduction of acetophenone in the presence of diethylzinc and a chiral ligand

Chiral ligand	Reaction time (h)	Yield (%)	ee(%)
A	24	88	17 (*R*)
B	24	97	22 (*S*)
C	24	66	5 (*S*)
D (-)	24	74	8 (*S*)
E (+)	24	64	6 (*S*)

Chiral 1,10-phenanthroline ligands gave conversion of up to 97 % isolated yield (**B** ligand). However the enantioselectivity was very low. A possible explanation for this could be $ZnEt_2$ activation. Mimoun *et al.*[4] reported that chiral diimines can also activate $ZnEt_2$ to catalyze the reaction (Figure 7.1).

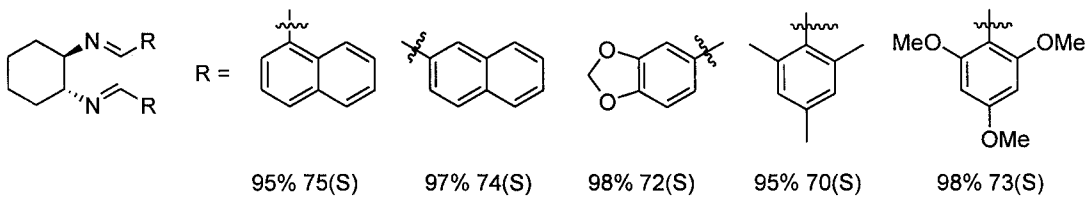
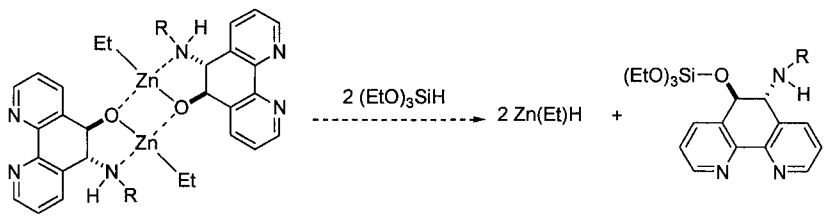


Figure 7.1 Reported $ZnEt_2$ activated-diimines

As seen in Table 7.1, chiral diamines give very good isolated yields (88-97%) and the highest enantioselectivity (17 and 22 % ee). In comparison amino alcohols give lower yields (64-74%) and almost no new stereoselectivity (5-8% ee). It can be explained by the bond strength of the Si-O versus the Zn-O, as reported by Mimoun.[4] The amino alcohol reacts with $ZnEt_2$ to form a dimeric-zinc complex which subsequently reacts with

the ketone substrate and reducing agent, $(EtO)_3SiH$, to produce a silyl ether. The latter was isolated by Mimoun. However, because the electron affinity of the Si-O bond (covalent) is higher than Zn-O bond (ionic), after addition of $(EtO)_3SiH$ in the second step the dimeric-zinc complex can react with the reducing agent to generate EtZnH and the corresponding silyl ether. The reaction between the dimeric-zinc complex and $(EtO)_3SiH$ results in a reduced catalyst lifetime that is responsible for low yields for the reduction of acetophenone. We suspect that amino alcohol ligands form similar silyl ethers as seen in Scheme 7.4.



Scheme 7.4 Likely reaction of dimeric-zinc complex with $(EtO)_3SiH$ reagent

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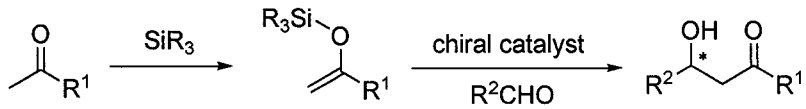
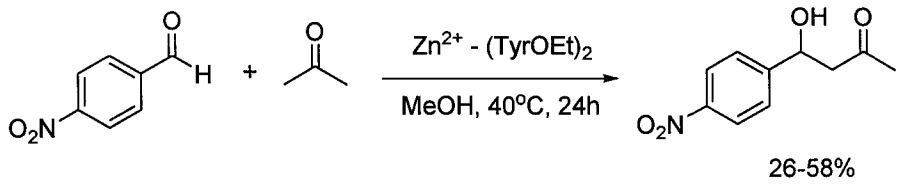
CHAPTER 8: ZINC CATALYZED DIRECT ALDOL REACTION

The aldol reaction, the simple addition of an enolate donor to a carbonyl acceptor, is one of the most fundamental tools for the construction of new carbon-carbon bonds in organic synthesis. It is a useful method for preparing β-hydroxy carbonyl compounds. The ability to control the newly formed stereogenic centers is very important for the synthesis of natural products. In general, control of stereochemistry has been achieved by either the use of chiral aldehyde substrates or of stoichiometric chiral auxiliaries attached to the enolate donor. However, the preconversion of the ketone moiety to a more reactive species such as silyl enol ethers or enol methyl ethers is typically required of these asymmetric aldol reactions (Scheme 8.1).



Scheme 8.1 Mukaiyama-type reaction

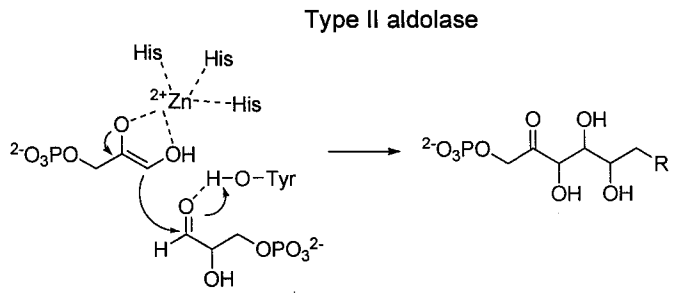
Watanabe reported the aldol reaction of *p*-nitrobenzaldehyde with acetone catalyzed by Zn^{2+} complexes of α-amino acid esters in 1985, and these mild reaction conditions afforded the aldol products along with some dehydrated aldol product (Scheme 8.2).[1]



Scheme 8.2 Zn(II) catalyzed aldol reaction (Watanabe)

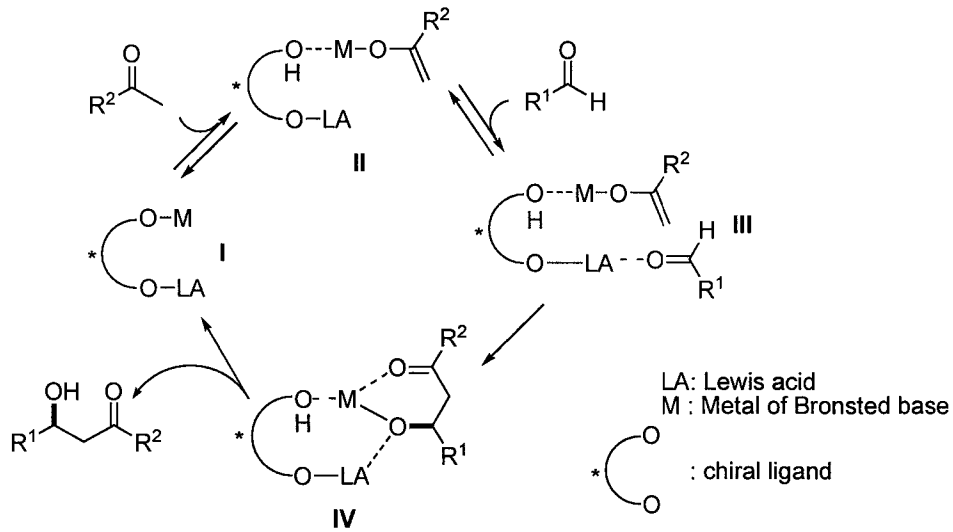
The Watanabe aldol reaction scheme has given an entry point into the direct aldol reaction. In 1999, Shibasaki *et al.*[2] developed a direct asymmetric aldol reaction in which unmodified ketones directly react with aldehydes using a chiral metal complex in catalytic amounts ($LaLi_3$-trisbinaphthoxide, LLB). This catalyst behaved like a DAHP-aldolase enzyme (Scheme 3),[3] affording aldol products of up to 94% *ee*.

The aldolase mechanism is believed to involve cocatalysis by the function of a Zn^{2+} ion as a Lewis acid and a basic functional group in the enzyme's active site. Therefore, aldolases can be thought of as multifunctional catalysts exhibiting Lewis acidity and Brønsted basicity.



Scheme 8.3 Type II aldolase mechanism[4]

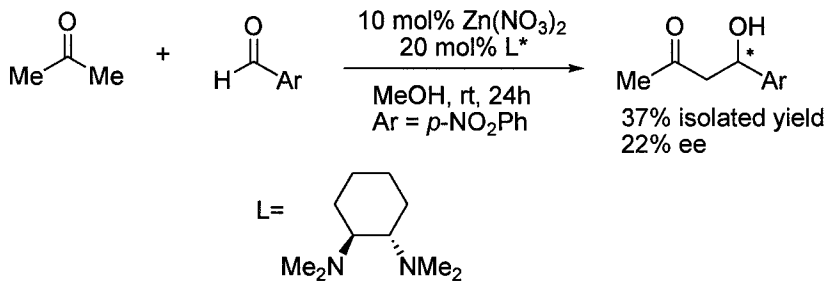
The catalytic cycle of the Shibasaki's asymmetric aldol reaction is shown in Scheme 8.4 The Brønsted base functionality (OM) in the heterobimetallic asymmetric catalyst (**I**) is proposed to abstract an α-proton from a ketone to generate the metal enolate (**II**). In the meantime the Lewis acid functionality (LA) activates the aldehyde component to yield complex (**III**), which can then react in a chelation-controlled asymmetric environment to afford a β-keto metal alkoxide (**IV**). Proton exchange between the metal alkoxide moiety and a proton source could then regenerate the catalyst (**I**) and liberate an optically active aldol product (Scheme 8.4).[2]



Scheme 8.4 Catalytic cycle of direct catalytic asymmetric aldol reactions[2]

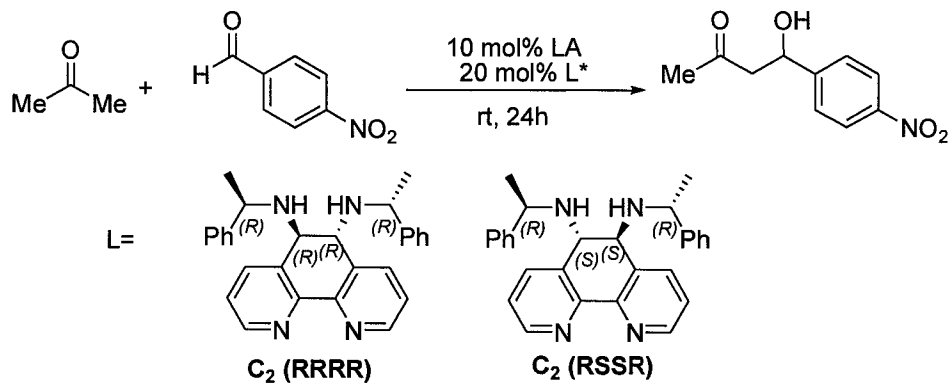
Recently, Michael A. Calter reported[5] an approach that is similar to the type II aldolase and the Watanabe aldol reaction method in which the bifunctional amine-zinc

catalysts containing Lewis acid and basic functionalities, were used to perform the direct aldol reaction. Particularly the zinc-(1*S*,2*S*)-tetramethylcyclo-hexane-1,2-diamine complex, which was generated *in situ* by the reaction of (1*S*,2*S*)-tetramethylcyclohexane-1,2-diamine (20 mol%) with $Zn(NO_3)_2$ (10 mol%) in methanol, catalyzed the aldol reaction of acetone (5.0 equiv.) and *p*-nitrobenzaldehyde (1.0 equiv.) to produce only one aldol product. 4-Hydroxy-4-(4-nitrophenyl)butan-2-one was isolated in 37% yield and 22% enantiomeric excess (Scheme 8.5).



Scheme 8.5 Direct aldol reaction with zinc-diamines complex[5]

Based on Calter's report[5] we investigated our C_2 diamine-1,10-phenanthroline ligands in the direct aldol reaction of acetone and *p*-nitrobenzaldehyde. The reaction was carried out in the presence of C_2 diamine ligand or Lewis acid alone, neither reaction showed conversion. However, when we used a combination of C_2 ligand (20 mol %) and Lewis acid (10 mol %), likely forming a bifunctional catalyst, the reaction produced the aldol product (Scheme 8.6). Several Lewis acids were used to test the reaction such as $Zn(NO_3)_2.6H_2O$, $Zn(OTf)_2$, $ZnCl_2$, $Sn(OTf)_2$, $Ni(NO_3)_2.6H_2O$, $Cu(OTf)_2$.



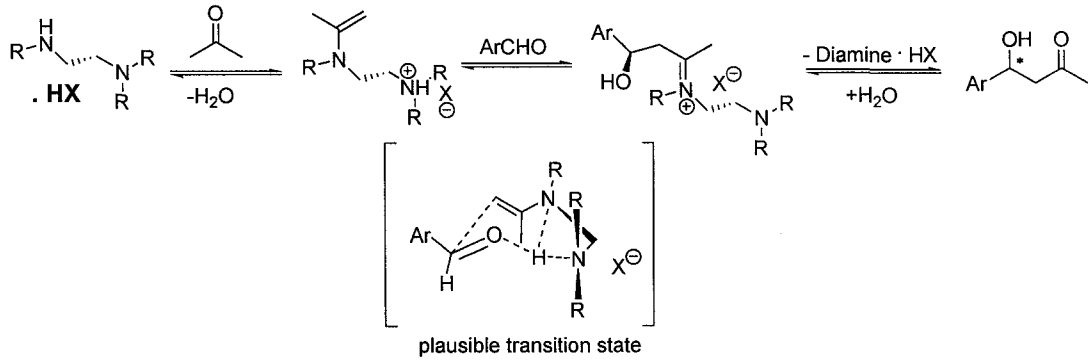
Scheme 8.6 Direct aldol reaction with diamine-1,10-phenanthroline complexes

Among the screened Lewis acids, we found that only $Zn(NO_3)_2.6H_2O$ and $Zn(OTf)_2$ could react with C_2-diamine ligands to form a catalyst for the direct aldol reaction in 47% and 8% yield, respectively. We also found some dehydrated aldol product as a by-product when $Zn(OTf)_2$ was used. The investigation was then focused on the use of $Zn(NO_3)_2.6H_2O$ as Lewis acid with C_2-diamine ligands for the direct aldol reaction to optimize the conditions. There was no temperature and solvent effect when the reactions were conducted in MeOH, MeCN or a room temperature to 40°C. The Lewis acid to ligand ratios (10:20, 20:20, and 30:20 mol%) was also studied. The best yields (30-47%) of the aldol product 4-hydroxy-4-(4-nitrophenyl)butan-2-one was observed with 10 mol% Lewis acid and 20 mol% C_2-diamine ligands. The enantiomeric excess of 4-hydroxy-4-(4-nitrophenyl)butan-2-one was determined to be 99% by chiral HPLC analysis on Chiralcel OD-H column. The results are summarized in Table 8.1.

Table 8.1 Chiral diamine ligands for direct aldol reaction with $Zn(NO_3)_2$

Ligand	Zn^{2+}/ligand ratio (mol%)	Time (h)	Isolated yield (%)	ee (%)
C_2 (RRRR)	5:10 mol%	48	47	99 (*R*)
C_2 (RRRR)	20:20 mol%	48	29	99 (*R*)
C_2 (RRRR)	30:20 mol%	48	25	99 (*R*)
C_2 (RSSR)	10:20 mol%	48	39	99 (*S*)
C_2 (RSSR)	20:20 mol%	48	24	99 (*S*)

Because the reaction yields were low to moderate we tried to apply an alternative method that was published by Nakadai.[6] They replaced the Lewis acid with protonic acid for the direct aldol reaction of *p*-nitrobenzaldehyde with acetone using a mixture of chiral diamine-protonic acid (10 mol%, 1:1 ratio) as catalyst. A plausible mechanism of the catalytic pathway to aldol adducts involves the interaction of the amine with acetone to form the corresponding enamine after dehydration. The next step involved a six-membered chair-like transition state in which the aldehyde's aromatic ring adopted a pseudoequatorial position to yield the aldol product (Scheme 8.7).



Scheme 8.7 Mechanism for the diamine-catalyzed aldol reaction proposed by Nakaida[6]

Following the literature procedure,[6] we used a mixture of trifluoromethanesulfonic acid (triflic acid, CF_3SO_3H) as protonic acid (10 mol%) with C_2-diamine-1,10-phenanthroline ligand (10 mol%) to catalyze the direct aldol reaction of *p*-nitrobenzaldehyde in acetone. Unfortunately, the reactions were deactivated after 4 days under argon atmosphere at 40-50°C. The acidic and basic functions of triflic acid and diamine are likely incompatible. Possibly the enamine intermediate, which derived from the C_2-diamine-triflic acid adduct and acetone, could not form a six-member chair-like transition state with *p*-nitrobenzaldehyde or it could react with *p*-nitrobenzaldehyde and the resulting ammonium intermediate inactive to acetone. Furthermore, triflic acid could protonate the C_2 ligand at the diimine moiety, which could prevent the formation of a six-member chair-like transition state.

Finally, Calter's reaction conditions with addition of a small amount of Et_3N, gave the product in good yield (76%) but without changing enantioselectivity previously observed. A small amount of dehydrate by-product was also produced (less than 3%).

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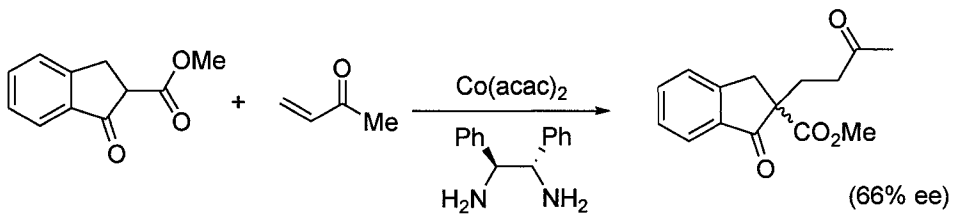
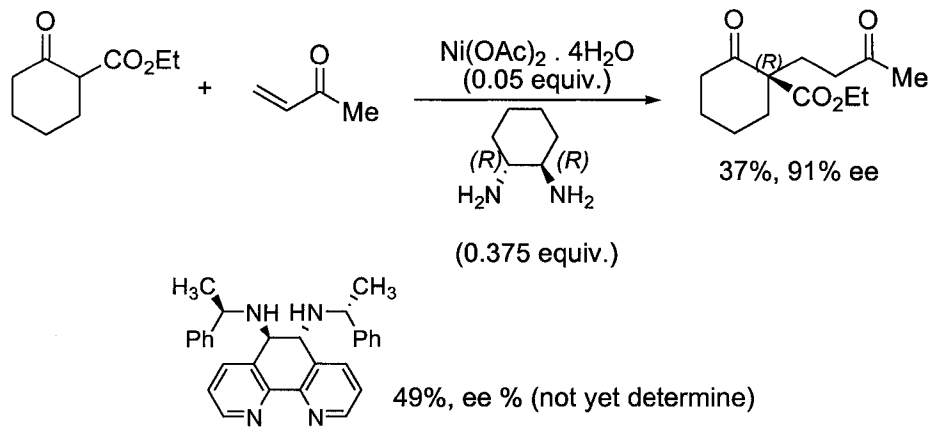
CHAPTER 9: PRELIMINARY STUDIES OF CATALYTIC MICHAEL ADDITION REACTION

The Michael addition reaction involves the addition of a carbanion nucleophile to α,β-unsaturated systems. Carbon-carbon bond formation via Michael additions are most frequently performed under basic conditions, however, this method suffers from side reaction such as aldol-cyclization products. The conjugate addition of 1,3-dicarbonyl compounds to enones such as methyl vinyl ketone (MVK) can be catalyzed by metal complexes and also allows asymmetric catalysis with chiral ligands. The cobalt-catalyzed Michael addition of methyl-1-oxo-2-indanecarboxylate to MVK was first reported by Brunner and Hammer (Scheme 9.1).[1] In the presence of (1*S*,2*S*)-(-)-1,2-diphenylethylene diamines as chiral ligand the Michael product was formed with 66% enantiomeric excess.



Scheme 9.1 Michael addition with diamine-cobalt complex

Recently, Christoffers *et al.*[2] reported the addition of ethyl 2-oxocyclohexane-carboxylate to MVK using (*R*,*R*)-*trans*-1,2-diamino-cyclohexane. The reaction was conducted under aerobic conditions, at ambient temperature with an enantioselectivity of up to 91% ee (Scheme 9.2).



Scheme 9.2 Michael addition with diamine-nickel complex, comparison of Christoffers' work and our result

We conducted preliminary studies for the addition of ethyl 2-oxocyclohexanecarboxylate to MVK in the presence of our chiral C_2 diamine-1,10-phenanthroline ligand and nickel salt. The C_2 (RRRR) diamine-1,10-phenanthroline-nickel complex was generated *in situ* and catalyzed the Michael addition reaction under aerobic conditions at ambient temperature. The Michael product formed in 49% yield and was confirmed by ^{1}H, ^{13}C NMR, and IR spectroscopy.

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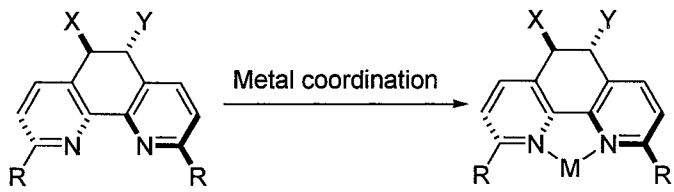
CHAPTER 10: SUMMARY AND OUTLOOK

Organometallic catalysis is a rapidly growing area in synthetic chemistry. In this research project we have demonstrated new conditions to prepare high quality 1,10-phenanthroline epoxide in good yield and high purity. We also prepared new 1,10-phenanthroline derivatives (5,6-aminoalcohol, 5,6-oxazolidinone, and C_2 symmetrically diamine-1,10-phenanthro-line) using 1,10-phenanthroline epoxide as a key intermediate. The introduction of stereogenic centers in the B-ring was achieved by nucleophilic ring opening of 1,10-phenanthroline epoxide in the presence of Lewis acid, $Mg(ClO_4)_2$. The chiral aminoalcohol derivatives were produced in good yield (62-97%). NMR spectroscopy, X-ray analysis and computational analysis have been applied to investigate conformational preferences of the new 1,10-phenanthroline derivatives. The interchange of 5- and 6-subtituents between pseudoaxial (anti) and equatorial positions (syn) alters the ligand twist that affects the ligand chelation site (NCCN). Cyclization of 5,6-aminoalcohol-1,10-phenanthroline derivatives, obtained through carbonylation with triphosgene, permanently locked the 5- and 6-subtituents in the syn conformation. The complexation of 1,10-phenanthroline derivatives with transition metals was investigated to test their coordination capabilities. We screened several ligand applications. Metal-catalyzed reactions included allylic substitution, aminohalogenation, direct aldol, and ketone reduction. So far, our research showed that 5,6-oxazolidinone ligands can catalyze allylic substitution of rac-(*E*)-1,3-diphenyl-2-propenyl acetate with dimethyl malonate in good yield (80-86%), however, without asymmetric induction affects. The allylpalladium-oxazolidinone-chloride complex can also catalyze chloroamination of

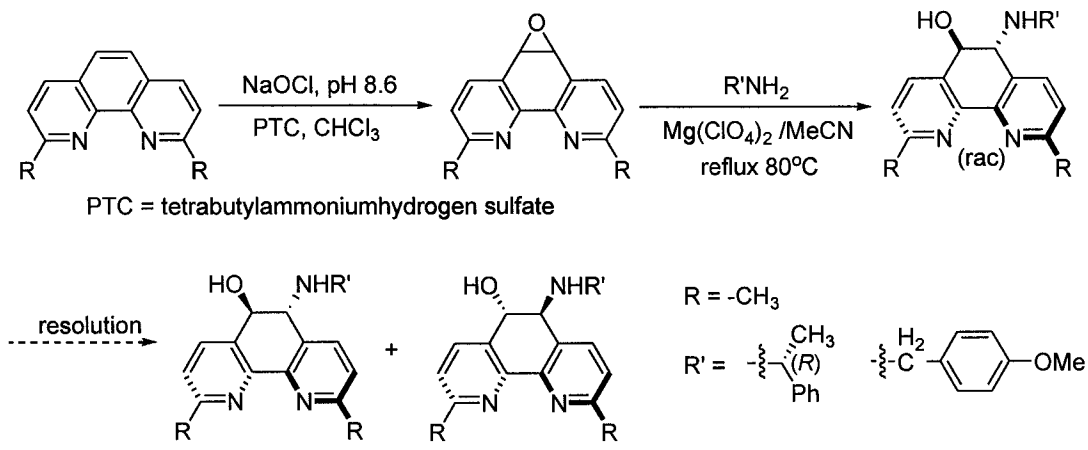
methyl cinanamate with good control of regio- and stereoselectivity but further studies are needed to improve yields and test enantioselectivity. C_2-symmetrical diamine-1,10-phenanthroline ligands gave good performance for the direct aldol reaction of *p*-nitrobenzaldehyde with acetone. As proposed the C_2 diamine-zinc complex served as a bifunctional catalyst for the formation of the aldol product with 99% ee in good yield (76%). The reduction of acetophenone was accomplished in good yields (88-97%) but low ee when using C_2 diamine ligands.

Additional work showed that the complexes of Pd-**(±)-oxa-4-MeO**, **(-)-oxa-4-MeO**, **(*S,S*)-oxa-α(+)**, **C_2 (*RRRR*)**, and **C_2 (*RSSR*))** promote allylic substitution reactions. However, there was no asymmetric induction and racemic mixtures were isolated. It is likely that coordination of the ligand to the metal overrides the dihedral angle (N-C-C-N). Therefore, the attachment of a group (R) replacing hydrogen at either the 2- and/or 9- position may be needed to amplify the effect of the B-ring stereocenters, thus improving stereocontrol. The new ligand template in Scheme 10.1 could be described as a mix of template **Ia** and **III** (page 9).



Scheme 10.1 Complexation of phenanthroline with substituents in the 2- and 9- position

Additional derivatives like 2,9- and 5,6-tetrasubstituted phenanthrolines were prepared in the same manner as 5,6-disubstituted-1,10-phenanthroline as outlined in Scheme 10.2.



Scheme 10.2 Preparation of 2,9-disubstituted-5,6-aminoalcohol-1,10-phenanthroline derivatives

The 2,9-dimethyl-1,10-phenanthroline-5,6-epoxide (**2,9-phen-epoxide**) was successfully prepared by oxidizing 2,9-dimethyl-1,10-phenanthroline, with commercial bleach (NaOCl) in the presence of a phase transfer catalyst (PTC) in chloroform. After purification by silica gel chromatography, **2,9-phen-epoxide** was obtained in good yield (78%).

The epoxide ring opening of **2,9-phen-epoxide** with different amine nucleophiles was achieved under refluxing conditions in acetonitrile in the presence of $Mg(ClO_4)_2$. The diastereoisomeric (5*R*,6*R*) and (5*S*,6*S*)-6-((*R*)-1-phenylethyl-amino)-5,6-dihydro-2,9-

dimethyl-1,10-phenanthroline-5-ol mixture product, (**2,9-diMe-α(+)-L**), and racemic 6-(4-methoxybenzylamino)-5,6dihydro-2,9-dimethyl-1,10-phenanthroline-5-ol, (**2,9-diMe-(4-MeO-benzyl)-L**), were obtained when using α(+)-methylbenzylamine and *p*-methoxybenzylamine as nucleophiles, respectively.

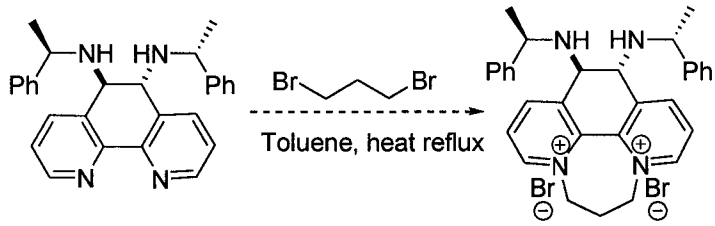
So far, we have been unable to separate the stereoisomers of **2,9-diMe-α(+)-L** by column chromatography or recrystallization. Unfortunately, resolution attempts of the **2,9-diMe-α(+)-L** mixture with chiral acid such as S-mandelic, S-tartaric, and D-camphoric acid were also unsuccessful. We anticipated that the diastereomeric salts would have different property in solubility, which then can be separated from each other.

The **2,9-diMe-α(+)-L** mixture was converted to the corresponding copper complexes through coordination with copper sulfate. The diastereoisomeric complexes could also not be separated. Additional research is necessary to develop the 2,9-substituted phenanthroline template.

One approach could involve reactions with bulky chiral acids to facilitate diastereomeric salt crystallization. Alternatively, one could convert the 2,9-diubstituted aminoalcohols into 2,9-disubstituted 5,6-oxazolidinone derivatives and test the resolution at that stage.

For the reduction of acetophenone, we suspect that the low ee was due to competing chelation of $ZnEt_2$ between the diamine and diimine. To corroborate this and

to improve enantioselectivity one could convert the diimine into a diiminium moiety (Scheme 10.3).



Scheme 10.3 Proposed preparation of C_2 diamonium-diamine ligand

The new C_2 diamonium-diamine ligand could be tested with Carpentier's new method,[1] involving direct ketones reduction to alcohols with polymethylhydro-siloxane (PMHS) in the presence of $ZnEt_2$ and 1,2-diamine ligand in a one step procedure.

We also conducted preliminary studies for the Michael addition reaction which showed that C_2-diamine ligands with $Ni(OAc)_2.4H_2O$ catalyzed the formation of the Michael adduct product. Additional optimization of reaction conditions and enantioselectivity is needed.

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APPENDIX A

EXPERIMENTAL SECTION

EXPERIMENTAL SECTION

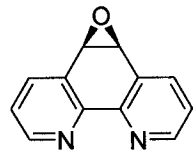
Reagents and Solvents

All reagents and solvents used in this research project were purchased from Acros, Lancaster, Aldrich or TCI Chemical Companies. Chemicals were more than 99% purity and were used without further purification. All commercial solvents used were of reagent grade. Dichloromethane was dried by distillation from P_2O_5 before use. Silica gel (32 – 63 mesh, Dynamic Absorbents, LLC) was used for column chromatography. Silica and alumina TLC plates (UV/254) were purchased from AllTech.

Characterization of Compounds and Instrumentation

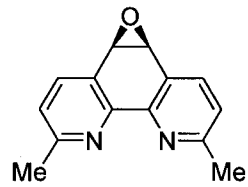
^1H NMR spectra were recorded with at 400 MHz and ^{13}C NMR spectra were obtained with a 100 MHz JEOL Eclipse nuclear magnetic resonance spectrometer, with tetramethylsilane (TMS) as an internal standard. Chemical shifts are given as δ values (ppm) and coupling constants J are given in Hz. Melting points were taken using a Thomas-Hoover Unimelt instrument and reported in degree Celcius. FT-IR spectra were recorded on a Bruker Equinox 55 and Perkin Elmer 1710 Fourier Transform Infrared Spectrometers. Optical rotations $[\alpha]_D$ were measured at 20°C in a 1.0 dm cell, using a Perkin-Elmer 341 spectrophotometer. The enantiomeric excess (ee) was determined by HPLC analysis, performed on a Waters HPLC system consisting of the following: 515 HPLC pump, 2487 Dual λ Absorbance Detector, measured at 254 nm; column DAICEL

CHIRALPAK OD-H (250 x 4.6 mm); mobile phase, hexane/2-propanol. NuMega Resonance Labs, Inc., San Diego, CA, performed microanalyses.



1,10-Phenanthroline-5,6-epoxide, (Phen-oxide)

To mechanically stirred commercial bleach (6%, 100 mL), adjusted to pH 8.6 with concentrated sulfuric acid, was added a mixture of tetrabutylammonium hydrogen sulfate (1.8 g, 5.3 mmol, 0.5 eq.) and phenanthroline monohydrate (2.0 g, 11 mmol, 1.0 eq.) dissolved in chloroform (20 ml). The reaction mixture was agitated vigorously at room temperature for 15-30 min, depending on the quality of bleach. After the reaction was complete as observed by reverse phase TLC, the organic layer was separated and the aqueous layer was extracted with chloroform (3 x 25 mL). The combined organic layers were washed with several portions of water and brine, dried over anhydrous sodium sulfate, filtered, and the solvent removed in vacuo to yield the light yellow compound (1.75 -1.85 g, 80-85%). The crude epoxide was purified by recrystalization from chloroform and hexanes to give pure product (50-75%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (2H, d, J = 4.76 Hz), 8.02 (2H, d, J = 7.69 Hz), 7.41 (2H, dd, J = 4.76, 7.69 Hz), 4.62 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 149.6, 138.4, 129.2, 123.9, 55.4; (m.p. 163 °C; lit. m.p. 165°C).



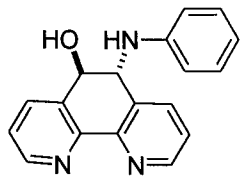
2,9-Dimethyl-1,10-phenanthroline-5,6-epoxide, (2,9-Phen-epoxide)

Commercially available bleach (NaOCl, 46 mL) was adjusted to pH 8.6 with conc. sulfuric acid. To this solution was added a mixture of (1.0 g, 4.61 mmol) of 2,9-dimethyl-1,10-phenanthroline and (0.781 g, 2.3 mmol) tetrabutylammonium hydrogen sulfate (PTC) in chloroform (10 mL). The biphasic mixture was stirred at room temperature for about 1hr. After the conversion was completed the layers were separated and the aqueous layer extracted with $CHCl_3$ (3 x 10 mL). The combined organic layer was washed with water and brine and dried over anhydrous Na_2SO_4. Filtration and evaporation gave the crude product. The crude epoxide was purified by silica gel chromatography ($CHCl_3$/5% MeOH) and yielded the pure product (0.81g), (m.p. 184°C) in 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (2H, d, J = 7.69 Hz), 7.23 (2H, d, J = 7.69 Hz), 4.56 (2H, s), 2.74(6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 149.1, 138.7, 126.6, 123.7, 55.5, 25.3; FT-IR (NaCl, DCM solution) ν/cm-1 3029, 2964, 2925, 1570, 1482, 1456, 1398, 1140, 822, 735; Anal Calcd for $C_{14}H_{12}N_2O$. ½ H2O: C, 72.09; H, 5.62; N, 12.01. Found C, 72.4; H, 5.81; N, 12.21.

General Procedure for epoxide opening with $Mg(ClO_4)_2$

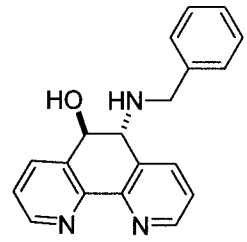
1,10-phenanthroline-5,6-epoxide (500 mg, 2.5 mmol) and $Mg(ClO_4)_2$ (850 mg, 3.8 mmol) were dissolved in CH_3CN (10 mL) and the solution was heated at 40°C for 20

minutes, followed by the addition of the amine nucleophile (1.1-1.5 eq.). The reaction mixture was stirred and heated at 80°C for 24-72 hrs while monitored by TLC (Al_2O_3, $CHCl_3$/5% MeOH). Upon completion, the reaction was quenched with water and the crude material was washed with hexanes to remove excess nucleophile. The aqueous layer was extracted with chloroform and the combined organic layer washed with water and brine. Drying with anhydrous Na_2SO_4, followed by filtration and concentration gave the crude material.



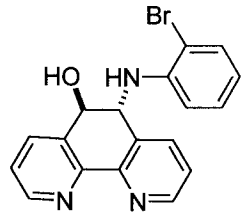
***trans*-5,6-Dihydro-6-anilylamino-1,10-phenanthroline-5-ol, (anilyl adduct)**

Purification by crystallization from $CHCl_3$/Hexanes yielded a solid (m.p. 210°C) in 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.7 (2H, dd, J = 4.76, 4.76 Hz), 8.07 (1H, d, J = 7.69 Hz), 7.79 (1H, d, J = 7.69 Hz), 7.36 (1H, dd, J = 4.76, 7.69 Hz), 7.26 (1H, dd, J = 4.76, 7.69 Hz), 7.17 (2H, t, J = 7.32, 8.06 Hz), 6.77 (1H, t, J = 7.69, 6.96 Hz), 6.70 (2H, d, J = 7.69 Hz), 5.08 (1H, d, J = 10.62 Hz), 4.82 (1H, d, J = 10.62 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.18, 150.11, 149.64, 147.10, 135.00, 134.17, 134.10, 133.10, 129.81, 124.42, 124.29, 119.19, 113.83, 70.54, 58.62; FT-IR (NaCl, DCM solution) ν/cm-1 3054, 2923, 2851, 1601, 1498, 1419, 1263, 1077, 797, 746, 694.



***trans*-5,6-Dihydro-6-benzylamino-1,10-phenanthroline-5-ol, (benzyl adduct)**

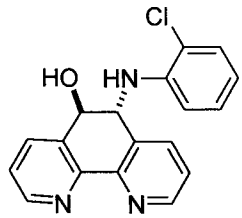
Purification by column chromatography (SiO_2, $CHCl_3$/5% MeOH) yielded a solid in 87% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (1H, d, J = 4.76 Hz), 8.65 (1H, d, J = 4.76 Hz), 7.90 (1H, d, J = 6.96 Hz), 7.80 (1H, d, J = 7.32 Hz), 7.27-7.34 (m, 7H), 4.87 (1H, d, J = 9.15 Hz), 4.03 (1H, d, J = 9.15 Hz), 4.02 (1H, d, J = 13.18 Hz), 3.87 (1H, d, J = 13.18 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9, 149.9, 149.7, 149.6, 139.4 134.8, 134.4, 133.2, 128.7, 128.2, 127.6, 124.3, 124.0, 70.1, 61.2, 51.2; FT-IR (NaCl, DCM solution) ν/cm-1 3260, 3061, 2967, 2850, 2355, 1581, 1562, 1494, 1453, 1419, 1265, 1207, 1128, 1073, 845, 802, 780, 746, 701.



***trans*-5,6-Dihydro-6-(2-bromo-anilylamino)-1,10-phenanthroline-5-ol, (2-Br-anilyl adduct)**

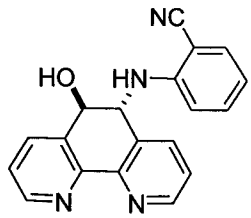
Purification by crystallization from $CHCl_3$/Hexanes yielded a solid (m.p. 130°C) in 83% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 (1H, d, J = 7.69 Hz), 7.71 (1H, d, J = 8.06 Hz), 7.48 (2H, d, J = 8.06 Hz), 7.47 (2H, d, J = 7.69 Hz), 7.38 (1H, dd, J = 4.76, 7.69 Hz), 7.28 (1H, dd, J = 4.76, 7.69 Hz), 7.13 (1H, t, J = 8.42, 7.32 Hz), 6.73 (1H, d, J = 7.69 Hz), 6.66 (1H, t, J = 7.32, 7.69 Hz), 5.13 (1H, d, J = 10.62 Hz), 4.91 (1H, t, J =

7.69, 10.25 Hz), 4.78 (1H, d, J = 8.42 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 149.9, 149.8, 149.2, 144.2, 134.9, 134.5, 134.4, 133.0, 132.8, 128.9, 124.6, 124.5, 119.7, 112.7, 110.7, 70.6, 59.0; FT-IR (NaCl, DCM solution) ν/cm-1 3197, 3064, 2957, 2924, 2853, 1593, 1560, 1507, 1458, 1420, 1321, 1283, 1126, 1076, 1034, 1019, 798, 744, 664.



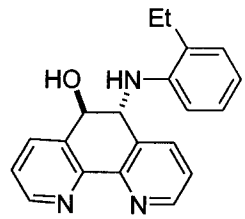
trans-5,6-Dihydro-6-(2-chloro-anilylamino)-1,10-phenanthroline-5-ol, (2-Cl-anilyl adduct)

Purification by crystallization from $CHCl_3$/Hexanes yielded a solid (m.p. 155°C) in 86% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (2H, t, J = 4.76, 4.39 Hz), 8.05 (1H, d, J = 7.69 Hz), 7.72 (1H, d, J = 7.69 Hz), 7.41 (1H, dd, J = 4.76, 8.06 Hz), 7.33 (1H, dd, J = 4.76, 8.06 Hz), 7.24 (1H, d, J = 7.69 Hz), 7.04 (1H, t, J = 6.96, 7.32 Hz), 6.68 (1H, d, J = 8.06 Hz), 6.62 (1H, t, J = 7.32, 8.06 Hz), 5.21 (1H, d, J = 6.59 Hz), 5.03 (1H, d, J = 10.62 Hz), 4.78 (1H, t, J = 6.59, 10.25 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 149.5, 149.3, 149.2, 144.1, 136.5, 135.9, 135.2, 134.0, 129.5, 128.2, 124.7, 124.6, 119.4, 118.1, 112.5, 69.4, 58.4; FT-IR (NaCl, DCM solution) ν/cm-1 3175, 3065, 2956, 2917, 2849, 1596, 1560, 1507, 1458, 1419, 1323, 1123, 1075, 1033, 797, 742, 668.



***trans*-5,6-Dihydro-6-(2-cyano-anilylamino)-1,10-phenanthroline-5-ol, (2-CN-anilyl adduct)**

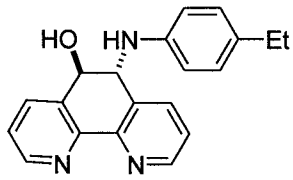
Purification by crystallization from $CHCl_3$/Hexanes yielded a solid (m.p. 149°C) in 73% yield. . ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (2H, t, J = 3.66, 4.39 Hz), 8.13 (1H, d, J = 7.69 Hz), 7.70 (1H, d, J = 7.69 Hz), 7.34-7.34 (m, 3H), 7.28 (1H, dd, J = 4.76, 7.69 Hz), 6.75 (1H, d, J = 6.59 Hz), 6.72 (1H, t, J = 4.76, 7.69 Hz), 5.55 (1H, d, J = 7.69 Hz), 5.37 (1H, d, J = 10.25 Hz), 4.98 (1H, t, J = 8.97, 8.97 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9, 150.1, 150.0, 149.8, 149.6, 135.0, 134.8, 134.7, 134.6, 133.4, 132.2, 124.7, 124.4, 117.8, 117.6, 111.6, 96.4, 70.0, 58.6; FT-IR (NaCl, DCM solution) ν/cm-1 3243, 2213, 1604, 1578, 1520, 1420, 1327, 1077, 1042, 798, 746, 668.



***trans*-5,6-Dihydro-6-(2-ethyl-anilylamino)-1,10-phenanthroline-5-ol, (2-Et-anilyl adduct)**

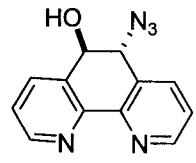
Purification by crystallization from $CHCl^3$/Hexanes yielded a solid (m.p. 146°C) in 97% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.66 (1H, d, J = 4.76 Hz), 8.63 (1H, d, J = 4.76 Hz), 8.06 (1H, d, J = 7.69 Hz), 7.70 (1H, d, J = 7.69 Hz), 7.32 (2H, dd, J = 4.76, 7.69), 7.23 (2H, dd, J = 4.76, 7.69 Hz), 7.09 (1H, d, J = 7.32 Hz), 7.03 (1H, t, J = 7.69,

7.69 Hz), 6.75 (1H, t, J = 7.32, 7.32 Hz), 6.57 (1H, d, J = 8.06Hz), 5.17 (1H, d, J = 10.62 Hz), 4.85 (1H, d, J = 10.62 Hz), 2.5 (2H, q, J = 7.32, 7.69 Hz), 1.17 3H, (t, J = 7.69, 7.32 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 149.8, 149.78, 149.4, 144.5, 135.5, 134.8, 134.5, 133.5, 128.6, 128.5, 127.3, 124.5, 124.4, 118.8, 111.1, 70.3, 58.4, 24.1, 13.2; FT-IR (NaCl, DCM solution) ν/cm-1 3339, 3190, 3063, 2964, 2930, 2872, 1603, 1585, 1563, 1515, 1453, 1419, 1307, 1265, 1126, 1076, 1042, 909, 882, 799, 747.



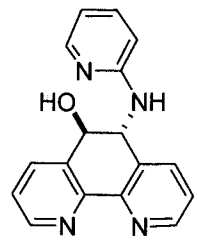
trans-5,6-Dihydro-6-(4-ethyl-anilylamino)-1,10-phenanthroline-5-ol, (4-Et-anilyl adduct)

Purification by crystallization from $CHCl_3$/Hexanes yielded a solid (m.p. 208°C) in 78%. ^1H NMR (400 MHz, $CDCl_3$) δ 8.72 (1H, d, J = 4.76 Hz), 8.69 (1H, d, J = 3.30 Hz), 8.06 (1H, d, J = 7.69 Hz), 7.79 (1H, d, J = 7.69 Hz), 7.35 (2H, dd, J = 5.13, 4.76 Hz), 7.25 (2H, dd), 7.01 (2H, d, J = 8.42 Hz), 6.66 (2H, d, J = 8.42 Hz), 5.05 (1H, d, J = 10.62 Hz), 4.79 (1H, d, J = 10.62 Hz), 2.55 (2H, q, J = 7.69, 7.69 Hz), 1.18 (3H, t, J = 7.69, 7.69 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.0, 149.5, 149.0, 145.1, 135.6, 134.9, 134.8, 134.7, 134.0, 129.0, 124.6, 124.5, 113.8, 70.2, 58.9, 28.0, 16.0; FT-IR (NaCl, DCM solution) ν/cm-1 3285, 3055, 2962, 2928, 2869, 1616, 1582, 1563, 1519, 1420, 1322, 1266, 1184, 1125, 1077, 1041, 823, 799, 746, 735



***trans*-5,6-Dihydro-6-azido-1,10-phenanthroline-5-ol, (azido alcohol)**

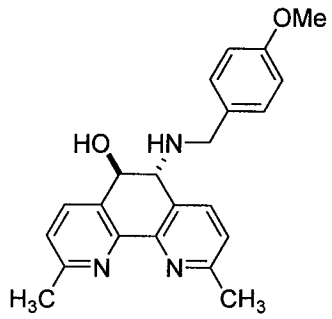
Purification by column chromatography (SiO_2, $CHCl_3$/5% MeOH) yielded a solid (m.p. 83°C) in 87% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.71 (2H, dd, J = 4.76, 4.76 Hz), 8.06 (1H, d, J = 7.32 Hz), 7.91 (1H, d, J = 7.69 Hz), 7.37 (2H, dd, J = 4.76, 7.69 Hz), 5.06 (1H, d, J = 10.25 Hz), 4.87 (1H, d, J = 9.89 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.16, 149.74, 149.68, 149.05, 135.35, 134.93, 134.28, 130.05, 124.72, 124.49, 71.77, 64.97; FT-IR (NaCl, DCM solution) ν/cm-1 3205, 3064, 2925, 2855, 2239, 2108, 1582, 1564, 1420, 1298, 1264, 1074, 800, 744.



***trans*-5,6-Dihydro-6-(pyridin-2-ylamino)-1,10-phenanthrolin-5-ol (FSL)**

Purification by column chromatography (SiO_2, $CHCl_3$/5% MeOH) and recrystalization in $CHCl_3$ yielded a white solid (m.p. 220°C) in 47%. ^1H NMR (400 MHz, MeOD) δ 8.67 (2H, dd, J = 4.76, 4.76 Hz), 8.04 (1H, d, J = 7.69 Hz), 7.96 (1H, d, J = 5.13 Hz), 7.84 (1H, d, J = 7.69 Hz), 7.38-7.48 (3H, m), 6.62 (2H, d overlap dd, J = 8.42, 6.22 Hz), 5.39 (1H, d, J = 8.79 Hz), 5.02 (1H, d, J = 8.79 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 151.1, 150.2, 149.8, 149.7, 134.5, 134.3, 134.2, 133.5, 131.8, 129.4,

124.3, 124.0, 114.2, 70.4, 61.1, 55.4, 50.9; FT-IR (NaCl, DCM solution) ν(cm-1) 3270, 3063, 2835, 2208, 1611, 1583, 1564, 1512, 1418, 1247, 1178, 1035, 802, 747, 730;

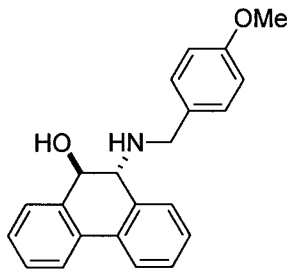


6-(4-Methoxybenzylamino)-5,6-dihydro-2,9-dimethyl-1,10-phenanthrolin-5-ol, (2,9-diMe-(4-MeO-benzyl) adduct)

Purification by column chromatography (SiO_2, $CHCl_3$/3% MeOH) yielded a solid (m.p. 80 °C) in 33%. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (1H, d, J = 7.69 Hz), 7.62 (1H, d, J = 7.69 Hz), 7.23 (2H, d, J = 8.42 Hz), 7.13 (2H, dd, J = 7.69; 7.69 Hz), 6.84 (2H, d, J = 8.42 Hz), 4.73 (1H, d, J = 8.42 Hz), 3.91 (1H, d, J = 8.06 Hz), 3.89 (1H, d, J = 12.81 Hz), 3.76 (4H, d, J = 11.35 Hz), 2.65 (2H, d, J = 2.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 159.0, 158.8, 150.3, 149,1, 135.3, 135.2, 131.7, 131.3, 130.3, 129.4, 124.0, 123.6, 114.1, 70.5, 61.1, 55.4, 50.8, 24.9, 24.8; FT-IR (NaCl, DCM solution) ν/cm^{-1} 3310.5, 3060.7, 2956.3, 2917.5, 2848.7, 1611.2, 1582.9, 1571.0, 1540.8, 1512.0, 1448.3, 1372.5, 1300.8, 1247.0, 1176.4, 1034.5, 831.2, 734.2.

General method for resolution of racemic and diastereomeric aminoalcohol-1,10-phenanthroline derivatives

To a solution of aminoalcohol (1.0 equiv) in absolute methanol was added S-mandelic acid (1.0-1.2 equiv). The mixture was heated to reflux while stirring and after 1 hour allowed to cool to room temperature. After one day white precipitate or crystals of the diastereomeric salt formed which were filtered and washed with cold methanol. Repeated heating and cooling steps with the remaining solution gave more diastereomeric salts, which were separately basicified with aqueous NaOH solution (1N) to pH 8.0-9.0 and then extracted with $CHCl_3$. Combined $CHCl_3$ layer was dried over $MgSO_4$, filtered, concentrated of solvent to afford enantiopure aminoalcohol products.

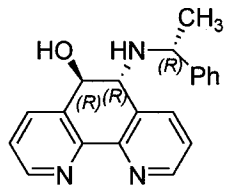


(+)- and (-)-*trans*-6-(4-Methoxy-benzylamino)-5,6-dihydro-1,10-phenanthroline-5-ol, ((+) and (-)-4-MeO-benzyl adduct)

Purification by column chromatography (SiO_2, $CHCl_3$/5% MeOH) yielded a solid (m.p. 190°C) in 62-74%. ^1H NMR (400 MHz, $CDCl_3$) δ 8.65 (2H, d, J = 4.76 Hz), 7.91 (1H, d, J = 6.96 Hz), 7.79 (1H, d, J = 7.69 Hz), 7.26-7.30 (2H, m), 7.24 (2H, d, J = 8.42 Hz), 6.48 (2H, d, J = 8.79 Hz), 4.83 (1H, d, J = 9.52 Hz), 4.00 (1H, d, J = 9.52 Hz), 3.94 (1H, d, J = 12.81 Hz), 3.79 (1H, d, J = 12.45 Hz), 3.77 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 151.1, 150.2, 149.8, 149.7, 134.5, 134.3, 134.2, 133.5, 131.8, 129.4, 124.3, 124.0,

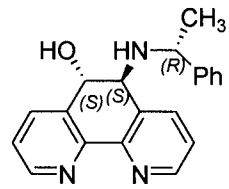
114.2, 70.4, 61.1, 55.4, 50.9; FT-IR (NaCl, DCM solution) ν(cm-1) 3270, 3063, 2835, 2208, 1611, 1583, 1564, 1512, 1418, 1247, 1178, 1035, 802, 747, 730; Anal Calcd for C20H19N3O2: C, 72.05; H, 5.74; N, 12.60. Found: C, 71.66; H, 6.14; N, 12.75. After resolution (+)-4-MeO-benzyl adduct $[\alpha]_D$ = +12.1° (c =0.038g/mL MeOH); (-)-4-MeO-benzyl adduct $[\alpha]_D$ = -13.4° (c =0.04g/mL MeOH).

X-ray analysis: X-ray quality crystals were grown from a chloroform/hexanes mixture. A colorless sample approximately 0.25 x 0.25 x 0.1 mm was chosen by size, habit, and polarized light microscopy. The compound crystallized in the monoclinic system in the space group $P2_1/c$ (#14)' a=10.4198(0.0018)Å, b=14.6148(0.0023) Å, c=11.5805(0.0021) Å, β=109.8220(0.0146)°, V=1659.01 Å^3, data collected (total/unique/$I_0>4\sigma I_0$)=3414/2858/1821, scan method ω/2θ, Z=4, d_{calc}=1.33 g/cc, μ=0.09 mm^{-1}, T=295K, λ=0.7107Å, F_{000}= 696e, structural parameters = 227, R_1=0.0729, wR_1=0.2321 ($w=([\Sigma\ (F_o^2) + (0.1318P)^2 + 1.34P])^{-1}$ where $P=(Max(F_o^2,0)+2F_c^2)/3$). Nonius CAD4, $2\theta_{max}$=49.88°. The structure was solved by direct methods using SHELXS and refined on F^2 in full matrix least squares using SHELXL. All non-hydrogen atoms were refined anisotropically. Hydrogens were placed in a combination of observed and calculated positions. The data were corrected for absorption by an empirical psi-scan determination. The largest unassigned peak in the final difference map was 0.5e/Å^3 located near N3. CCDC 221492 X-ray data may be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Rd, Cambridge CB21EZ, UK, or ccdc.cam.ac.uk



***trans*-(5*R*,6*R*)-6-((*R*)-1-Phenylethylamino-5,6-dihydro-1,10-phenanthroline-5-ol, ((*R*,*R*)-α-(+) adduct)**

^{1}HNMR (400MHz, $CDCl_3$) δ 8.62 (2H, dd, J = 3.30; 4.76 Hz), 7.91 (1H, d, J = 7.69 Hz), 7.62 (1H, d, J = 7.69 Hz), 7.34-7.17 (7H, m), 4.76 (1H, d, J = 9.15 Hz), 4.06 (1H, q, J = 6.59 Hz), 3.94 (1H, d, J =9.15 Hz), 1.33 (3H, d, J = 6.59 Hz); ^{13}CNMR (100MHz, $CDCl_3$) δ 150.74, 149.84, 149.77, 149.44, 145.43, 1134.85, 1134.79, 134.52, 134.36, 128.88, 127.59, 126.98, 126.63, 124.25, 124.06, 70.83, 59.68, 56.65, 24.45; FT-IR (NaCl, DCM solution) ν/cm^{-1} 3281, 3060, 3029, 2967, 2923, 2867, 1653, 1581, 1560, 1541, 1456, 1428, 1418, 1127, 1074, 1039, 801, 747, 702; (m.p. 72°C); $[\alpha]_D$ = -5.28° (c =0.05g/mL MeOH).



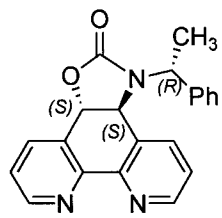
***trans*-(5*S*,6*S*)-6-((*R*)-1-Phenylethylamino-5,6-dihydro-1,10-phenanthroline-5-ol, ((*S*,*S*)-α-(+) adduct)**

^{1}HNMR (400MHz, $CDCl_3$) δ 8.73 (2H, dd, J = 4.03; 3.36 Hz), 7.82 (1H, d, J = 7.32 Hz), 7.66 (1H, d, J = 7.32 Hz), 7.36-7.26 (7H, m), 4.68 (1H, d, J = 5.86 Hz), 3.97 (1H, q, J = 6.22, 5.86 Hz), 3.73 (1H, d, J = 7.69 Hz), 1.38 (3H, d, J = 6.22 Hz); ^{13}CNMR (100MHz, $CDCl_3$) δ 150.71, 150.22, 149.78, 149.66, 144.80, 135.53, 134.92, 134.06, 133.95, 128.91, 127.61, 126.99, 124.26, 123.75, 71.25, 58.91, 56.66, 25.16; FT-IR (NaCl, DCM

solution) ν/cm^{-1} 3289, 3060, 2963, 2924, 2859, 1652, 1582, 1561, 1491, 1456, 1428,1372, 1267, 1217, 1126, 1073, 1044, 1026, 800, 756, 702; (m.p. 75°C); $[\alpha]_D$ = +29.82° (c = 0.05g/mL MeOH).

General method for the preparation of 5,6-oxazolidinone-1,10-phenanthroline derivatives

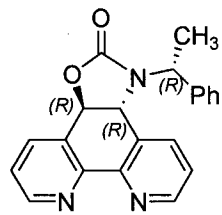
Amino alcohol (1.0 eq.) was added to a solution (2.5-3.0 eq.) of Li^{t}OBu in DCM under argon. The mixture was stirred at room temperature for 20 min and placed in an ice bath. Triphosgene (1.0 eq.), pre-dissolved in DCM, was added dropwise to the solution, stirred 2 hrs at 0°C and then allowed to warm to room temperature. After the reaction was completed after ca. 16 hrs (monitored by TLC, alumina, $CHCl_3$/5% MeOH), it was quenched with water. The layers were separated; the aqueous layer adjusted to pH 9.0-10.0 and extracted with $CHCl_3$. The combined organic layers were washed with water and brine, dried over anhydrous Na_2SO_4, and filtered. Evaporation of the solvent gave the crude product.



(3a*S*,11b*S*)-3,3a-Dihydro-3-((*R*)-1-phenylethyl)oxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one, ((*S,S*)-oxa-α-(+) adduct)

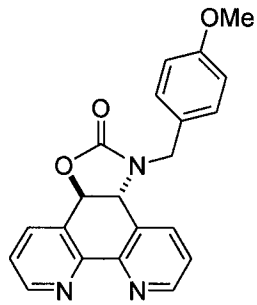
Purification by column chromatography (SiO_2, $CHCl_3$/3% MeOH) yielded a solid (m.p. 208 °C) in 91%. ^{1}HNMR (400MHz, $CDCl_3$) δ 8.83 (1H, d, J = 4.39 Hz), 8.70 (1H,

app t, J = 3.66, 2.56 Hz), 7.88 (1H, d, J = 7.69 Hz), 7.48 (2H, d, = 7.32 Hz), 7.33-7.42 (4H, m), 7.06 (2H, d, J = 4.03 Hz), 5.42 (1H, q, J = 7.32, 7.32 Hz), 5.26 (1H, d, J = 13.91 Hz), 4.77 (1H, d, J = 13.91 Hz), 1.80 (3H, d, J = 7.32 Hz); ^{13}CNMR (100MHz, $CDCl_3$) δ 160.1, 150.6, 150.5, 149.7, 149.5, 141.0, 131.7, 131.0, 130.9, 130.0, 129.0, 128.2, 127.0, 124.3, 123.6, 75.8, 61.1, 54.2, 15.9; FT-IR (NaCl, DCM solution) ν/cm^{-1} 3058, 2980, 2941, 1762, 1653, 1557, 1541, 1421, 1363, 1282, 1179, 1122, 1032, 798, 748, 702, 648; $[\alpha]_D$ = +11°; Anal Calcd for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.36; H, 4.83; N, 12.33.



(3a*R*,11b*R*)-3,3a-Dihydro-3-((*R*)-1-phenylethyl)oxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one, ((*R*,*R*)-oxa-α-(+) adduct)

Purification by column chromatography (SiO_2, $CHCl_3$/3% MeOH) yielded a solid (m.p. 229 °C) in 79%. ^{1}HNMR (400MHz, $CDCl_3$) δ 8.84 (1H, d, J = 4.76 Hz), 8.78 (1H, d, J = 4.76 Hz), 7.90 (1H, d, J = 7.69 Hz), 7.75 (2H, d, = 8.06 Hz), 7.53 (2H, d, J = 7.69 Hz), 7.37-7.45 (3H, m), 7.28-7.32 (2H, m), 5.26 (1H, d, J = 13.91 Hz), 5.06 (1H, q, J = 6.96, 6.96 Hz), 4.75 (1H, d, J = 13.91 Hz), 1.87 (3H, d, J = 6.96 Hz); ^{13}CNMR (100MHz, $CDCl_3$) δ 159.2, 150.6, 150.5, 149.9, 149.4, 139.5, 131.2, 131.1, 130.5, 130.0, 129.0, 128.0, 127.0, 124.4, 123.7, 75.9, 62.0, 60.0, 17.8; FT-IR (NaCl, DCM solution) ν/cm^{-1} 3058, 2976, 2936, 1769, 1554, 1422, 1371, 1278, 1173, 1149, 1018, 955, 800, 776, 748, 696; $[\alpha]_D$ = +1.16° (c = 0.037/mL $CHCl_3$).

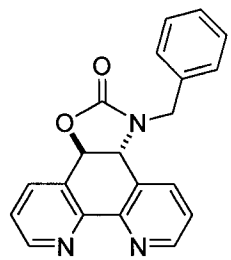


(+) and (-)-3-(4-Methoxybenzyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2 (11bH)-one, ((+) and (-)-oxa-4-MeO adduct)

Purification by column chromatography (SiO_2, $CHCl_3$/5% MeOH) yielded a solid (m.p. 199°C) in 78% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.81 (2H, m), 7.86 (2H, m), 7.40-7.36 (2H, m), 7.23 (2H, d, J = 8.2 Hz), 5.24 (1H, d, J = 13.9 Hz), 5.06 (1H, d, J = 15.2 Hz), 4.60 (1H, d, J = 15.2 Hz), 4.41 (1H, d, J = 13.9 Hz), 3.73(3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 159.8, 150.5, 150.0, 149.4, 131.1, 131.0, 130.5, 130.0, 129.9, 126.4, 124.3, 123.8, 114.5, 75.9, 60.0, 55.3, 49.3; FT-IR (NaCl, DCM solution) ν/cm^{-1} 3063, 3002, 2956, 2838, 1769, 1611, 1557, 1514, 1419, 1248, 1175, 1027, 800. Anal Calcd for $3C_{21}H_{17}N_3O_3 \cdot CHCl_3 \cdot H_2O$: C, 63.24; H, 4.48; N, 10.37. Found: C, 63.14; H, 4.81; N, 10.36; (+)-oxa-4-MeO $[\alpha]_D$ = +2.35° (c = 0.023g/mL MeOH), (-)-oxa-4-MeO $[\alpha]_D$ = -13.6° (c = 0.029g/mL MeOH) .

X-ray analysis: X-ray quality crystals were grown from chlorofom/hexanes mixture. A colorless sample approximately 0.3 x 0.3 x 0.3 mm was cut from multilayered plates and chosen by size, habit, and polarized light microscopy. The compound crystallized in the monoclinic system in the space group $P2_1/n$ (non-standard setting of $P2_1/c$ #14), a=15.7246(0.0092)Å, b=5.5890(0.0012) Å, c=28.745(0.0075) Å, β=120.5951(0.0371)°, V=2174.61 $Å^3$, data collected (total/unique/$I_0>4\sigma I_0$)=4779/3716/1781, scan method

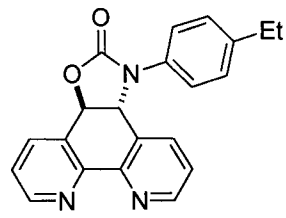
$\omega/2\theta$, Z=4, d_{calc}=1.10 g/cc, μ=0.45 mm^{-1}, T=295K, λ=0.7107Å, F_{000}=984e, structural parameters=283, R1=0.0947, wR1=0.3083 (Weight = $([\Sigma\ (F_o^2) + (0.1458P)^2 + 4.63P])^{-1}$ where $P=(Max(F_o^2,0)+2F_c^2)/3$). Nonius CAD4, $2\theta_{max}$=49.83°. The structure was solved by direct methods using SIR, and refined in full matrix least squares using SHELXL. All non-hydrogen atoms were refined anisotropically. Hydrogens were placed in a combination of observed and calculated positions. There was one molecule of chloroform in each asymmetric unit. Application of absorption corrections did not improve the model. There was some disorder of the chloroform. Adjusting for variable site occupancy for the chlorine atoms resulted in unit occupancy within experimental error. No attempt beyond adjusting the site occupancy for the chlorine atoms was applied to account for this disorder. The largest unassigned peak in the final difference map was 0.51 e/$Å^3$ located near Cl1. CCDC 221493 X-ray data may be obtained free of charge from the Cambridge Crystallographic Data Centre, 12 Union Rd, Cambridge CB21EZ, UK, or ccdc.cam.ac.uk



(3aR,11bR)-3-Benzyl-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one, (oxa-benzyl adduct)

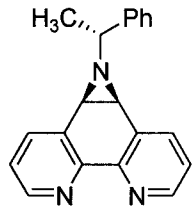
Purification by column chromatography (SiO_2, $CHCl_3$/5% MeOH) yields a solid (m.p. 169°C) in 74% yield. ^1H NMR δ 8.80 (2H, d, J = 4.76 Hz), 7.86 (1H, d, J = 7.69 Hz), 7.80 (1H, d, J = 7.69 Hz), 7.39 (1H, dd, J = 4.76, 4.76 Hz), 7.29-7.35 (6H, m), 5.26

(1H, d, J = 13.91 Hz), 5.05 (1H, d, J = 15.38 Hz), 4.70 (1H, d, J =15.38 Hz), 4.46 (1H, d, J = 13.91 Hz); 13C NMR δ 160.4, 150.5, 150.4, 150.0, 149.2, 134.6, 131.0, 130.7, 130.6, 130.2, 129.2, 128.6, 128.4, 124.4, 123.9, 75.9, 60.5, 49.9; FT-IR (NaCl, DCM solution) ν/cm^{-1} 3061, 3004, 2971, 1766, 1554, 1420, 1368, 1285, 1176, 1149, 1054, 1025, 800, 747; (m.p. 169°C).



3-(4-Ethylphenyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one, (oxa-4-Et-anilyl adduct)

Purification by column chromatography (SiO_2, $CHCl_3$/5% MeOH) yielded a solid (m.p. 227°C) in 73%. ^{1}H NMR (400 MHz, DMSO) δ 8.79 (1H, d, J = 4.76 Hz), 8.7 (1H, d, J = 4.03 Hz), 7.97 (1H, d, J = 7.69 Hz), 7.59 (1H, dd, J = 4.76, 4.76 Hz), 7.36 (6H, m), 7.15 (1H, d, J = 8.06 Hz), 5.78 (1H, d, J = 13.55 Hz), 5.66 (1H, d, J = 13.91 Hz), 2,66 (2H, q, J = 7.69, 7.69 Hz), 1.23 (3H, t, J = 7.69, 7.69 Hz); ^{13}C NMR (100 MHz, DMSO) δ 157.9, 150.9, 150.2, 149.8, 149.5, 142.5, 136.2, 131.5, 131.2, 130.9, 130.1, 129.1, 124.9, 124.3, 123.5, 76.0, 60.0, 28.2, 16.3; FT-IR (KBr) ν/cm^{-1} 3055, 2963, 1770, 1600, 1554, 1518, 1424, 1376, 1340, 1272, 1201, 1167, 1137, 1110, 1077, 1022, 967, 887, 850, 826, 797, 747, 679, 628.



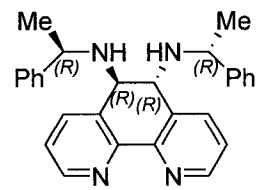
(1a*S*,9b*R*)-1a,9b-Dihydro-1-((*R*)-1-phenylethyl)-1H-azirino[2,3-f][1,10]phenanthroline, (α(+)-aziridine)

In a two-necked flask, fitted with an addition funnel, condenser and a magnetic stirrer, was added under argon atmosphere the diastereoisomeric mixture of (5*R*,6*R*,1'*R*) and/or (5*S*,6*S*,1'*R*) aminoalcohol derivative (1.59 g, 5 mmol), dry Et_3N (1.05 mL) and dry DCM (15 mL). The mixture was cooled to 0°C and to it was added dropwise a solution of methanesulfonyl chloride (0.63 g, 5.5 mmol) in dry DCM (5 mL). The reaction was stirred at 0°C until no more starting material (by TLC alumina, $CHCl_3$/ 5% MeOH), the *in situ* mesylated compounds were allowed to warm to room temperature and stirred further for 12 hrs. The reaction mixture was then quenched with water. The layers were separated and the aqueous layer was extracted several times with DCM (3 x 10 mL). The combined organic layer was washed with water, brine, and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by column chromatography (SiO_2, $CHCl_3$/5% MeOH) to give (1aS,9bR)-1a,9b-dihydro-1-((R)-1-phenylethyl)-1H-azirino [2,3-f][1,10]phenanthroline (1.19 g, 80%) as a thick yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (1H, d, J = 4.76 Hz), 8.77 (1H, d, J = 4.76 Hz), 7.90 (1H, d, J = 7.69 Hz), 7.46 (1H, d, J = 7.69 Hz), 7.34 (1H, dd, J = 4.76, 7.69 Hz), 7.25-7.30 (5H, m), 7.20 (1H, dd, J = 4.76, 7.69 Hz), 3.30 (1H, d, J = 5.86 Hz), 3.09 (1H, d, J = 6.22 Hz), 2.97 (1H, q, J = 6.59, 6.59 Hz), 1.51 (3H, d, J = 6.59 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 149.6, 149.4, 143.7, 139.3, 137.0, 131.0, 130.9, 128.5, 128.0,

127.3, 126.7, 123.7, 123.6, 69.6, 44.2, 42.7, 23.2; FT-IR (NaCl-DCM solution) ν/cm^{-1} 3393, 3058, 2970, 2926, 1560, 1494, 1427, 1131, 1096, 1071, 1039, 934, 792, 746, 704; $[\alpha]_D = -6.4^o$

(5*S*,6*S*)- and (5*R*,6*R*)-5,6-Dihydro-*N*5,*N*6-bis((*R*)-1-phenylethyl)-1,10-phenanthroline 5,6-diamine

In a dry two-neck flask, fitted with an addition funnel, condenser and magnetic stirrer, was placed with stirring under argon atmosphere 5,6-aziridine-1,10-phenanthroline (1.03 g, 3.45mmol) and anhydrous $Mg(ClO_4)_2$ (1.00 g, 4.48 mmol) in freshly dried acetonitrile (minimum amount) until complete dissolution of salt. The reaction mixture was cooled to 0°C and (*R*)-α-phenylethylamine (0.542g, 4.48 mmol) added. The resulting solution was then heated to reflux until the reaction was complete, which took ca. 2 days. A viscous residue formed. The reaction was quenched with water and washed with hexanes to get rid excess amine. The layers were separated and the aqueous layer was extracted with $CHCl_3$ (3 x 25 mL). The combined organic layers were washed with water and brine and dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give crude mixture of the 5,6-diamines. The mixture of 5,6-diamines was purified and separated by column chromatography (SiO_2, $CHCl_3$/3% MeOH) to give enantiopure material in 79% yield.



(5*R*,6*R*)-5,6-Dihydro-*N*5,*N*6-bis((*R*)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine

Recrystalization in $CHCl_3$ yielded a yellow solid (m.p. 108°C).^{1}H NMR (400 MHz, $CHCl_3$) δ 8.726 (2H, dd, J = 1.46, 3.30 Hz), 7.428 (2H, dd, J = 1.46, 6.22 Hz), 7.202-7.347 (12H, m), 3.955 (2H, s), 3.737 (2H, q, J = 6.59, 6.59 Hz), 1.160 (3H, d, J = 6.59 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.4, 150.1, 145.4, 138.0, 133.8, 129.3, 127.3, 126.8, 124.1, 56.1, 55.5, 24.5; FT-IR (NaCl-DCM solution) ν/cm^{-1} 3338, 3269, 3063, 3028, 2966, 2927, 2864, 2208, 1562, 1492, 1451, 1425, 1370, 1125, 909, 754, 730, 702; $[\alpha]_D$ = -138° (c =0.043g/mL MeOH).

X-ray analysis: C_2 (RRRR) diamine ligand

Table 1. Crystal data and structure refinement for vjc476fm (C_2 RRRR).

Identification code	vjc476fm	
Empirical formula	C29 H29 Cl3 N4	
Formula weight	539.91	
Temperature	100(2) K	
Wavelength	0.71073 ≈	
Crystal system	Tetragonal	
Space group	I4(1)	
Unit cell dimensions	a = 11.8038(3) ≈	= 90∞.
	b = 11.8038(3) ≈	= 90∞.
	c = 19.8714(8) ≈	= 90∞.

Volume	2768.68(15) $\approx^3$
Z	4
Density (calculated)	1.295 Mg/m^3
Absorption coefficient	0.356 mm^{-1}
F(000)	1128
Crystal size	0.39 x 0.25 x 0.10 mm^3
Theta range for data collection	2.01 to 27.47∞.
Index ranges	-15<=h<=15, -15<=k<=15, -25<=l<=25
Reflections collected	11723
Independent reflections	2721 [R(int) = 0.0303]
Completeness to theta = 27.47∞	85.9 %
Absorption correction	sadabs
Max. and min. transmission	0.9653 and 0.8733
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2721 / 163 / 225
Goodness-of-fit on F^2	0.932
Final R indices [I>2sigma(I)]	R1 = 0.0378, wR2 = 0.0923
R indices (all data)	R1 = 0.0427, wR2 = 0.0946
Absolute structure parameter	-0.01(6)
Largest diff. peak and hole	0.252 and -0.127 $e.\approx^{-3}$

Table 2. Bond lengths [≈] and angles [∞] for vjc476fm.

Cl(1)-C(1S)	1.750(4)
Cl(2)-C(1S)	1.698(4)
Cl(2)-C(1S)#1	1.761(4)
C(1S)-C(1S)#1	1.165(8)
C(1S)-Cl(2)#1	1.761(4)
N(1)-C(5)	1.347(2)
N(1)-C(1)	1.348(3)
C(1)-C(2)	1.381(4)
N(2)-C(6)	1.470(2)
N(2)-C(7)	1.472(2)
C(2)-C(3)	1.379(3)
C(3)-C(4)	1.394(3)
C(4)-C(5)	1.395(3)
C(4)-C(6)	1.510(3)
C(5)-C(5)#2	1.473(4)
C(6)-C(6)#2	1.551(3)
C(7)-C(9)	1.500(3)
C(7)-C(8)	1.526(3)
C(7)-C(9A)	1.529(4)
C(9)-C(14)	1.343(12)
C(9)-C(10)	1.369(3)

C(10)-C(11)	1.365(11)
C(11)-C(12)	1.38(2)
C(12)-C(13)	1.28(2)
C(13)-C(14)	1.455(17)
C(9A)-C(10A)	1.362(7)
C(9A)-C(14A)	1.399(7)
C(10A)-C(11A)	1.372(9)
C(11A)-C(12A)	1.374(9)
C(12A)-C(13A)	1.373(9)
C(13A)-C(14A)	1.400(5)

C(1S)-Cl(2)-C(1S)#1	39.3(3)
C(1S)#1-C(1S)-Cl(2)	73.3(4)
C(1S)#1-C(1S)-Cl(1)	173.8(4)
Cl(2)-C(1S)-Cl(1)	107.7(2)
C(1S)#1-C(1S)-Cl(2)#1	67.4(3)
Cl(2)-C(1S)-Cl(2)#1	113.7(2)
Cl(1)-C(1S)-Cl(2)#1	107.0(2)
C(5)-N(1)-C(1)	116.4(2)
N(1)-C(1)-C(2)	124.3(2)
C(6)-N(2)-C(7)	116.93(15)
C(3)-C(2)-C(1)	118.28(19)
C(2)-C(3)-C(4)	119.3(2)

C(5)-C(4)-C(3)	118.05(19)
C(5)-C(4)-C(6)	119.83(15)
C(3)-C(4)-C(6)	121.99(18)
N(1)-C(5)-C(4)	123.51(17)
N(1)-C(5)-C(5)#2	117.05(12)
C(4)-C(5)-C(5)#2	119.44(10)
N(2)-C(6)-C(4)	107.39(14)
N(2)-C(6)-C(6)#2	114.62(19)
C(4)-C(6)-C(6)#2	110.55(12)
N(2)-C(7)-C(9)	116.4(3)
N(2)-C(7)-C(8)	108.13(16)
C(9)-C(7)-C(8)	111.42(17)
N(2)-C(7)-C(9A)	108.7(2)
C(9)-C(7)-C(9A)	9.9(5)
C(8)-C(7)-C(9A)	110.10(18)
C(14)-C(9)-C(10)	117.1(6)
C(14)-C(9)-C(7)	123.3(6)
C(10)-C(9)-C(7)	119.0(2)
C(11)-C(10)-C(9)	123.7(7)
C(10)-C(11)-C(12)	115.5(10)
C(13)-C(12)-C(11)	124.9(13)
C(12)-C(13)-C(14)	117.7(13)
C(9)-C(14)-C(13)	120.3(10)

C(10A)-C(9A)-C(14A)	115.7(4)
C(10A)-C(9A)-C(7)	121.7(4)
C(14A)-C(9A)-C(7)	122.3(4)
C(9A)-C(10A)-C(11A)	125.0(5)
C(10A)-C(11A)-C(12A)	118.9(5)
C(13A)-C(12A)-C(11A)	118.6(5)
C(12A)-C(13A)-C(14A)	121.4(5)
C(9A)-C(14A)-C(13A)	120.3(4)

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,-y+0,z+0 #2 -x+2,-y+1,z+0

Table 3. Torsion angles [∞] for vjc476fm.

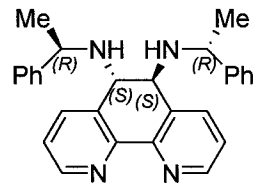
C(1S)#1-Cl(2)-C(1S)-Cl(1)	-173.6(3)
C(1S)#1-Cl(2)-C(1S)-Cl(2)#1	-55.2(3)
C(5)-N(1)-C(1)-C(2)	-2.1(3)
N(1)-C(1)-C(2)-C(3)	2.5(3)
C(1)-C(2)-C(3)-C(4)	0.4(3)
C(2)-C(3)-C(4)-C(5)	-3.4(3)
C(2)-C(3)-C(4)-C(6)	-179.24(18)
C(1)-N(1)-C(5)-C(4)	-1.2(3)
C(1)-N(1)-C(5)-C(5)#2	178.4(2)
C(3)-C(4)-C(5)-N(1)	3.9(3)
C(6)-C(4)-C(5)-N(1)	179.85(17)
C(3)-C(4)-C(5)-C(5)#2	-175.7(2)
C(6)-C(4)-C(5)-C(5)#2	0.3(3)
C(7)-N(2)-C(6)-C(4)	-164.63(15)
C(7)-N(2)-C(6)-C(6)#2	72.13(16)
C(5)-C(4)-C(6)-N(2)	-90.98(19)
C(3)-C(4)-C(6)-N(2)	84.8(2)
C(5)-C(4)-C(6)-C(6)#2	34.7(2)
C(3)-C(4)-C(6)-C(6)#2	-149.50(19)
C(6)-N(2)-C(7)-C(9)	61.7(3)
C(6)-N(2)-C(7)-C(8)	-171.99(16)

C(6)-N(2)-C(7)-C(9A)	68.5(2)
N(2)-C(7)-C(9)-C(14)	64.1(7)
C(8)-C(7)-C(9)-C(14)	-60.6(8)
C(9A)-C(7)-C(9)-C(14)	23.7(10)
N(2)-C(7)-C(9)-C(10)	-124.6(3)
C(8)-C(7)-C(9)-C(10)	110.82(15)
C(9A)-C(7)-C(9)-C(10)	-164.9(10)
C(14)-C(9)-C(10)-C(11)	-10.5(7)
C(7)-C(9)-C(10)-C(11)	177.6(5)
C(9)-C(10)-C(11)-C(12)	7.7(10)
C(10)-C(11)-C(12)-C(13)	-1.8(17)
C(11)-C(12)-C(13)-C(14)	-0.8(19)
C(10)-C(9)-C(14)-C(13)	7.3(13)
C(7)-C(9)-C(14)-C(13)	178.9(8)
C(12)-C(13)-C(14)-C(9)	-2.1(17)
N(2)-C(7)-C(9A)-C(10A)	-145.2(4)
C(9)-C(7)-C(9A)-C(10A)	-2.9(9)
C(8)-C(7)-C(9A)-C(10A)	96.5(4)
N(2)-C(7)-C(9A)-C(14A)	39.8(4)
C(9)-C(7)-C(9A)-C(14A)	-177.9(12)
C(8)-C(7)-C(9A)-C(14A)	-78.4(4)
C(14A)-C(9A)-C(10A)-C(11A)	-0.6(8)
C(7)-C(9A)-C(10A)-C(11A)	-175.9(5)

C(9A)-C(10A)-C(11A)-C(12A)	1.7(10)
C(10A)-C(11A)-C(12A)-C(13A)	-1.4(9)
C(11A)-C(12A)-C(13A)-C(14A)	0.1(8)
C(10A)-C(9A)-C(14A)-C(13A)	-0.8(6)
C(7)-C(9A)-C(14A)-C(13A)	174.5(3)
C(12A)-C(13A)-C(14A)-C(9A)	1.0(7)

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,-y+0,z+0 #2 -x+2,-y+1,z+0

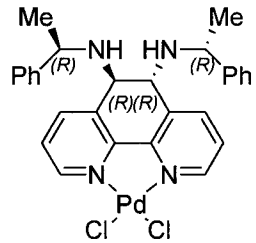


(5*S*,6*S*)-5,6-Dihydro-*N*5,*N*6-bis((*R*)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine

Yellow foam solid (m.p. 62 °C). ^{1}H NMR (400 MHz, $CHCl_3$) δ d 8.776 (2H, d, J = 3.66 Hz), 7.331-7.191 (14H, m), 3.693 (2H, s), 3.587 (2H, q, J = 6.59, 6.59 Hz), 1.021 (3H, d, J = 6.59 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ d 150.3, 150.1, 145.2, 137.8, 133.3, 129.1, 128.8, 128.5, 127.1, 126.8, 123.5, 58.1, 55.5, 25.7; FT-IR (NaCl-DCM solution) ν/cm^{-1} 3238, 3057, 3025, 2964, 2925, 2861, 1602, 1578, 1561, 1491, 1450, 1425, 1367, 1267, 1212, 1124, 1081, 1060, 812, 757, 737, 702; $[\alpha]_D$ = +23.7°.

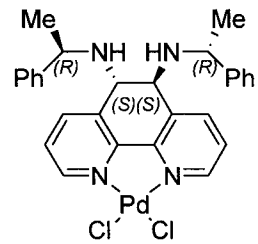
General method for the preparation of C_2 and 5,6-oxazolidinone-1,10-phenanthroline-Pd complexes

1,10-Phenanthroline ligand (1.0 eq.) was added to an equimolar solution of $Pd(MeCN)_2Cl_2$ in DCM (anhydrous). The mixture was stirred overnight at 30°C. The yellow precipitate was collected by filtration, washed with cold DCM and dried in a vacuum oven at 50° for 6 hrs.



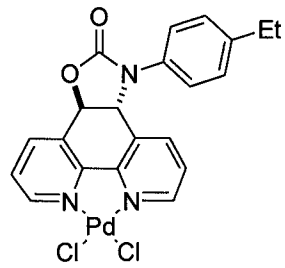
(5*R*,6*R*)-5,6Dihydro-*N*5,*N*6-bis((*R*)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine-$PdCl_2$ complex, (C_2(*RRRR*)-$PdCl_2$)

^{1}H NMR (400 MHz, DMSO_D_6) δ 8.81 (2H, d, J = 5.13 Hz), 7.81 (2H, d, J = 7.69 Hz), 7.62 (2H, t, J = 6.22, 6.59 Hz), 7.19-7.34 (10H, m), 4.01 (2H, broad s), 3.70 (2H, broad s), 2.71 (2H, broad s), 1.08 (6H, d, J = 5.86 Hz); ^{13}C NMR (100MHz, DMSO_D_6) δ 153.5, 148.0, 146.3, 142.0, 137.9, 128.9, 127.3, 127.1, 56.3, 55.7, 25.1.



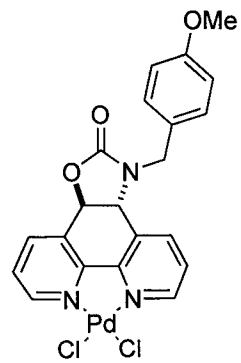
(5*S*,6*S*)-5,6Dihydro-*N*5,*N*6-bis((*R*)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine-$PdCl_2$ complex, (C_2(*RSSR*)-$PdCl_2$)

^{1}H NMR (400 MHz, DMSO_D_6) δ 8.90 (2H, t, J = 3.30, 3.30 Hz), 7.71 (4H, d, J = 3.66 Hz), 7.29-7.35 (6H, m), 7.17(4H, d, J = 6.60 Hz), 3.65 (2H, d, J = 8.79 Hz), 3.48 (2H, appear q, J = 3.30, 6.22 Hz), 2.68 (2H, dd, J = 2.93, 8.79 Hz), 0.96 (6H, d, J = 6.22 Hz).



3-(4-Ethylphenyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one Pd complex

^{1}H NMR (400 MHz, DMSO_D_6) δ 8.80 (1H, d, J = 5.49 Hz), 8.74 (1H, d, J = 5.49 Hz), 8.40 (1H, d, J = 7.69 Hz), 7.88 (1H, t, J = 6.22, 6.96 Hz), 7.66 (1H, t, J = 6.59, 6.59 Hz), 7.45 (1H, d, J = 7.69 Hz), 7.33-7.37 (4H, m), 6.15 (1H, d, J = 14.65 Hz), 6.02 (1H, d, J = 14.65 Hz), 2.67(2H, q, J = 7.69, 7.69, 7.32 Hz), 1.23 (3H, t, J = 7.69, 7.32 Hz); ^{13}C NMR (100MHz, DMSO_D_6) δ 157.3, 154.2, 153.3, 148.7, 148.1, 143.0, 135.6, 135.5, 135.3, 133.6, 133.3, 129.3, 128.3, 127.7, 123.7, 75.1, 59.4, 28.2, 16.0; (m.p. >250°C).

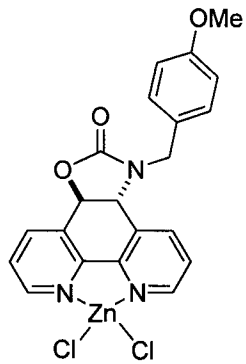


3-(4-Methoxybenzyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one Pd complex

^{1}H NMR (400 MHz, DMSO_D_6) δ 8.76 (2H, t, J = 6.59, 6.22 Hz), 8.44 (1H, d, J = 7.69 Hz), 8.27 (1H, d, J = 7.69 Hz), 7.79 (2H, dd, J = 8.06, 8.44 Hz), 7.29 (2H, d, J = 8.79 Hz), 6.90 (2H, d, J = 8.42 Hz), 5.88 (1H, d, J = 14.65 Hz), 5.04 (1H, d, J = 14.65 Hz), 4.77-4.92 (2H, ABqt, J = 15.38, 15.74 Hz); ^{13}C NMR (100MHz, DMSO_D_6) δ 159.8, 159.6, 154.1, 153.3, 148.4, 148.1, 135.8, 134.8, 133.6, 133.3, 130.1, 128.1, 127.7, 127.5, 114.9, 74.9, 59.2, 55.6, 48.2; FT-IR (KBr) ν/cm^{-1} 3096, 2837, 1780, 1610, 1513, 1428, 1379, 1248, 1178, 1155, 1110, 1044, 968, 898, 807, 728, 563; m.p. > 250°C

General method for the preparation of 5,6-oxazolidinone-1,10-phenanthroline-Zn complexes

The oxazolidinone ligand (1.0 equiv) was mixed with an equimolar solution of anhydrous $ZnCl_2$ in dry MeOH. The mixture was stirred under argon at room temperature overnight. Solvent evaporation yielded the complex.



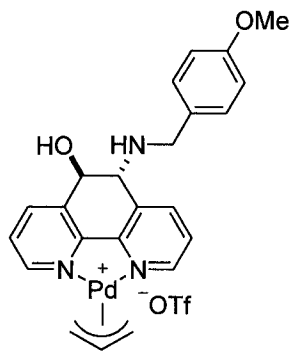
3-(4-Methoxybenzyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one-Zn complex

^{1}H NMR (400 MHz, $CHCl_3$) δ d 8.83 (2H, d, J = 5.13 Hz), 8.21 (2H, dd, J = 7.69, 8.06 Hz), 7.81 (2H, ddd, J = 5.49, 8.06 Hz), 7.21 (2H, d, J = 8.42 Hz), 6.85 (2H, d, J = 8.79

Hz), 5.41 (1H,d, J = 14.28 Hz), 5.11 (1H, d, J = 15.01 Hz), 4.61 (2H, dd, J = 15.38, 14.28 Hz), 3.75 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ d 160.2, 159.1, 149.0, 148.5, 145.3, 144.4, 135.4 135.1, 133.0, 132.3, 129.7, 128.2, 127.8, 125.4, 115.0, 74.2, 59.1, 55.4, 49.6.

General method for preparation of complexes [(L)-1,3-η^3-propenyl)Pd] CF_3SO_3.

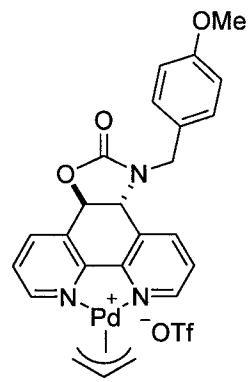
To chloroform (3 mL) (1.0 equiv) allylpalladium chloride dimer and (1.1 equiv) silver trifluromethansulfonate was added. The mixture was stirred for 10 min at room temperature under argon atmosphere, and then an equimolar amount of nitroligand was added. After a further 30 min the mixture was filtered and diethyl ether added to initiate the crystallization, followed by storage at –10°C.



5,6-Dihydro-6-(4-methoxybenzylamino)-1,10-phenanthrolin-5-ol (1,3-η^3-propenyl)Pd trifluoromethanesulfonate complex

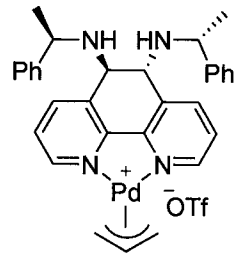
Recrystalization in $CHCl_3$/ether yielded yellow solid (m.p. 148°C). ^1H NMR (400 MHz, DMSO) δ 8.87 (2H, dd, J = 5.49, 6.22 Hz), 8.27 (1H, d, J = 8.06 Hz), 8.22 (1H, d, J = 7.69 Hz), 7.78 (2H, ddd, J = 7.69, 5.49 Hz), 7.22 (2H, d, J = 7.69 Hz), 6.86 (2H, d, J = 7.32 Hz), 6.07 (1H, tt, J = 10.25, 9.52 Hz), 5.99 (1H, d, J = 4.76 Hz), 5.03 (1H, s), 4.50 (2H, d, J = 6.22 Hz), 4.09 (1H, d, J = 3.28 Hz), 3.70 (3H, s), 3.64 (2H, s) 3.56 (2H, d, J =

11.72 Hz); ^{13}C NMR (100 MHz, DMSO) δ 158.7, 153.3, 152.9, 151.2, 151.1, 141.4, 141.3, 138.1, 137.4, 132.7, 129.7, 128.5, 128.1, 122.9, 120.3, 119.7, 114.1, 69.2, 63.1, 60.2, 55.6, 49.9; Anal Calcd for $C_{24}H_{23}F_3N_3O_5PdS$: C, 45.83; H, 3.69; N, 6.68; S, 5.10. Found C, 45.83; H, 3.73; N, 6.58; S, 4.77.



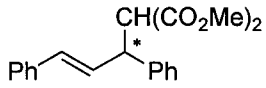
5,6-Oxazolidinone-6-*N*-(4-methoxybenzylamino)-1,10-phenanthrolin-5-ol (1,3-η^3-propenyl)Pd trifluoromethanesulfonate complex

^1H NMR (400 MHz, $CDCl_3$) δ 8.78 (2H, dd, J = 5.13, 5.49 Hz), 8.21 (1H, d, J = 7.69 Hz), 8.13 (1H, d, J = 7.69 Hz), 7.76 (2H, ddd, J = 8.06, 5.49 Hz), 7.23 (2H, d, J = 8.42 Hz), 6.80 (2H, d, J = 8.79 Hz), 5.92 (1H, m), 5.45 (1H, d, J = 14.65 Hz), 4.97 (1H, d, J = 15.74 Hz), 4.68 (2H, d, J = 15.38 Hz), 4.40 (2H, app t, J = 3.30, 5.86 Hz), 3.71 (3H, s), 3.55 (1H, d, J = 12.81 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 159.5, 153.1, 153.0, 150.8, 150.3, 135.1, 134.1, 133.4, 133.0, 129.7, 128.6, 128.4, 126.2, 122.4, 119.9, 114.7, 74.5, 63.2, 59.7, 55.4, 49.1.



(5*R*,6*R*)-5,6-Dihydro-*N*5,*N*6-bis((*R*)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine (1,3-η^3-propenyl)Pd trifluoromethanesulfonate complex

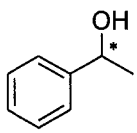
Recrystalization in $CHCl_3$/ether yielded yellow needle (m.p. 62°C). ^1H NMR (400 MHz, DMSO) δ 8.77 (2H, d, J = 4.76 Hz), 7.82 (2H, d, J = 7.69 Hz), 7.61 (2H, t, J = 5.49, 6.96 Hz), 7.30 (4H, t, J = 6.96, 7.32 Hz), 7.23 (2H, t, J 6.96, 7.32 Hz), 7.17 (4H, d, J = 7.32 Hz), 6.06 (1H, m), 4.46 (2H, d, J = 5.86 Hz), 4.06 (2H, d, J=4.76 Hz), 3.69 (2H, appt, J = 6.22, 5.49 Hz), 3.52 (2H, appt, J = 12.08, 11.72 Hz), 2.62 (2H, s), 1.08 (6H, d J = 6.96 Hz).



***General procedure for allylic alkylation reaction*: dimethyl 2-((E)-1,3-diphenylallyl) malonate**

A solution of the ligand (0.08 mmol, 10 mol %) and $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$ (8 mg, 2.5 mol%) in dry CH_2Cl_2 (2mL) was stirred at room temperature for 30 min. To this solution was added a solution of rac-(*E*)-1,3-diphenyl-2-propenyl acetate (200 mg, 0.79 mmol) in dry CH_2Cl_2 (1 mL), dimethyl malonate (316 mg, 2.4 mmol), *N,O*-bis(trimethylsilyl)-acetamide (BSA) (488 mg, 2.4 mmol) and sodium acetate (2.4 mg, 3.5 mol%). The

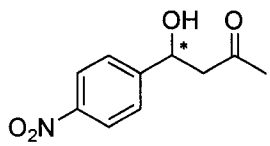
reaction mixture was stirred overnight until conversion was complete (monitored by TLC, SiO_2, petroleum/ether 3:1), diluted with ether (25 mL), and washed with cold saturated NH_4Cl. The organic phase was dried over Na_2SO_4 and concentrated in *vacuo*. The residue was purified by flash chromatography, SiO_2, petroleum/ether (3:1), to yield 1,3-diphenylprop-2-enylmalonate. The enantiomeric excess was determined by ^1H NMR in the presence of enantiomerically pure shift reagent, $(Eu(hfc)_3$. Splitting of the signals for one of the two methoxy groups was observed. Chiral HPLC was also performed with Daicel OD-H 25x0.46 cm (L x I.D.) at λ = 254 nm; flow rate 0.5 mL/min; eluent : Hexanes/IPA (200:1), t_R = 23.5 min t_S = 25.0 min. ^1H NMR (400 MHz, $CDCl_3$) δ 7.18-7.33 (10H, m), 6.5 (1H, d, J = 15.74 Hz), 6.36 (1H, dd, J = 15.74, 8.79 Hz), 4.29 (1H, dd, J = 10.98, 10.62 Hz), 3.98 (1H, d, J = 10.98 Hz), 3.71 (3H, s), 3.52 (3H, s).



***General procedure for Reduction of acetophenone reaction*: 1-phenylethanol**

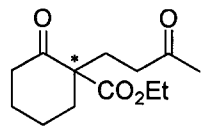
In a small flask, $ZnEt_2$ (0.014 mL, 1M in heptane, 0.083 mmol) and chiral ligand (0.083 mmol) in 1 mL of freshly distilled toluene were stirred under argon at room temperature for 10 min. Then (0.20 g, 1.66 mmol) acetophenone, and $(EtO)_3SiH$ were added slowly to the mixture. The reaction was stirred for 18-24 h. The solvent was removed by rotavap and the residue was purified by SiO_2 gel column with hexanes/EtOAc (10:1) as eluent. The silano product was dissolved in a small amount of MeOH, followed by the addition of KF aqueous solution and stirred for 2 hrs. This mixture was extracted with $CHCl_3$, dried over Na_2SO_4, filtered and evaporated to give the alcohol product as a colorless

liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.36 (5H, m), 4.87 (1H, q, J = 6.59, 6.22 Hz), 2.00(1H, s), 1.50 (3H, d, J = 6.22 Hz). The enantiomeric excess was determined from chiral HPLC Daicel OD-H 25x0.46 cm (L x I.D.) at λ = 254 nm; flow rate 0.5 mL/min; eluent: Hexanes/IPA (95:5), t_R = 16.3 min t_S = 19.3 min; Reference (*R*)-1-phenylthanol t_R = 16.7 min.



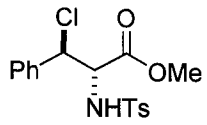
***General procedure for direct aldol*: 4-Hydroxy-4-(4-nitrophenyl)butan-2-one**

To a solution of the ligand (0.2 equiv.) in MeOH (0.1M with respect to the aldehyde) at room temperature was added $Zn(NO_3.6H_2O$ (0.1 equiv.). To the complex was then added *p*-nitrobenzaldehyde (1 equiv.), distilled acetone (20 equiv.) and small amount of Et_3N. The resulting solution was then stirred under argon atmosphere for 2 days. The crude mixture solvent was concentrated and the residue purified by column chromatography of (SiO_2, Hexanes/EtOAc 3:1) to afford the aldol product in 76% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (2H, d, J = 8.79 Hz), 7.52 (2H, d, J = 8.42 Hz), 5.22-5.26 (1H, m), 3.67 (1H, d, J = 3.30 Hz), 2.85 (1H, s), 2.83 (1H, d, J = 2.20 Hz), 2.22 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.6, 150.1, 147.3, 126.5, 123.8, 69.0, 51.6, 30.8; FT-IR (NaCl-DCM solution) ν/cm^{-1} 3432, 3112, 3080 3003, 2915, 1713, 1604, 1519, 1348, 1164, 1076, 857, 749, 698, 536.



***General procedure for Michael addition product*: Ethyl 2-oxo-1-(3-oxobutyl)cyclohexanecarboxylate**

$Ni(Oac)_2 . 4H_2O$ (7.3 mg, 0.05 equiv.) was added to a solution of **C_2(RRRR)** (25.0 mg, 0.10 equiv.) in $CHCl_3$ (1.0 mL/mmol ethyl 2-oxocyclohexanecarboxylate) and the mixture was stirred at room temperature for 1 hr. Then ethyl 2-oxocyclohexanecarboxylate (100 mg, 1.0 equiv.) was added, and after further stirring for 2 h, **MVK** (62 mg, 1.50 equiv.) was added. The resulting solution was stirred for additional 18 h. All volatile materials were removed in vacuo, and the residue was purified on SiO_2 (PE/MTB 1:1) to yield a colorless oil product (60%). ^1H NMR (400 MHz, $CDCl_3$) δ 4.15-24.23 (2H, m), 2.31-2.61(3H, m), 2.10 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.1, 207.9, 172.1, 61.5, 60.0, 41.1, 38.9, 36.8, 30.0, 28.5, 27.6, 22.6, 14.2; FT-IR (NaCl-DCM solution) ν/cm^{-1} 2940, 2868, 1716, 1559, 1540, 1489, 1419, 1364, 1245, 1188, 1136, 1021, 668.



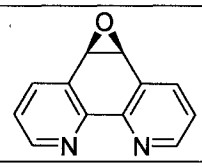
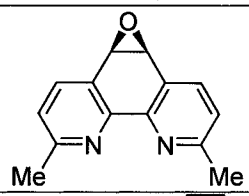
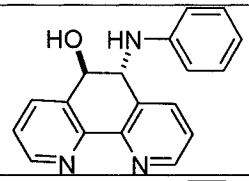
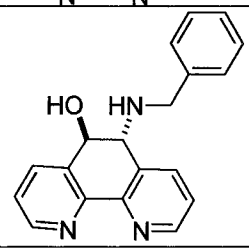
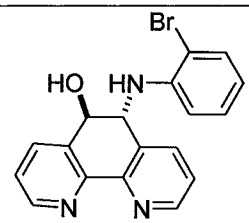
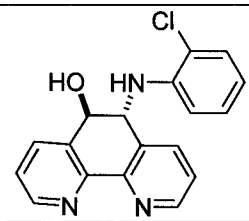
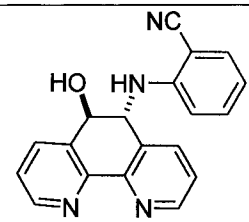
thyl 3-chloro-3-phenyl-2-(tosylamino)propanoate

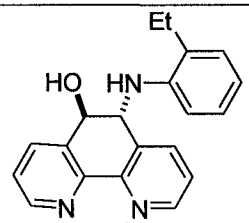
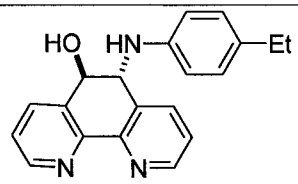
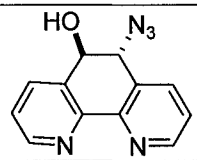
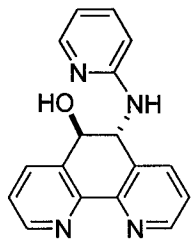
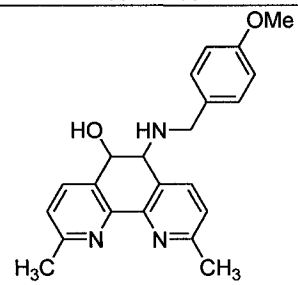
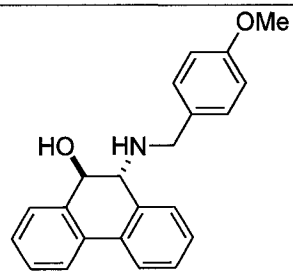
Solution of (*S,S*)-oxa-α(+) ligand (0.014 g, 10 mol%) and allylpalladium chloride dimer (0.004 g, 2.5 mol%) in dry DCM (2 mL) was stirred under argon atmosphere at room temperature for 30 min. A pre-dissolved solution of methyl cinanamate (0.065g, 0.4 mmol) and di-chloramine T (0.115g, 0.48 mmol) in dry DCM (2 mL) was added to the

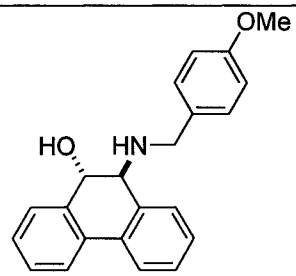
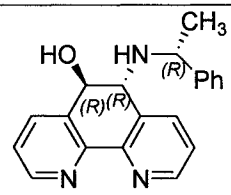
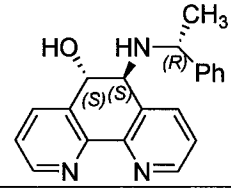
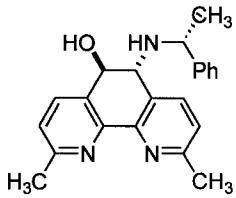
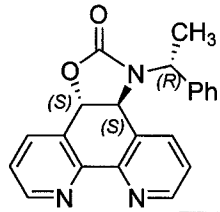
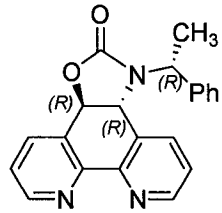
palladium-ligand solution. The resulting mixture was stirred at room temperature and was eventually quenched by slowly adding aqueous Na_2SO_3 (4 mL). The layers were separated and the aqueous layer was extracted with DCM (2 x 5 mL). The combined organic layers were washed with NH_4Cl solution (10 %), and brine, and dried over anhydrous $MgSO_4$. Finally the solution was filtered, concentrated and purified on SiO_2 (hexanes/EtOAc 3:1) to yield a white solid product (38%). ^1H NMR (400 MHz, DMSO) δ 8.76 (2H, d, J = 9.88 Hz), 7.27-7.43 (9H, m), 5.07 (1H, d, J = 10.25 Hz), 4.30 (1H, t, J = 10.25, 9.89 Hz), 3.37 (3H, s), 2.25 (3H, s); ^{13}C NMR (100 MHz, DMSO) δ 169.9, 143.4, 137.9, 137.3, 129.9, 129.5, 129.1, 128.7, 126.9, 61.7, 60.6, 52.6, 21.5. The enantiomeric excess was determined by chiral HPLC with Daicel OD-H 25x0.46 cm (L x I.D.) at λ = 254 nm; flow rate 0.5 mL/min; eluent: Hexanes/IPA (95:5), two peaks came out at 34.2 and 49.6 min.

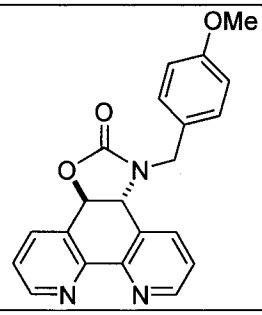
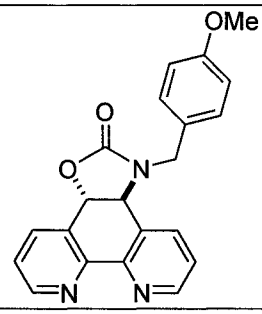
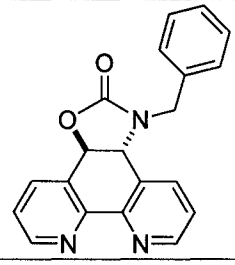
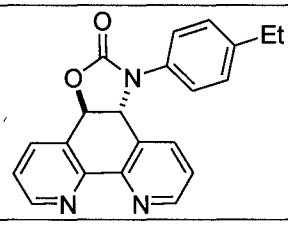
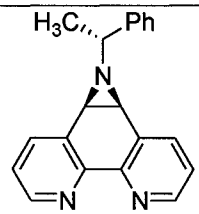
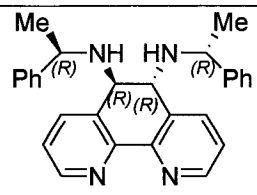
Appendix B

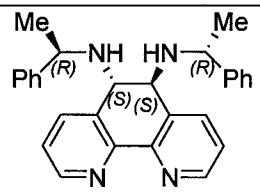
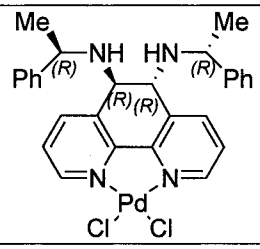
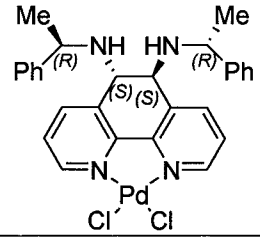
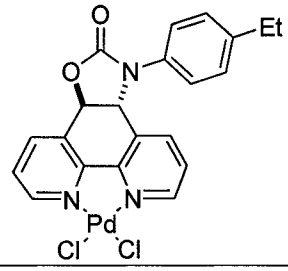
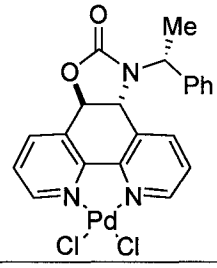
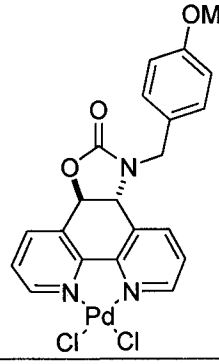
(^{1}H NMR, ^{13}C NMR and IR Spectral)

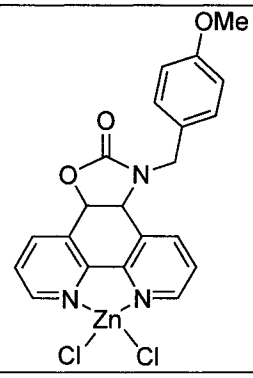
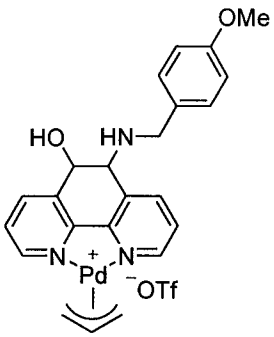
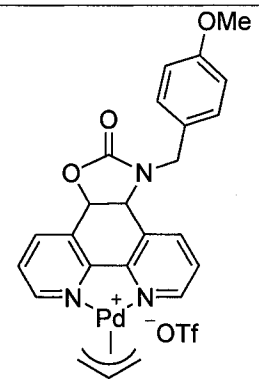
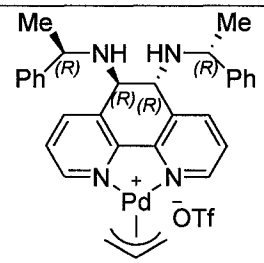
#	Name	Structure	Formular	Mol. Wt.
1	1,10-phenanthroline-5,6-epoxide Phen-epoxide		$C_{12}H_8N_2O$	196.20
2	2,9-dimethyl-1,10-phenanthroline-5,6-epoxide **2,9-Phen-epoxide**		$C_{14}H_{12}N_2O$	224.26
3	trans-5,6-dihydro-6-anilylamino-1,10-phenanthroline-5-ol **anilyl-L**		$C_{18}H_{15}N_3O$	289.33
4	trans-5,6-dihydro-6-benzylamino-1,10-phenanthroline-5-ol **benzyl-L**		$C_{19}H_{17}N_3O$	303.36
5	trans-5,6-dihydro-6-(2-bromo-anilylamino)-1,10-phenanthroline-5-ol **2-Br-anilyl-L**		$C_{18}H_{14}BrN_3O$	368.23
6	trans-5,6-dihydro-6-(2-chloro-anilylamino)-1,10-phenanthroline-5-ol **2-Cl-anilyl-L**		$C_{18}H_{14}ClN_3O$	323.78
7	trans-5,6-dihydro-6-(2-cyano-anilylamino)-1,10-phenanthroline-5-ol **2-CN-anilyl-L**		$C_{19}H_{14}N_4O$	314.34

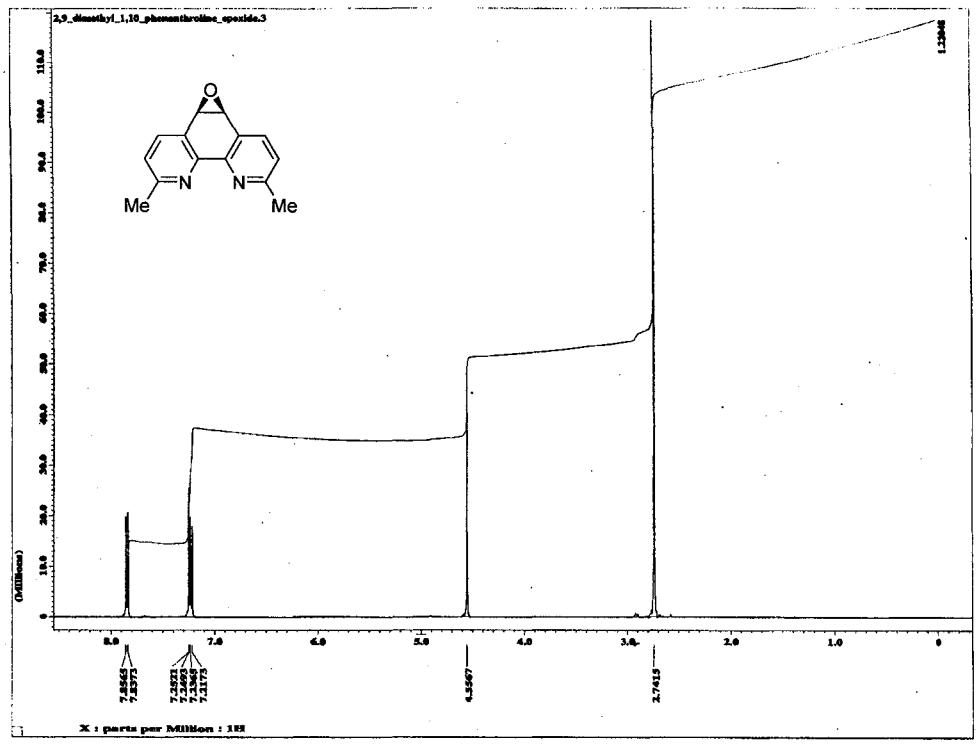
8	trans-5,6-dihydro-6-(2-ethyl-anilylamino)-1,10-phenanthroline-5-ol **2-Et-anilyl-L**		$C_{20}H_{19}N_3O$	317.38
9	trans-5,6-dihydro-6-(4-ethyl-anilylamino)-1,10-phenanthroline-5-ol **4-Et-anilyl-L**		$C_{20}H_{19}N_3O$	317.38
10	trans-5,6-dihydro-6-azido-1,10-phenanthroline-5-ol **azido alc.**		$C_{12}H_9N_5O$	239.23
11	5,6-dihydro-6-(pyridin-2-ylamino)-1,10-phenanthrolin-5-ol FSL		$C_{17}H_{14}N_4O$	290.32
12	6-(4-methoxybenzylamino)-5,6-dihydro-2,9-dimethyl-1,10-phenanthrolin-5-ol **2,9-diMe-(4-MeO-benzyl)-L**		$C_{22}H_{23}N_3O_2$	361.44
13	trans-6-(4-Methoxy-benzylamino)-5,6-dihydro-1,10-phenanthroline-5-ol **(+)-4-MeO-benzyl-L**		$C_{22}H_{21}NO_2$	331.41

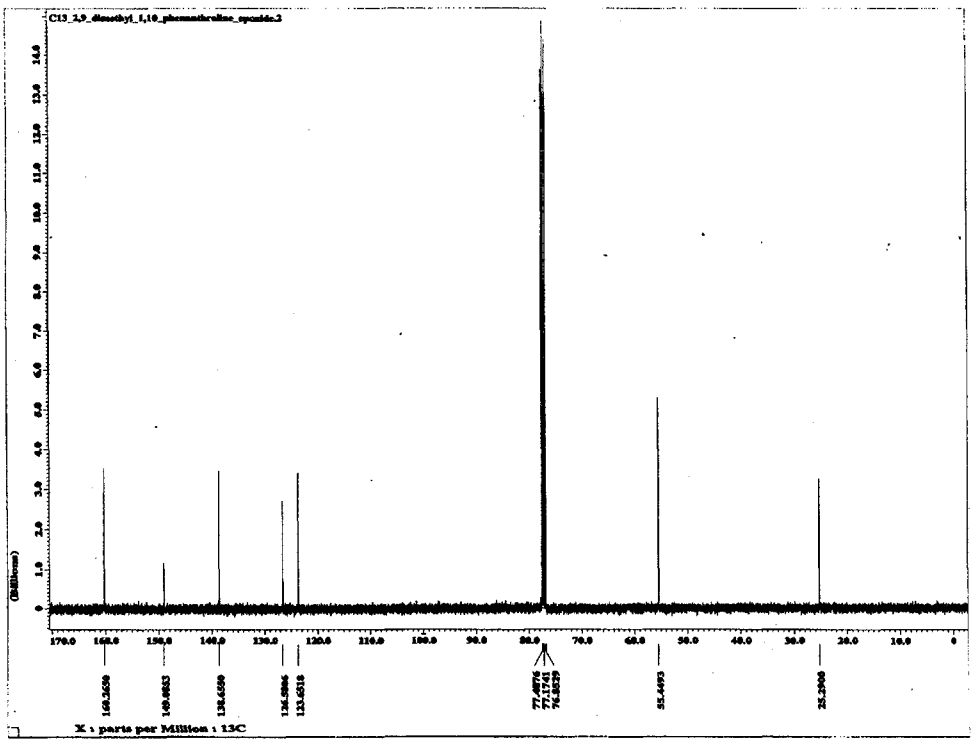
14	trans-6-(4-Methoxy-benzylamino)-5,6-dihydro-1,10-phenanthroline-5-ol **(-)-4-MeO-benzyl-L**		$C_{22}H_{21}NO_2$	331.41
15	trans-(5R,6R)-6-((R)-1-phenylethylamino-5,6-dihydro-1,10-phenanthroline-5-ol **(R,R)-α(+)-L**		$C_{20}H_{19}N_3O$	317.38
16	trans-(5S,6S)-6-((R)-1-phenylethylamino-5,6-dihydro-1,10-phenanthroline-5-ol **(S,S)-α(+)-L**		$C_{20}H_{19}N_3O$	317.38
17	6-((R)-1-phenylethylamino)-5,6-dihydro-2,9-dimethyl-1,10-phenanthrolin-5-ol **2,9-diMe-α(+)-L**		$C_{22}H_{23}N_3O$	345.44
18	(3aS,11bS)-3,3a-dihydro-3-((R)-1-phenylethyl)oxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one **(S,S)-oxa-α(+)**		$C_{21}H_{17}N_3O_2$	343.38
19	(3aR,11bR)-3,3a-dihydro-3-((R)-1-phenylethyl)oxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one **(R,R)-oxa-α(+)**		$C_{21}H_{17}N_3O_2$	343.38

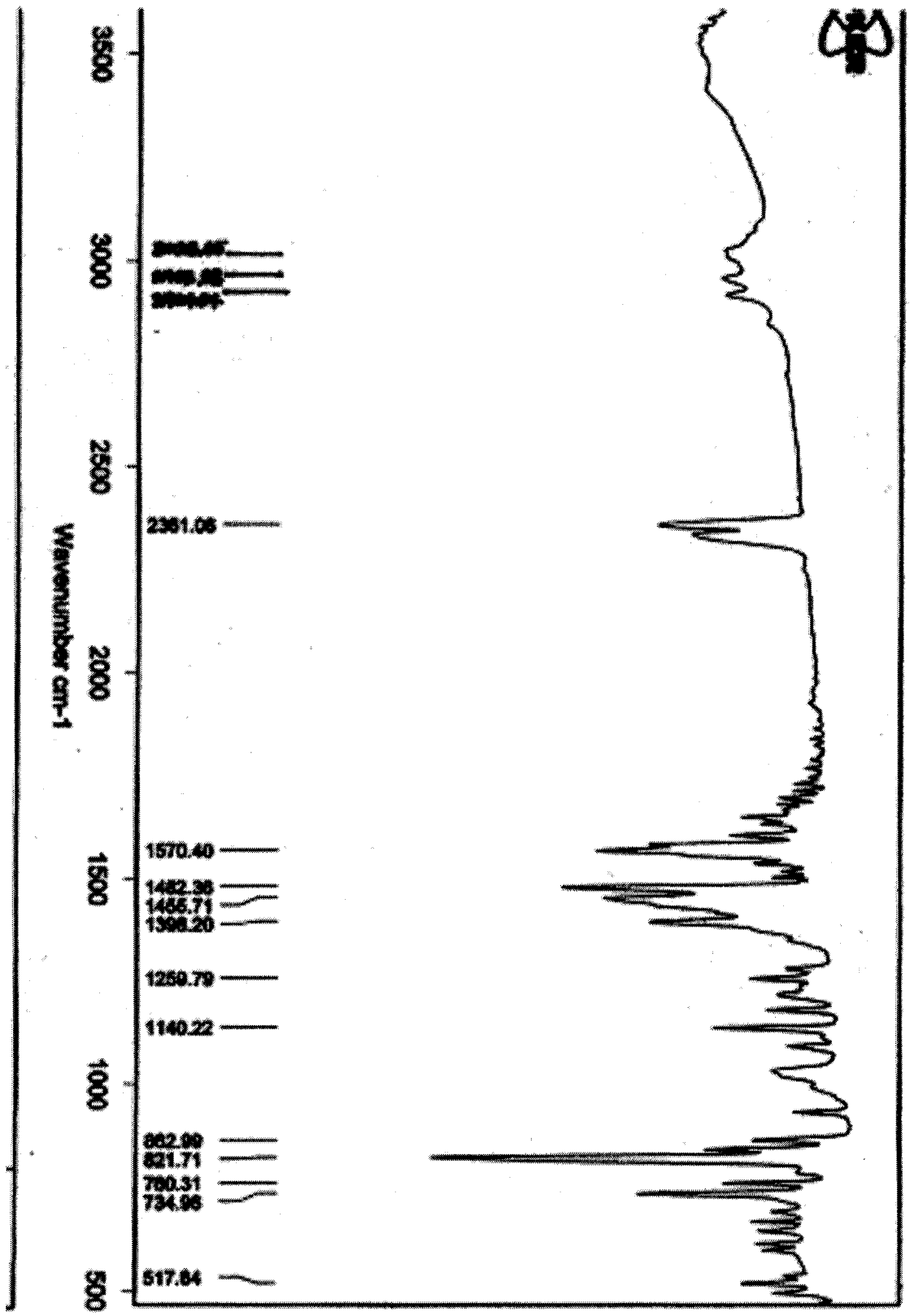
20	3-(4-methoxybenzyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one **(+)-oxa-4-MeO**		$C_{21}H_{17}N_3O_3$	359.38
21	3-(4-methoxybenzyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one **(-)-oxa-4-MeO**		$C_{21}H_{17}N_3O_3$	359.38
22	(3aR,11bR)-3-benzyl-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one oxa-benzyl		$C_{20}H_{15}N_3O_2$	329.35
23	3-(4-ethylphenyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one **oxa-4-Et-anilyl**		$C_{21}H_{17}N_3O_2$	343.38
24	(1aS,9bR)-1a,9b-dihydro-1-((R)-1-phenylethyl)-1H-azirino[2,3-f][1,10]phenanthrol-ine **α(+)-aziridine**		$C_{20}H_{17}N_3$	299.37
25	(5R,6R)-5,6-dihydro-N5,N6-bis((R)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine **C_2 (RRRR)**		$C_{28}H_{28}N_4$	420.55

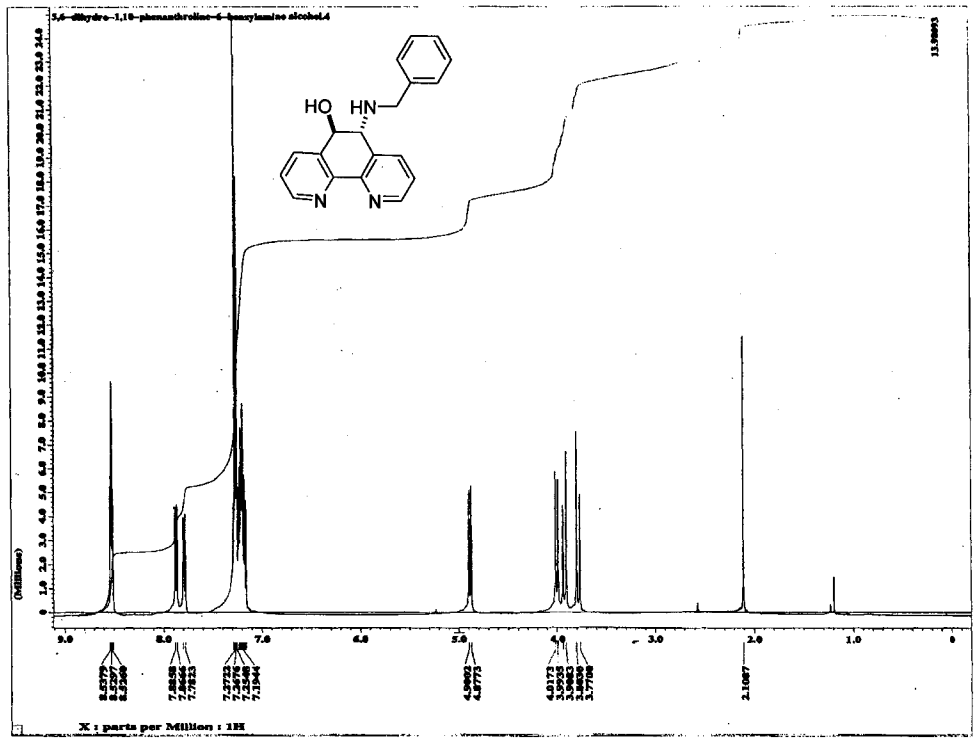
26	(5S,6S)-5,6-dihydro-N5,N6-bis((R)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine **C_2 (RSSR)**		$C_{28}H_{28}N_4$	420.55
27	(5R,6R)-5,6-dihydro-N5,N6-bis((R)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine-$PdCl_2$ complex **C_2 (RRRR)-$PdCl_2$**		$C_{28}H_{28}Cl_2N_4P$	597.87
28	(5S,6S)-5,6-dihydro-N5,N6-bis((R)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine-$PdCl_2$ complex **C_2 (RSSR)-$PdCl_2$**		$C_{28}H_{28}Cl_2N_4P$	597.87
29	3-(4-ethylphenyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one $PdCl_2$ complex **oxa-4-Et-anilyl-$PdCl_2$**		$C_{21}H_{17}Cl_2N_3O_2Pd$	520.70
30	3,3a-dihydro-3-((R)-1-phenylethyl)oxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one-$PdCl_2$ complex **oxa-α(+)-$PdCl_2$**		$C_{21}H_{17}Cl_2N_3O_2Pd$	520.7
31	3-(4-methoxybenzyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one Pd complex **oxa-4-MeO-$PdCl_2$**		$C_{21}H_{17}Cl_2N_3O_3Pd$	536.70

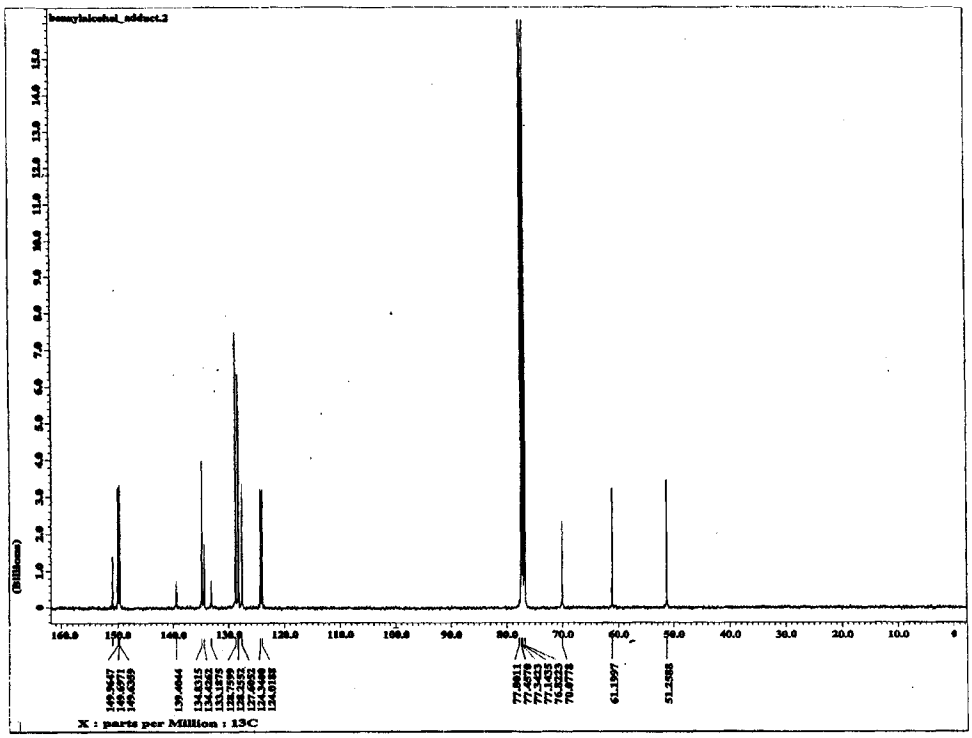
32	3-(4-methoxybenzyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one-Zn complex **oxa-4-MeO-ZnCl$_2$**		$C_{21}H_{17}Cl_2N_3O_3Zn$	495.67
33	5,6-dihydro-6-(4-methoxybenzylamino)-1,10-phenanthrolin-5-ol (1,3-η3-propenyl)Pd trifluoromethanesulfonate complex **4-MeO-benzyl-Pd-OTf**		$C_{25}H_{30}F_3N_3O_5PdS^-$	648.00
34	3-(4-methoxybenzyl)-3,3a-dihydrooxazolo[5,4-f][1,10]phenanthrolin-2(11bH)-one- (1,3-η3-propenyl)Pd trifluoromethanesulfonate complex **oxa-4-MeO-Pd-OTf**		$C_{26}H_{28}F_3N_3O_6PdS$	674.00
35	(5R,6R)-5,6-dihydro-N5,N6-bis((R)-1-phenylethyl)-1,10-phenanthroline-5,6-diamine-(1,3-η3-propenyl)Pd trifluoromethanesulfonate complex **C_2 (RRRR)-Pd-OTf**		$C_{33}H_{39}F_3N_4O_3PdS^+$	735.17

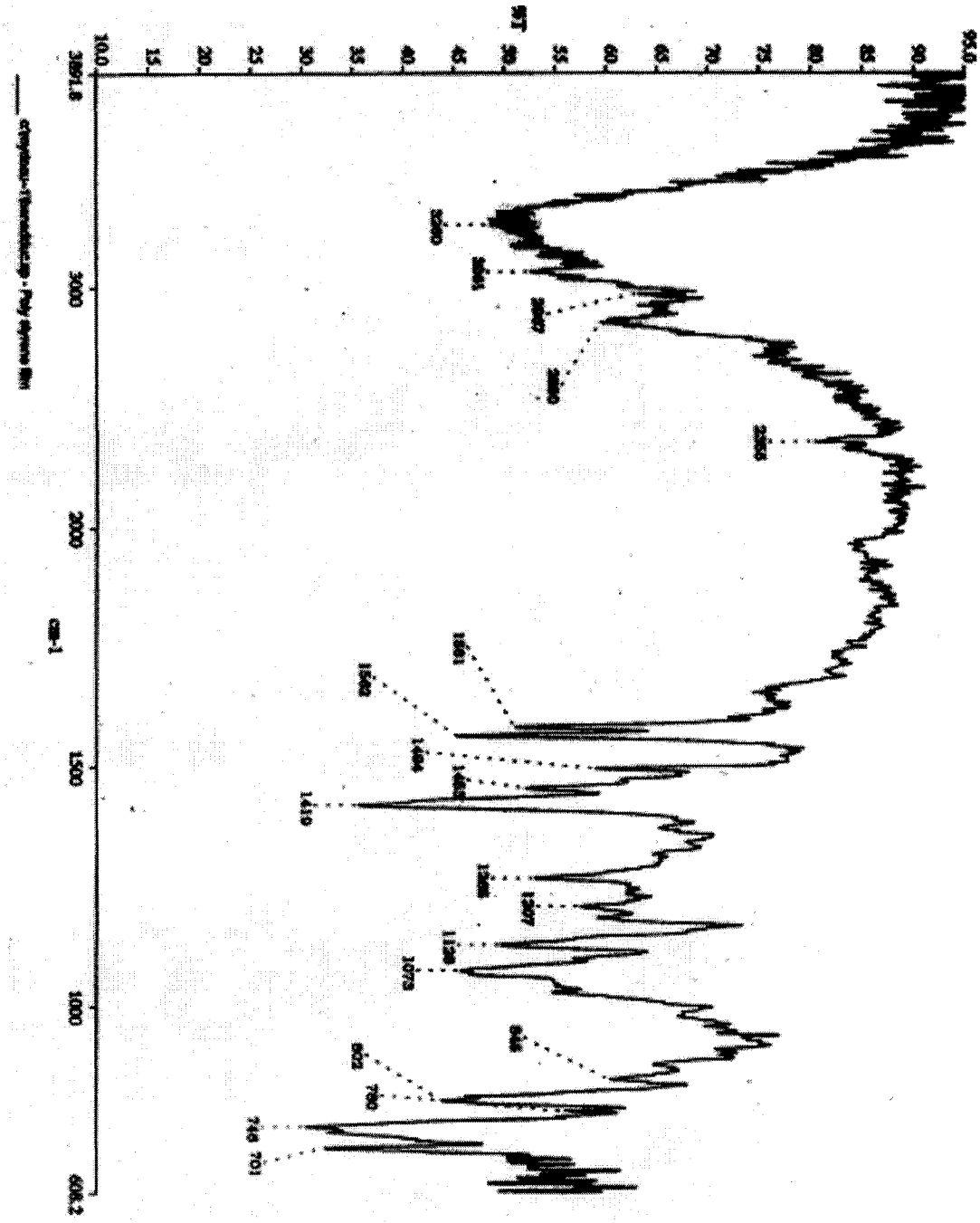


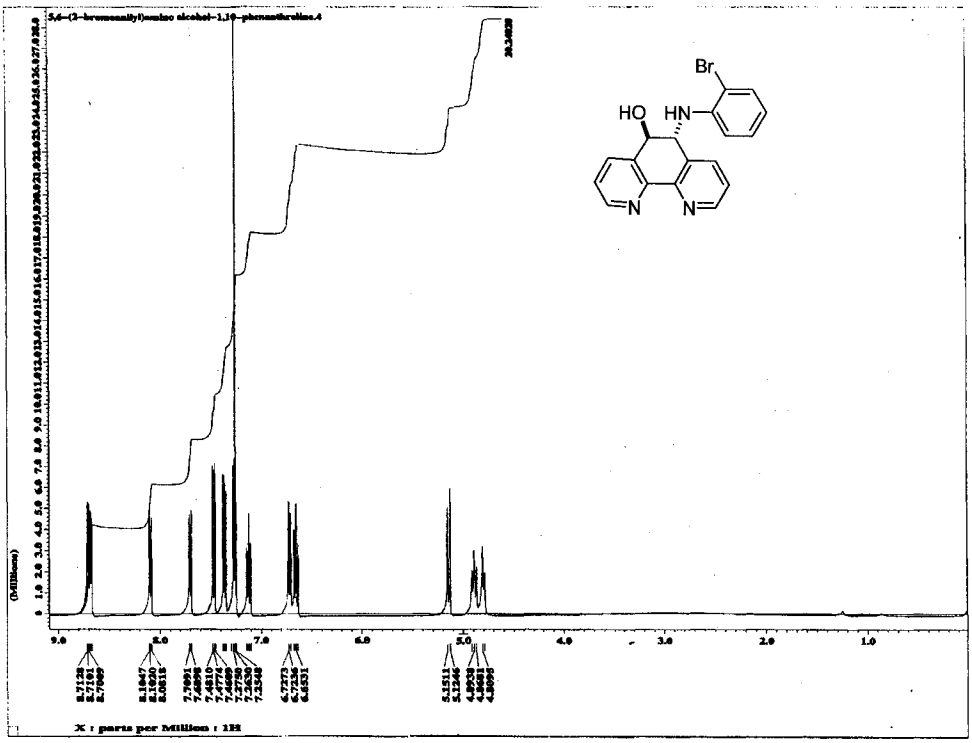


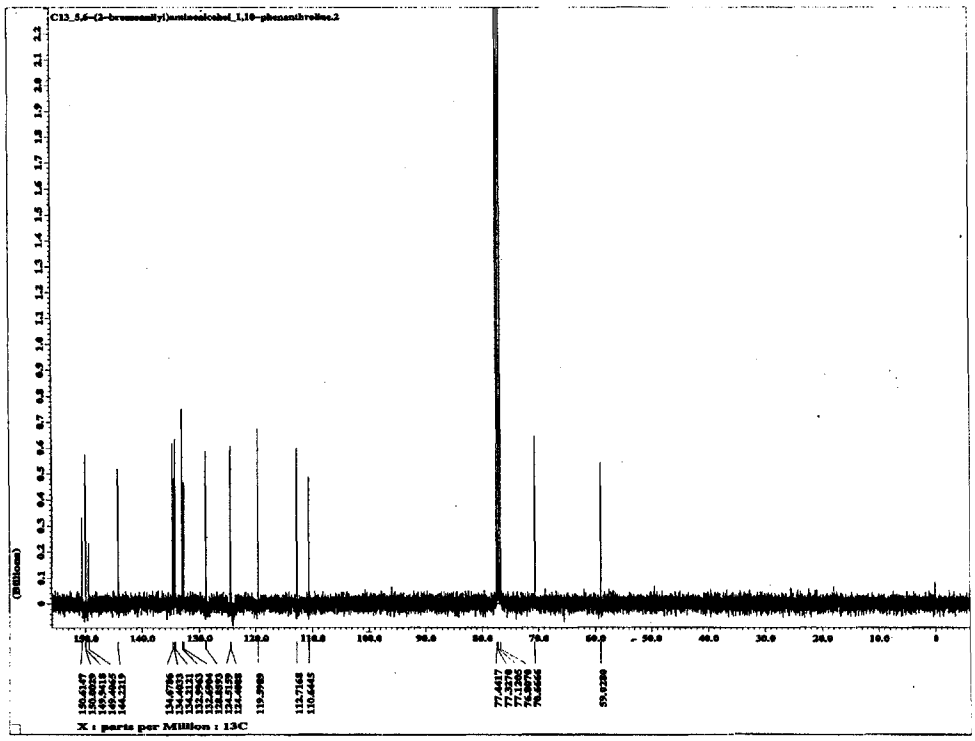


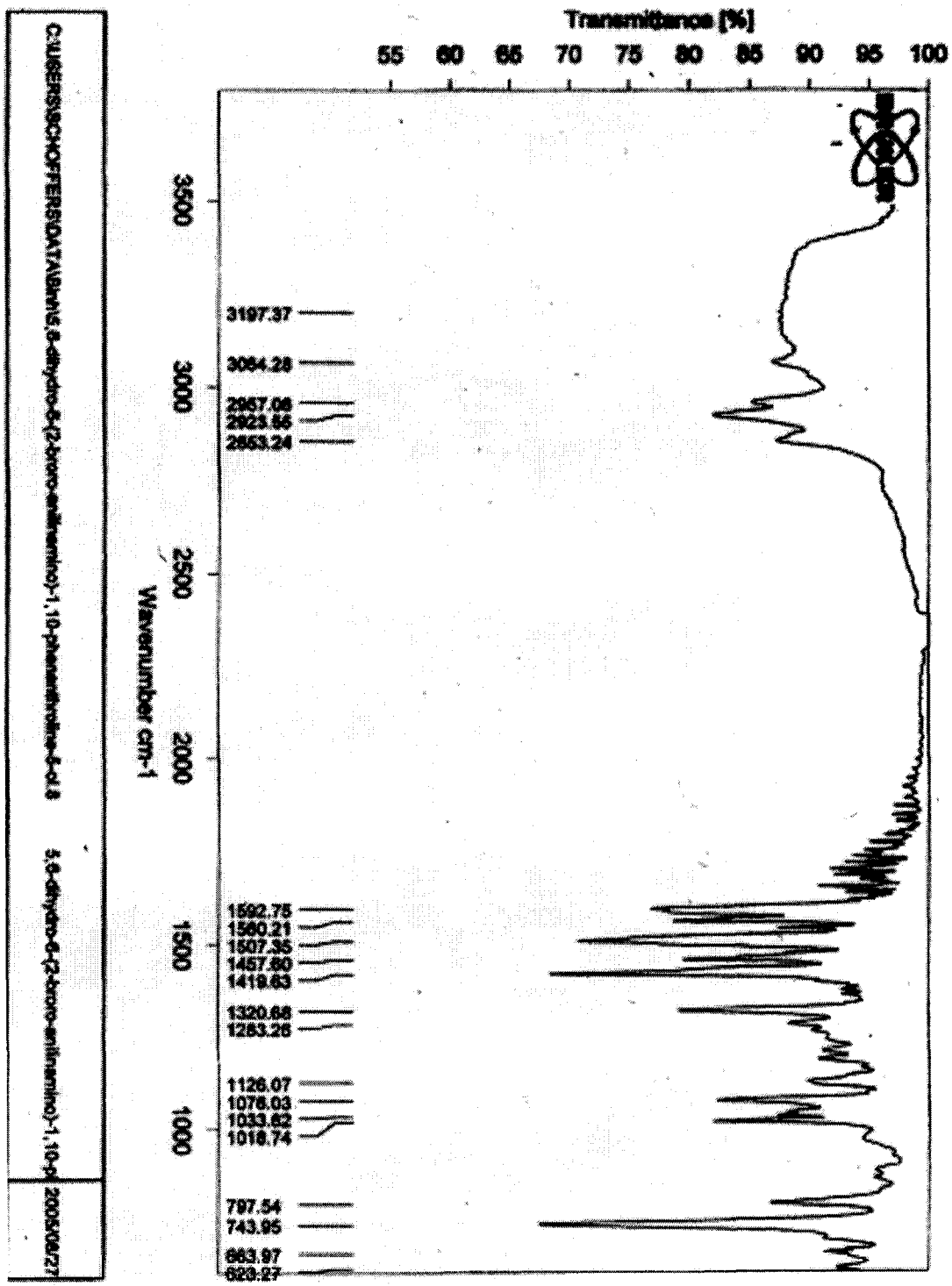


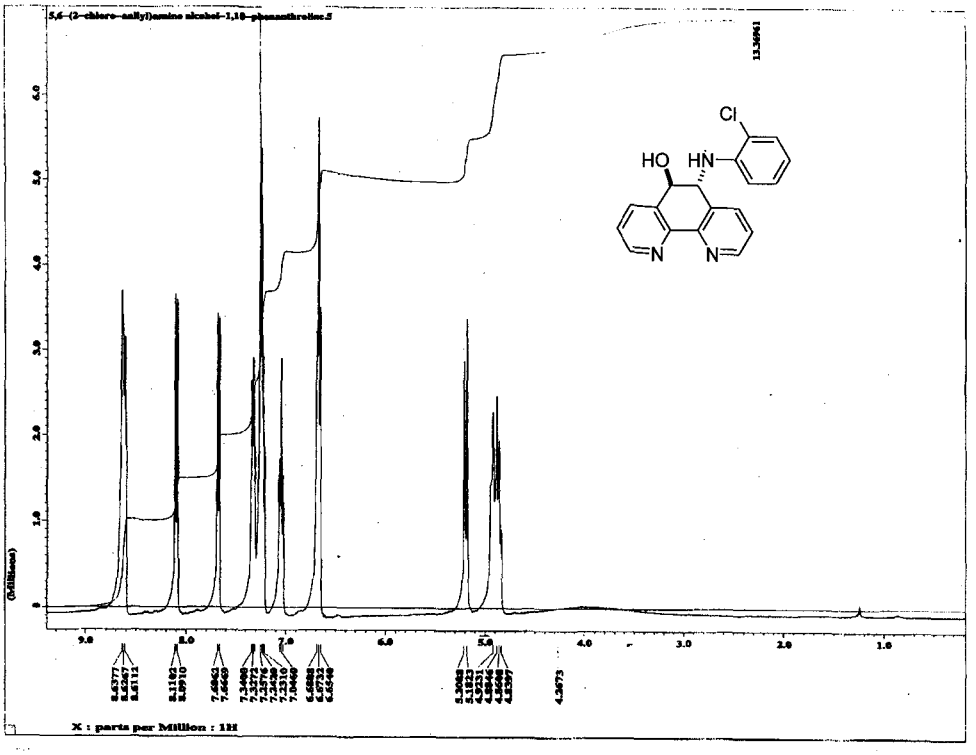


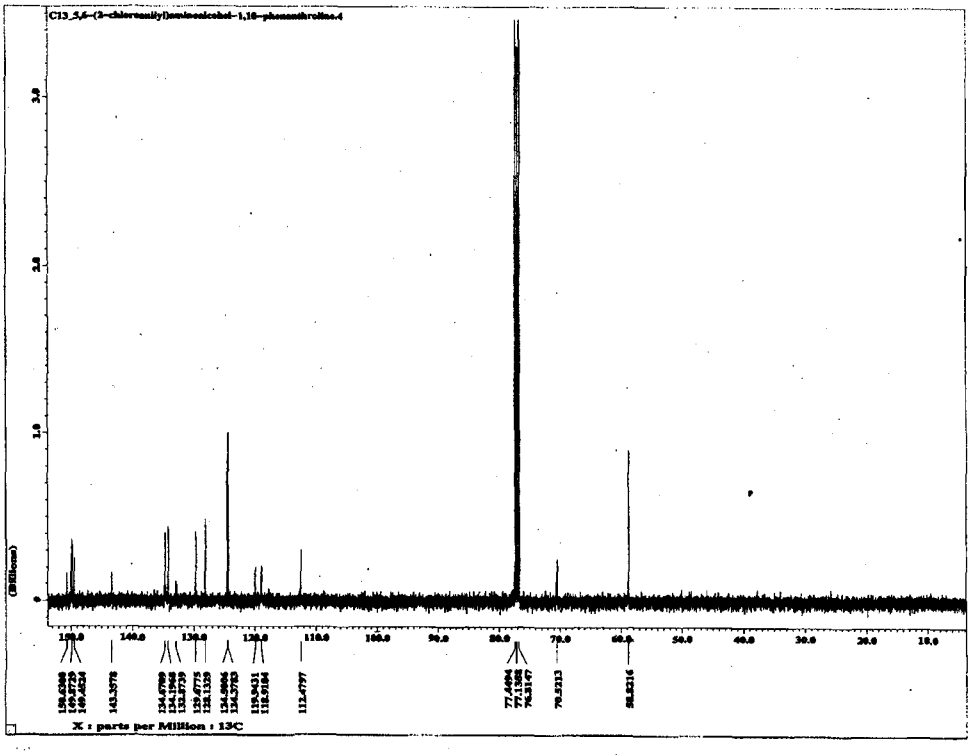


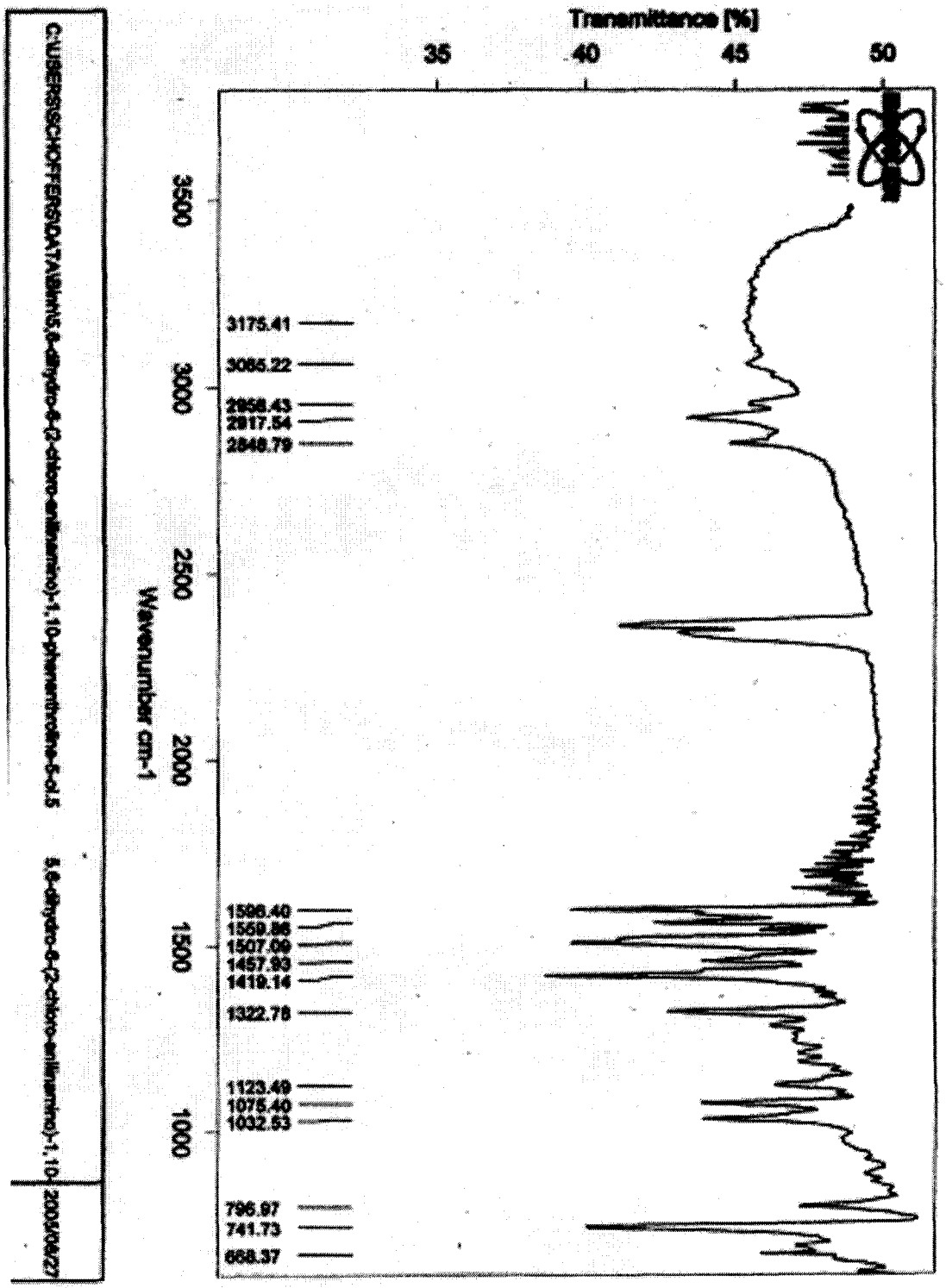


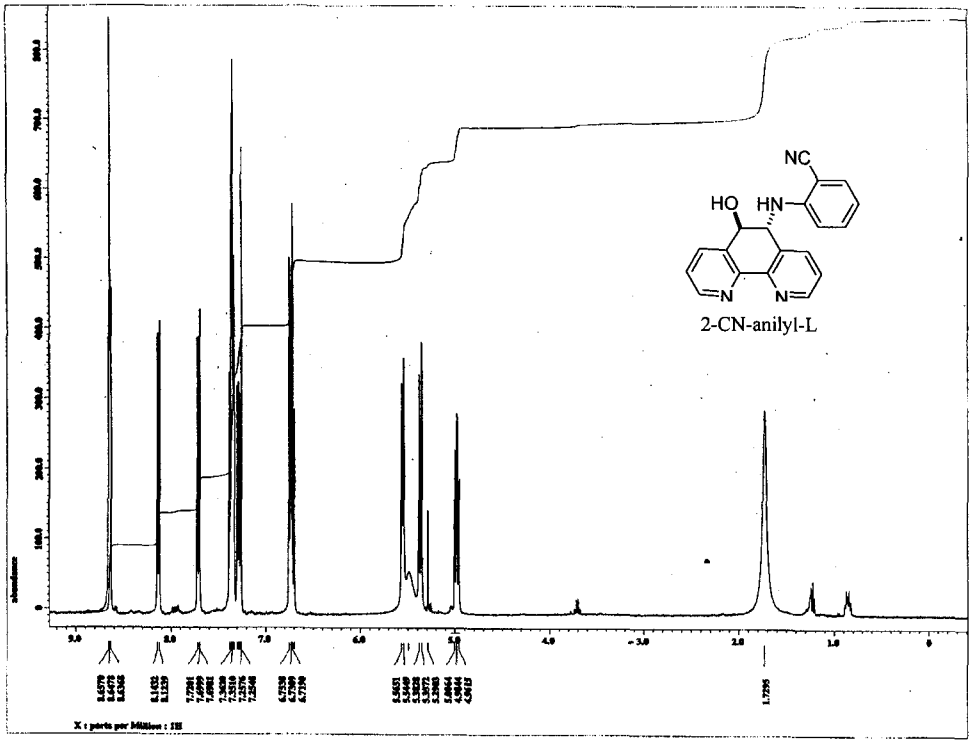












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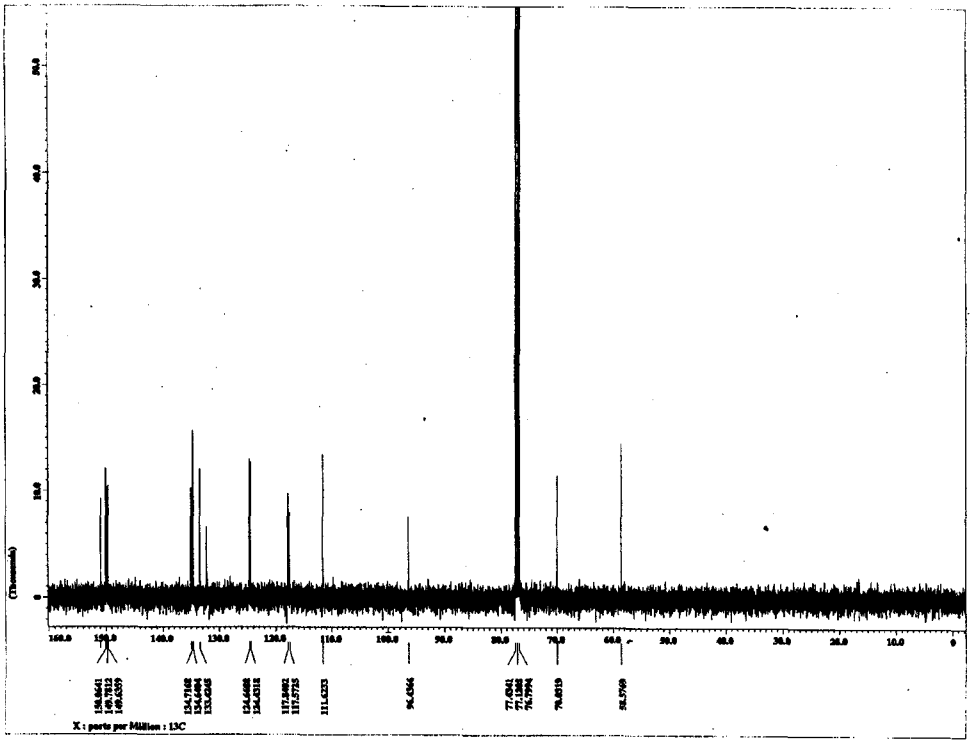

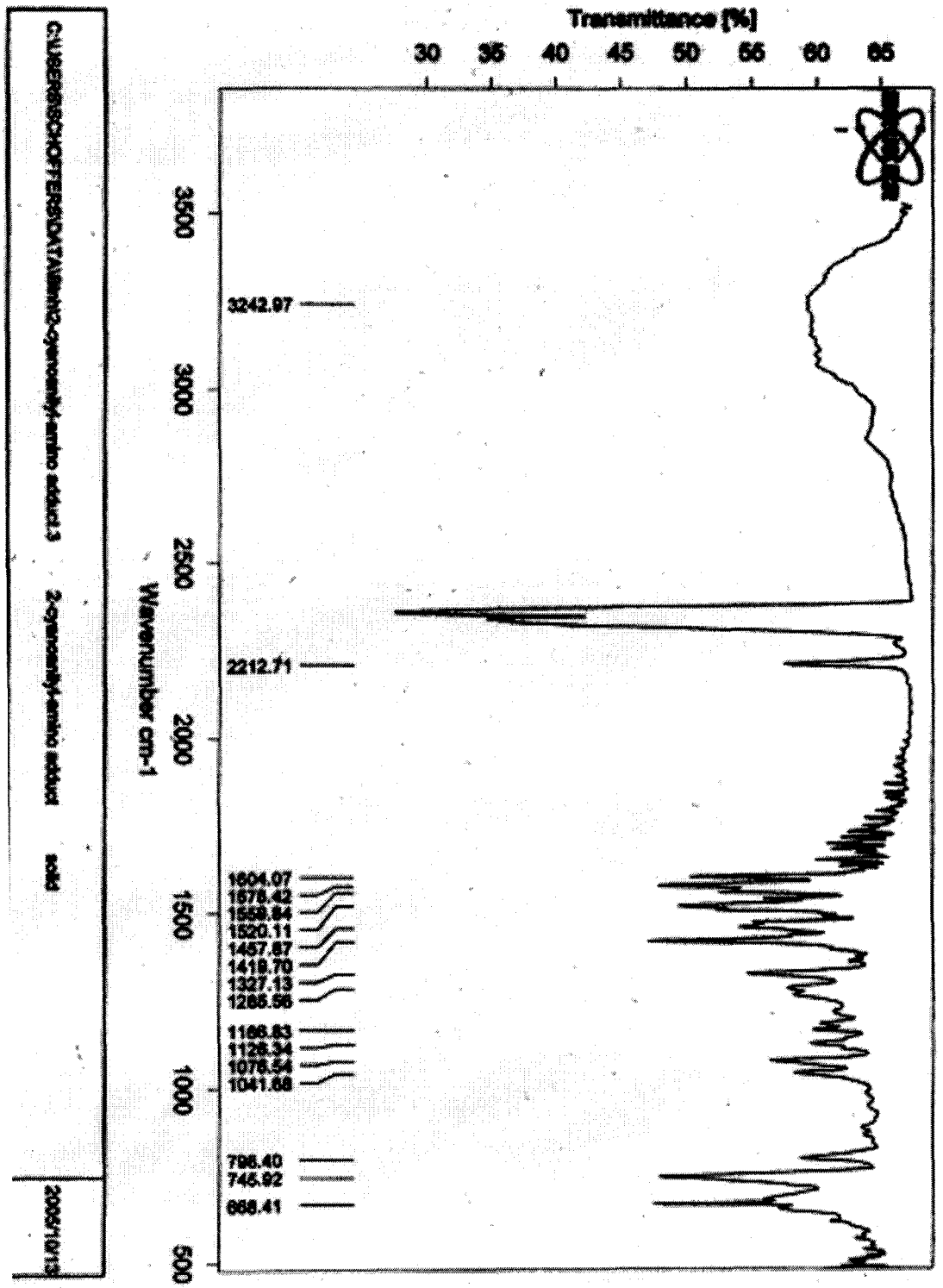

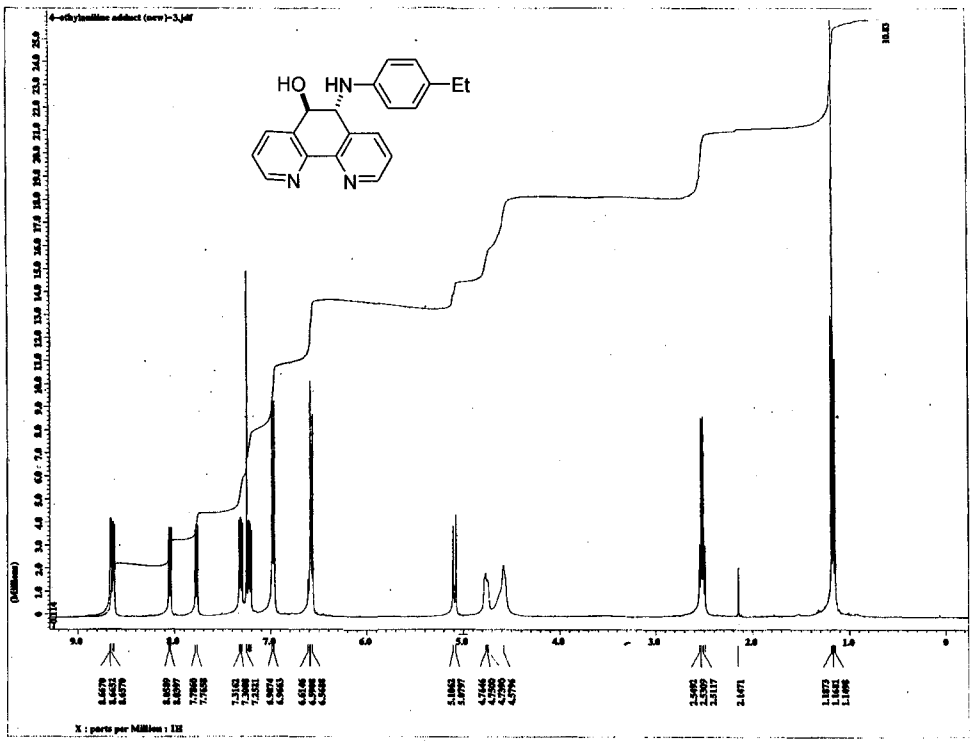

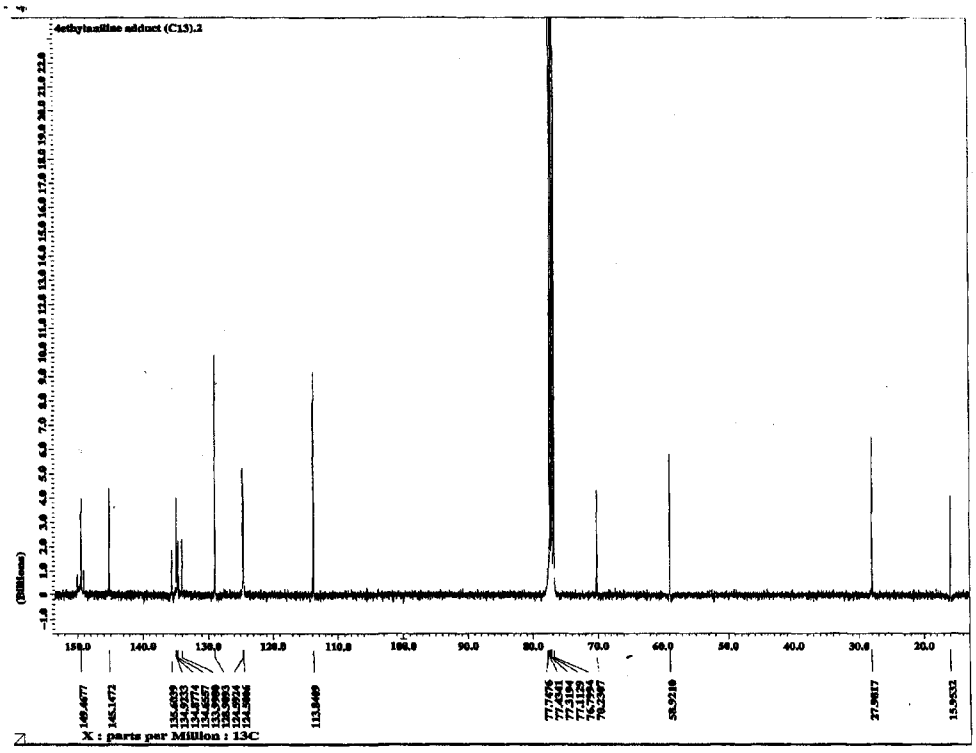

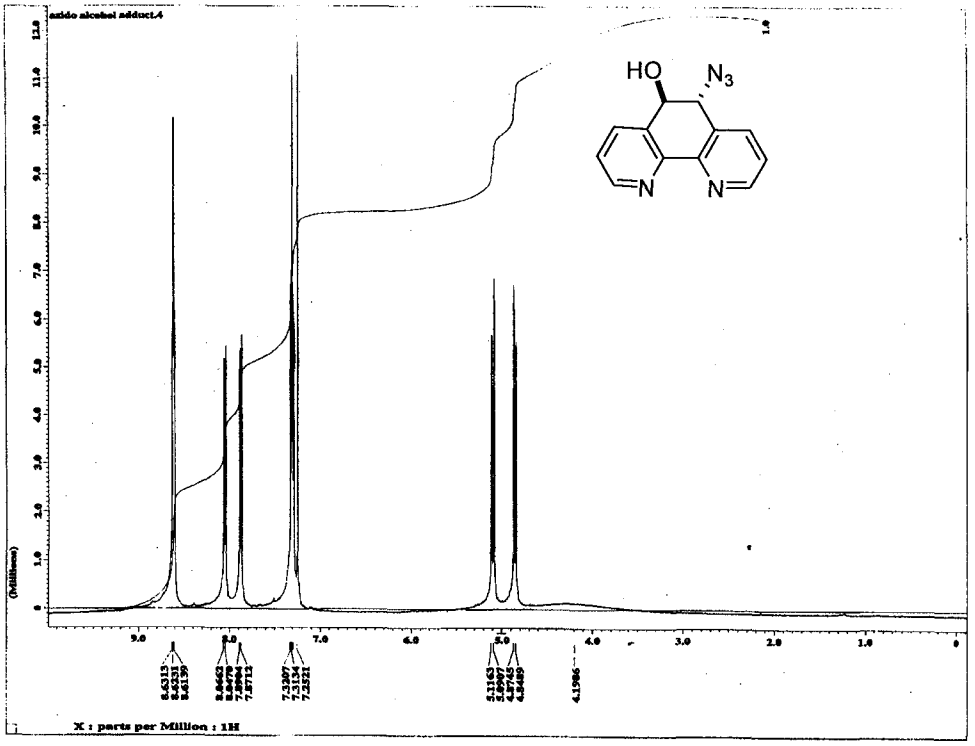

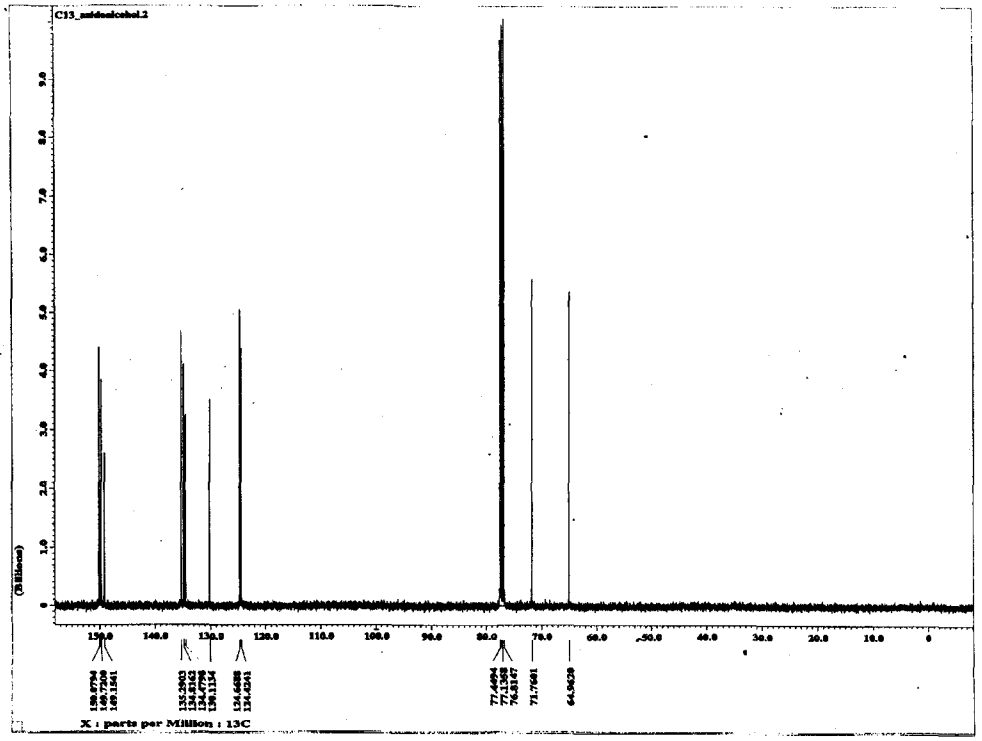

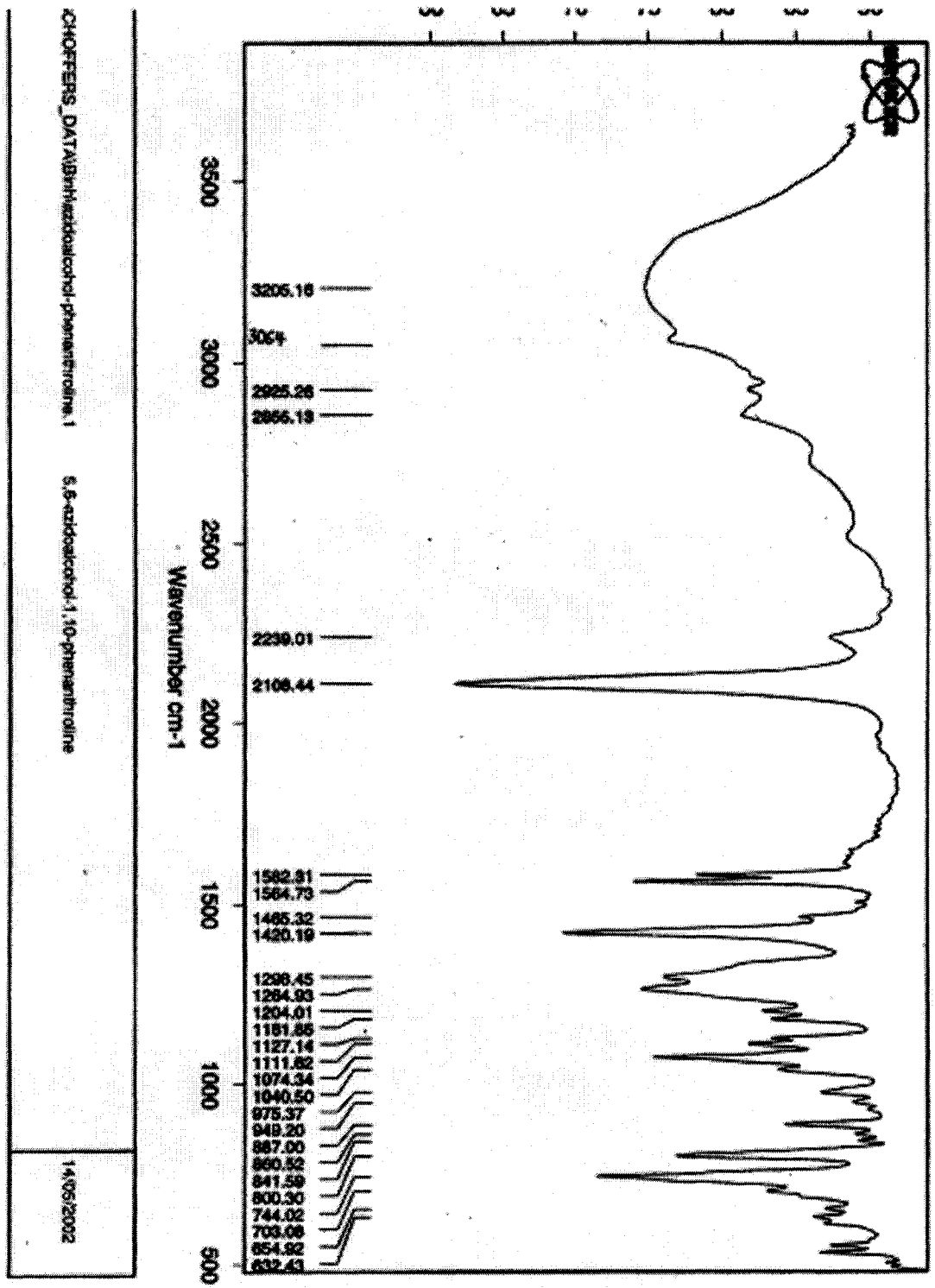

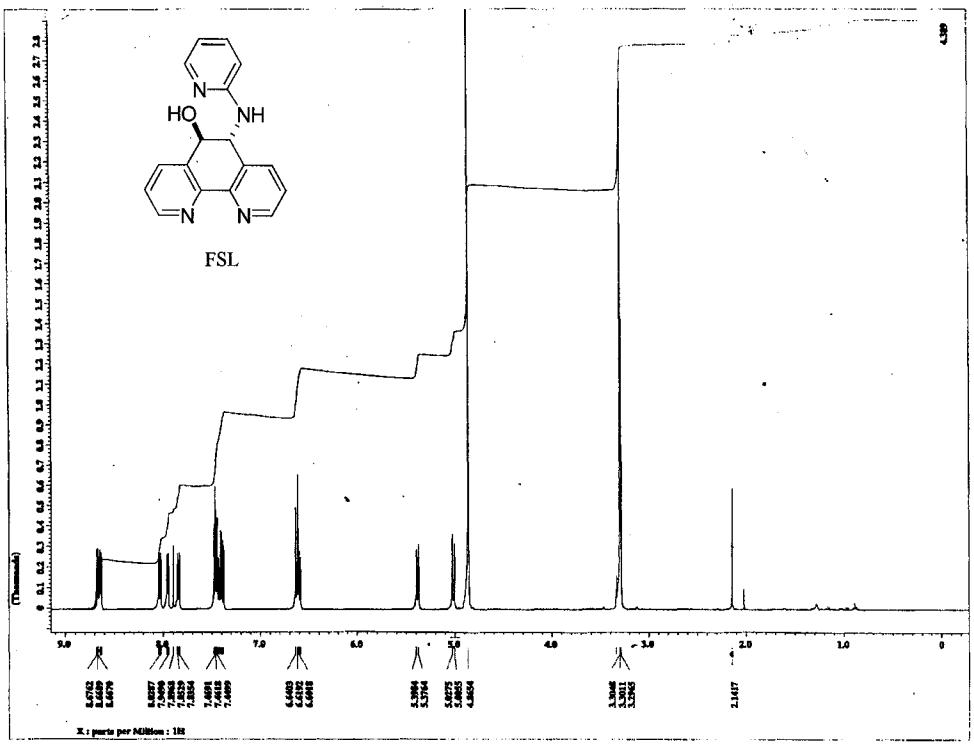

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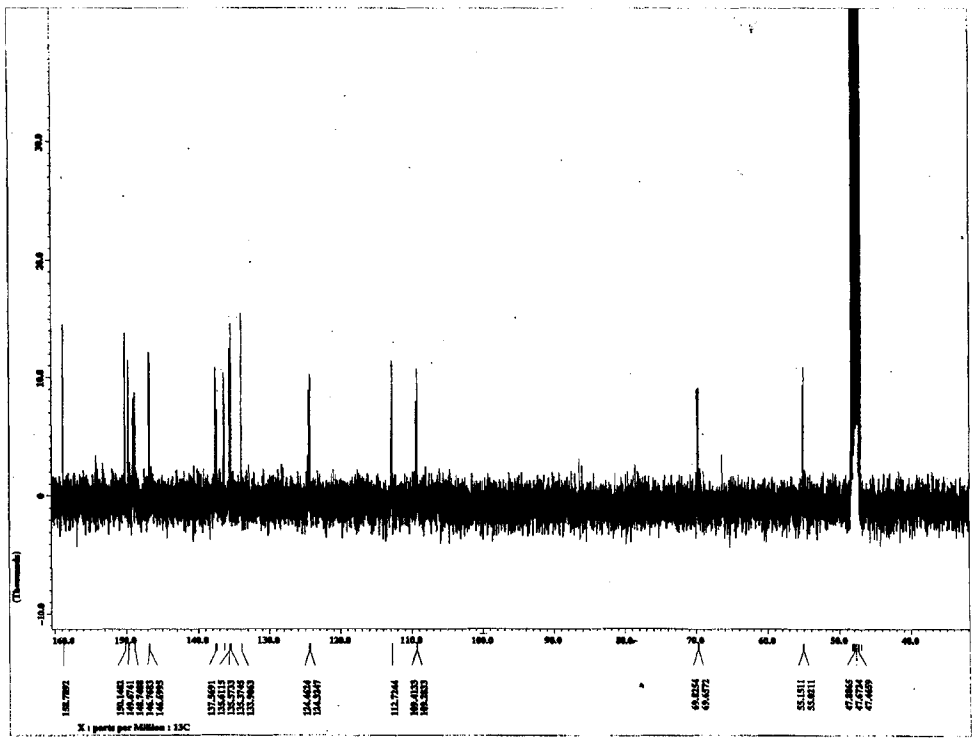
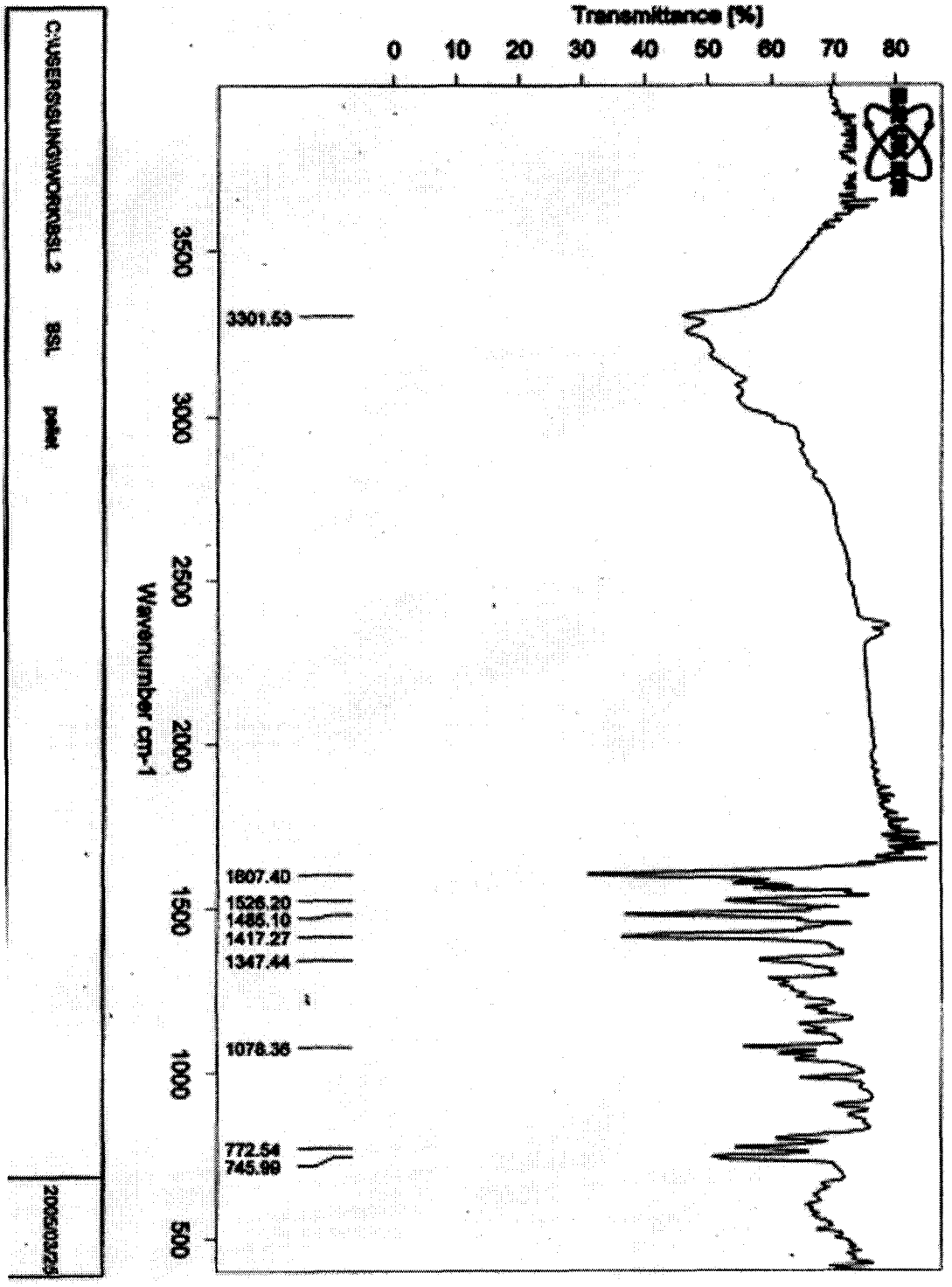
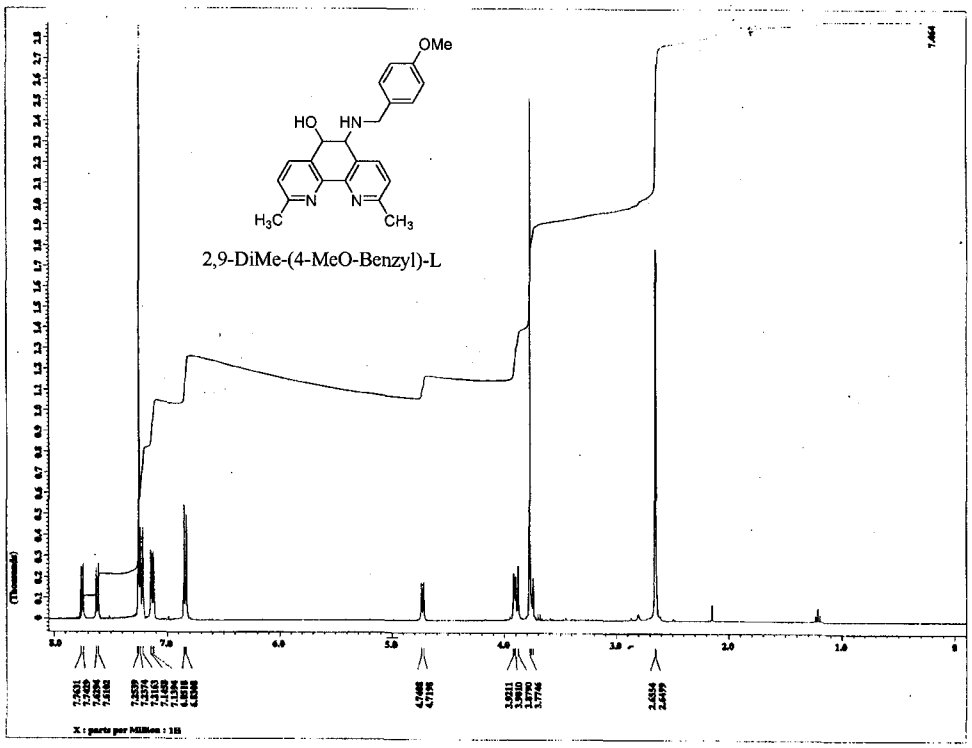
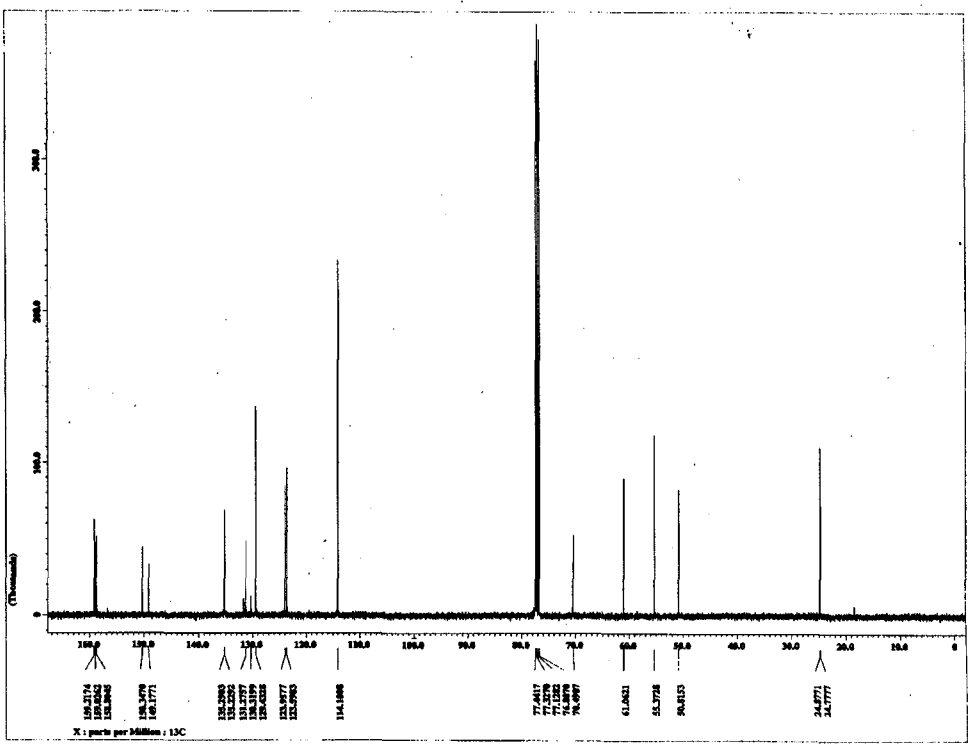
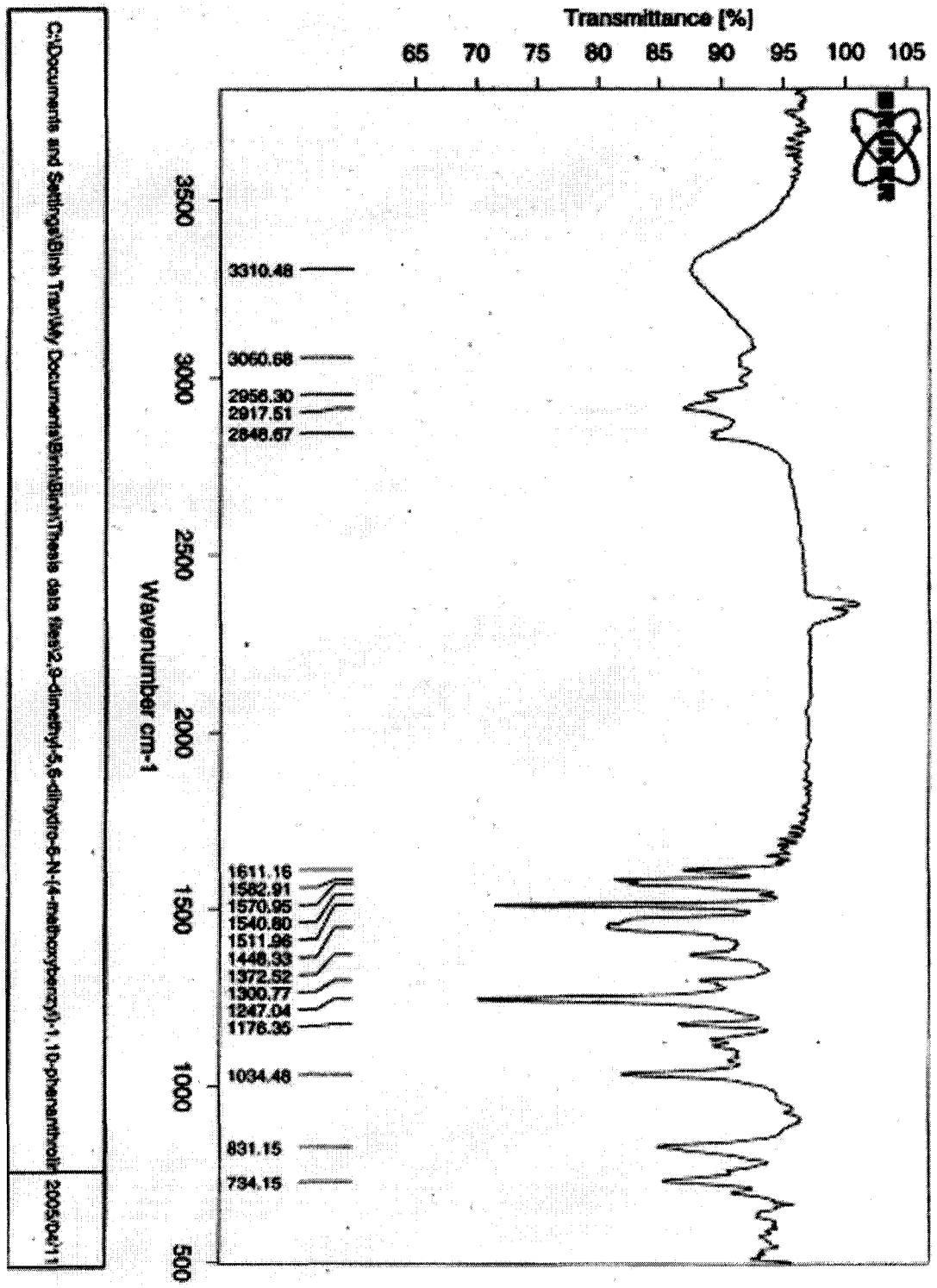


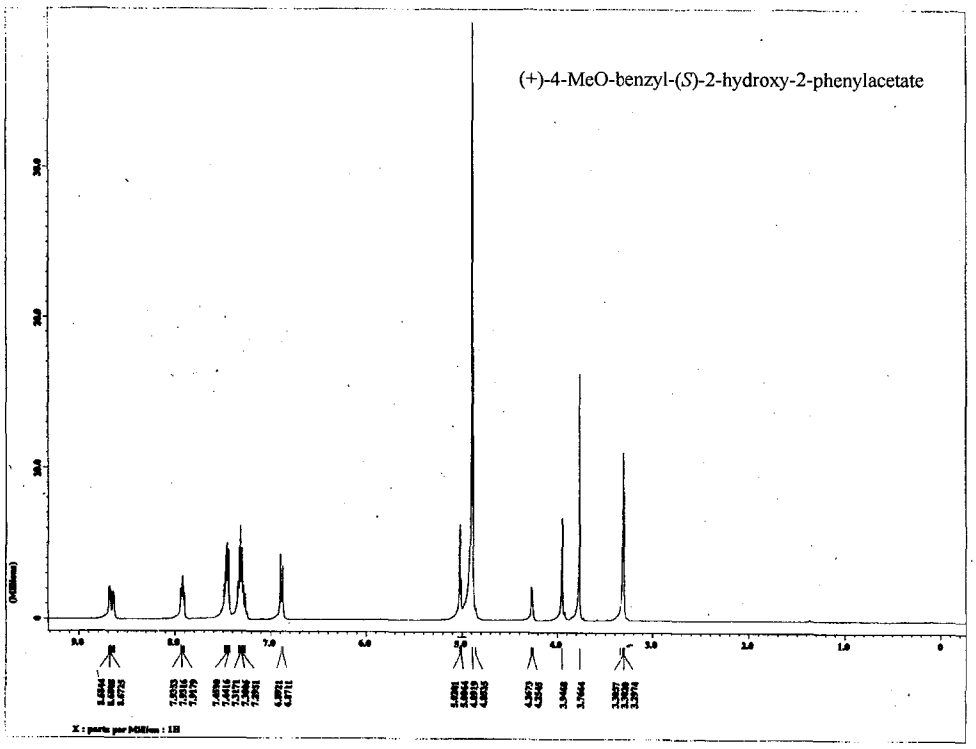


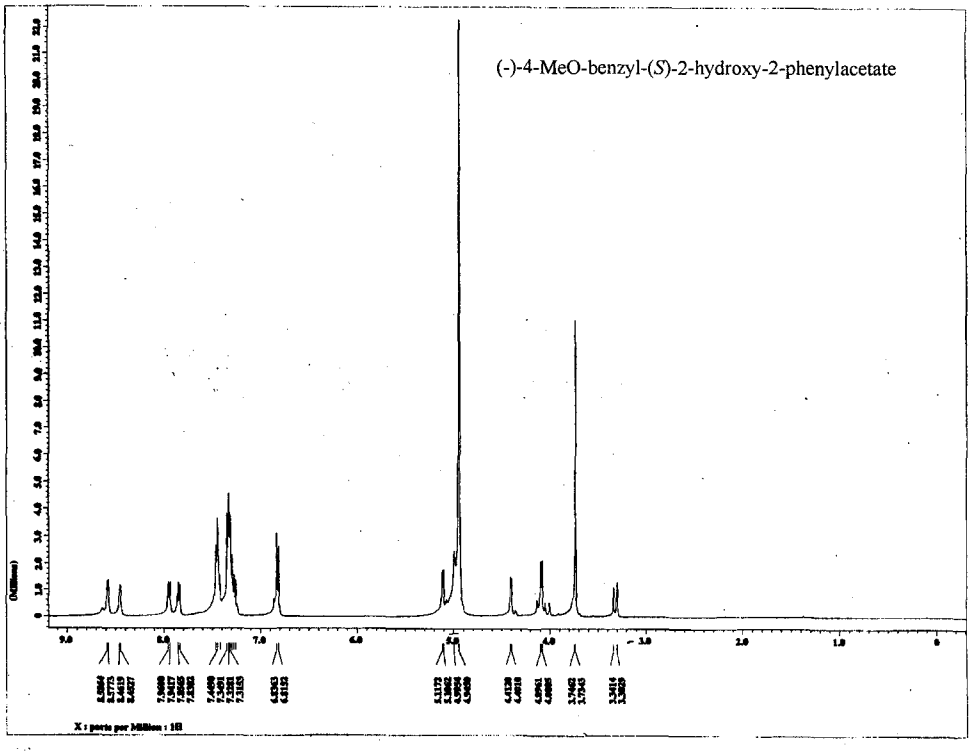


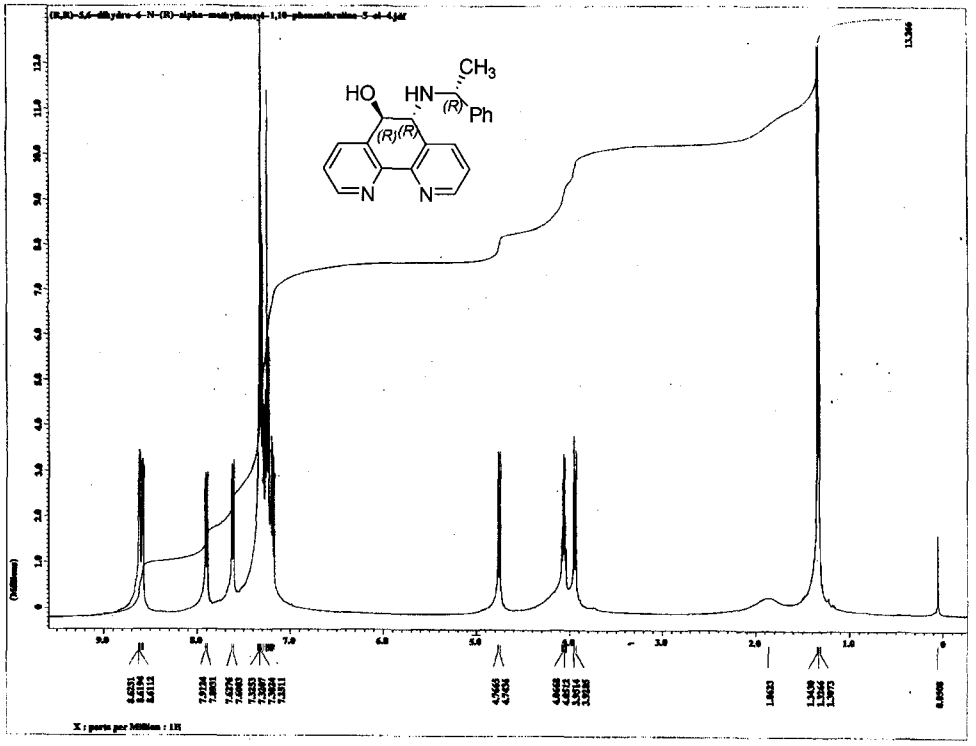
2,9-DiMe-(4-MeO-Benzyl)-L

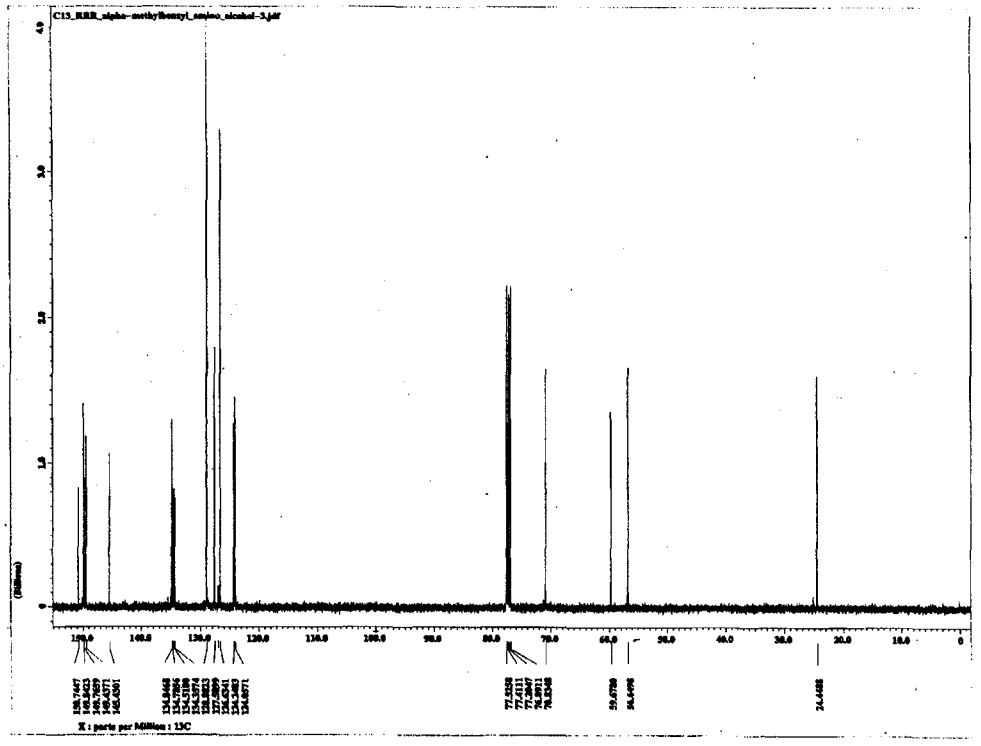


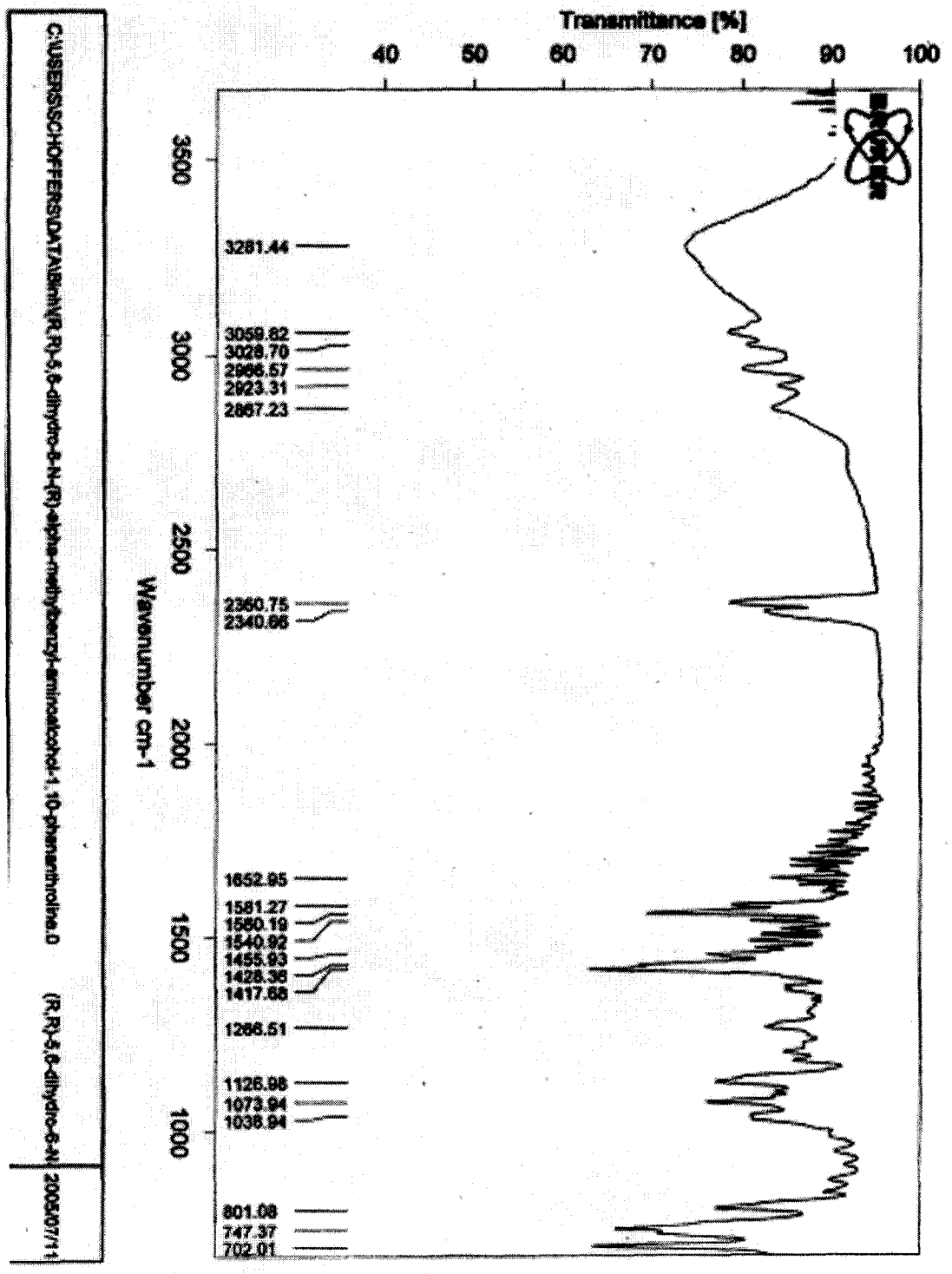


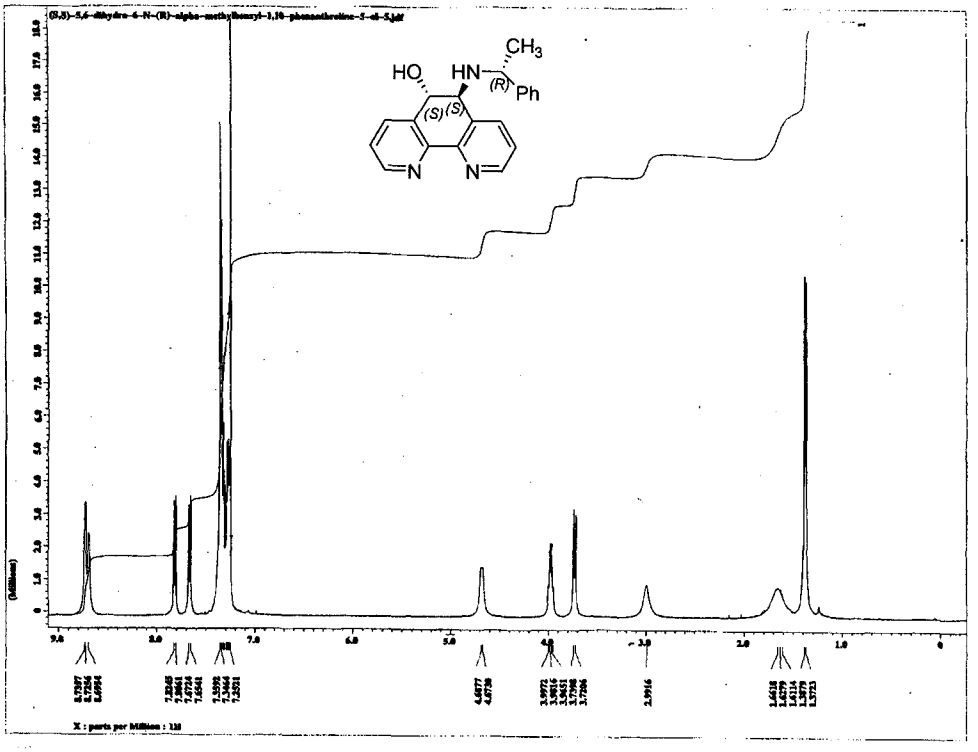


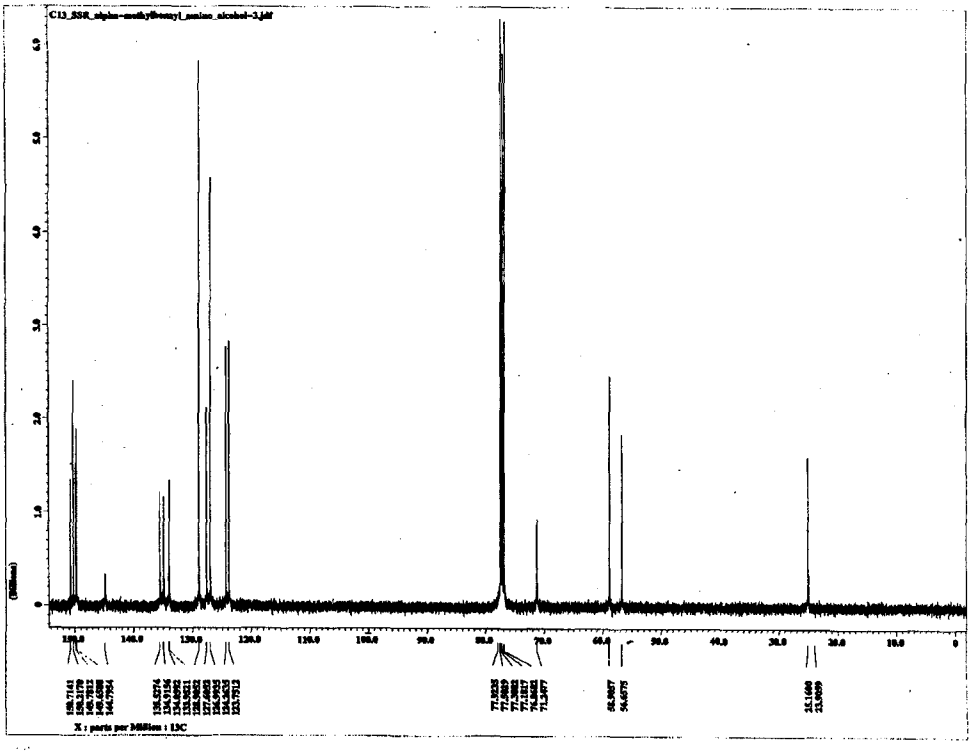


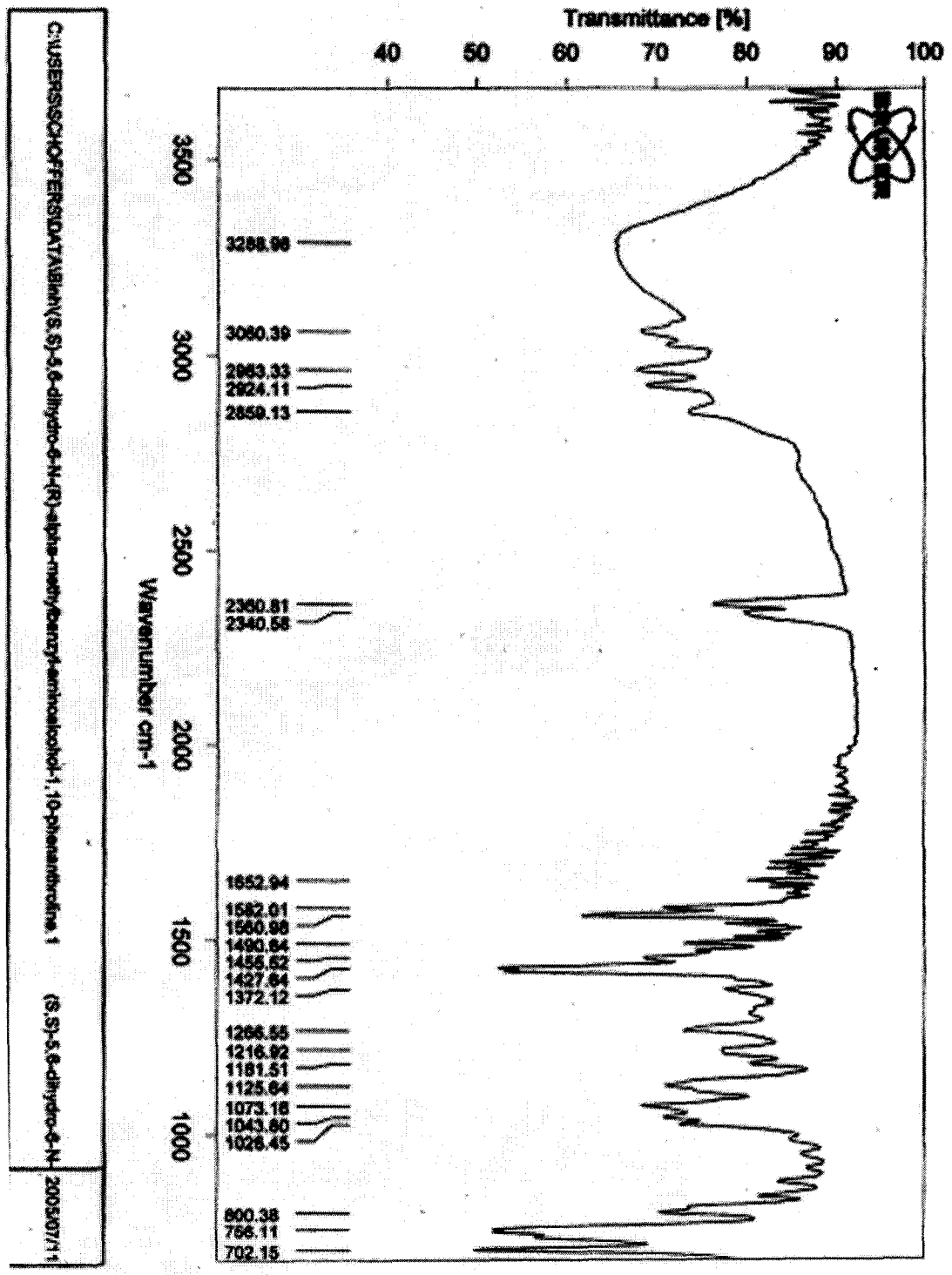


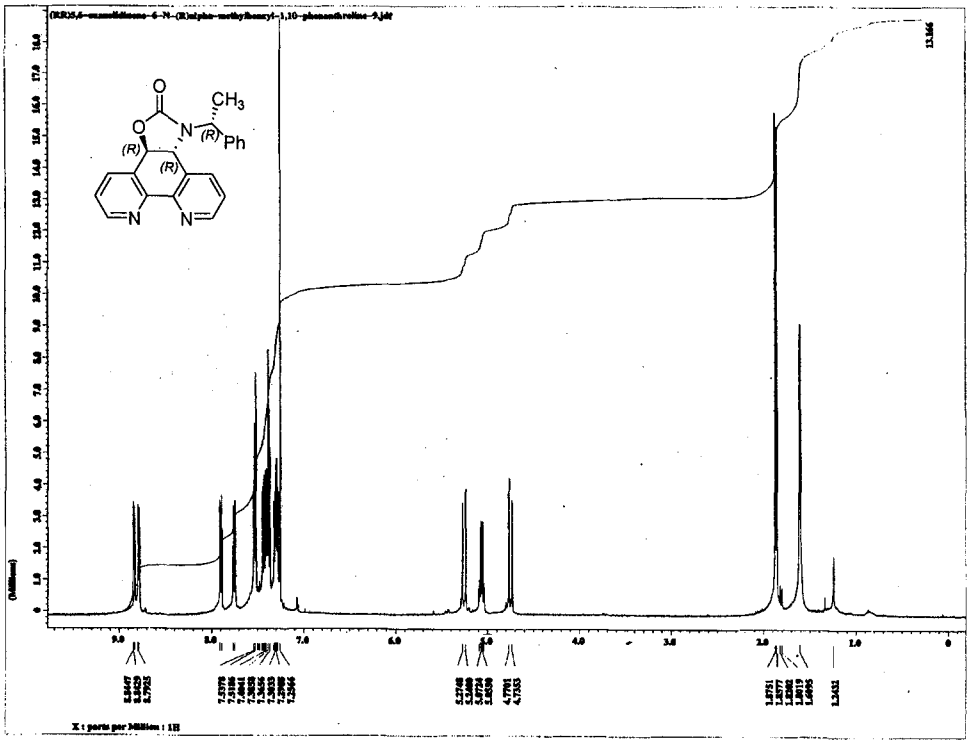


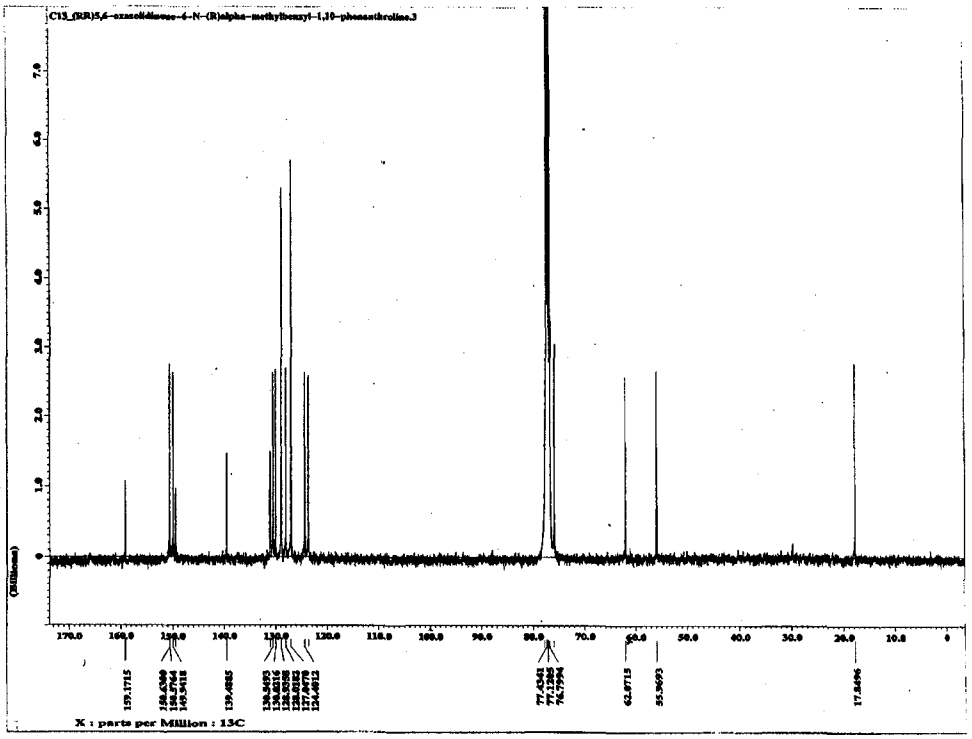


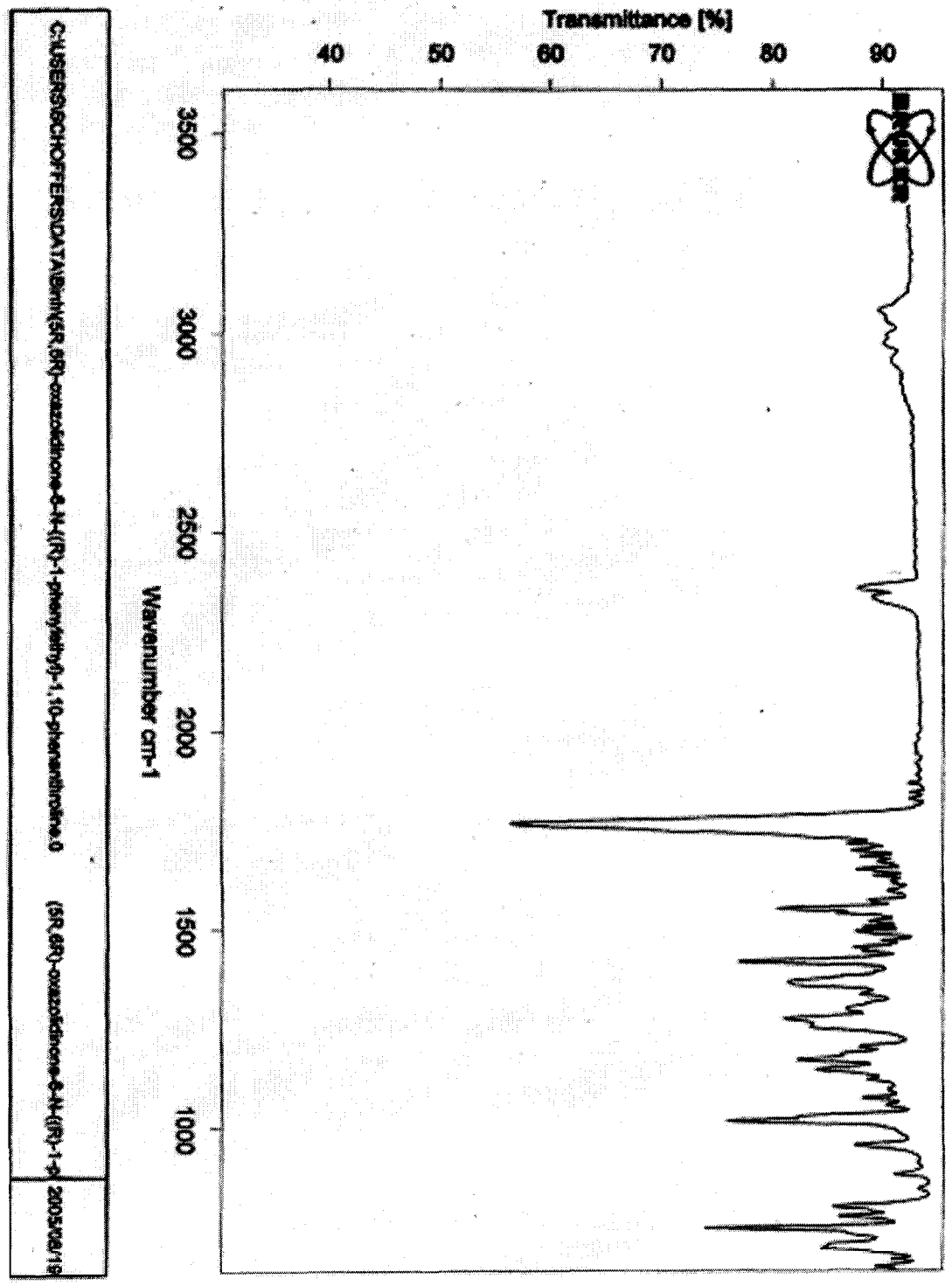


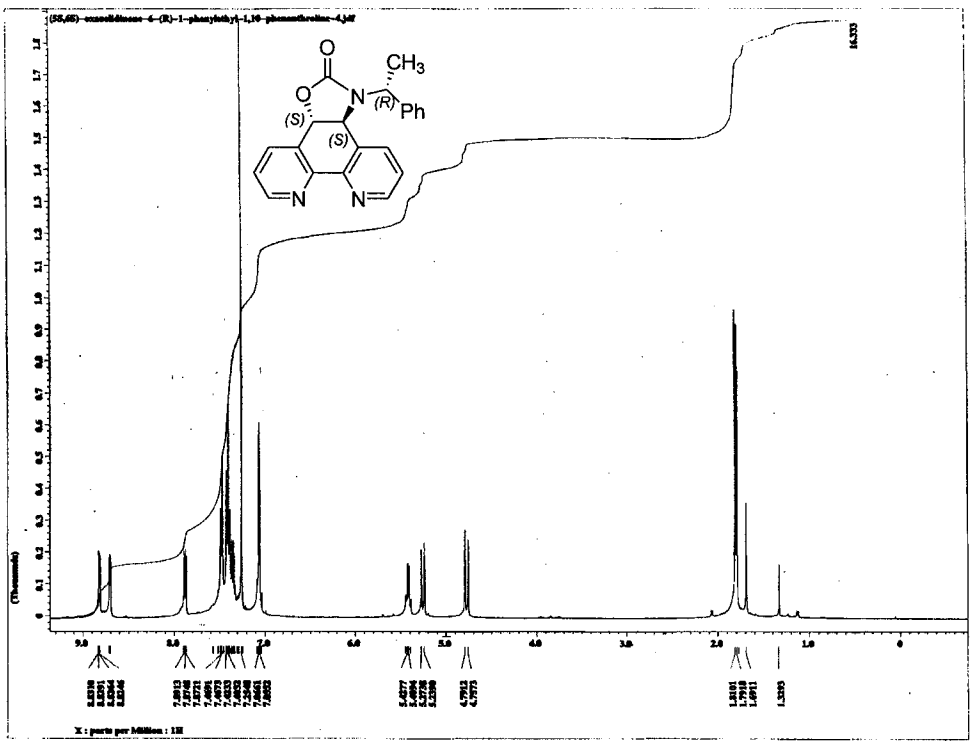


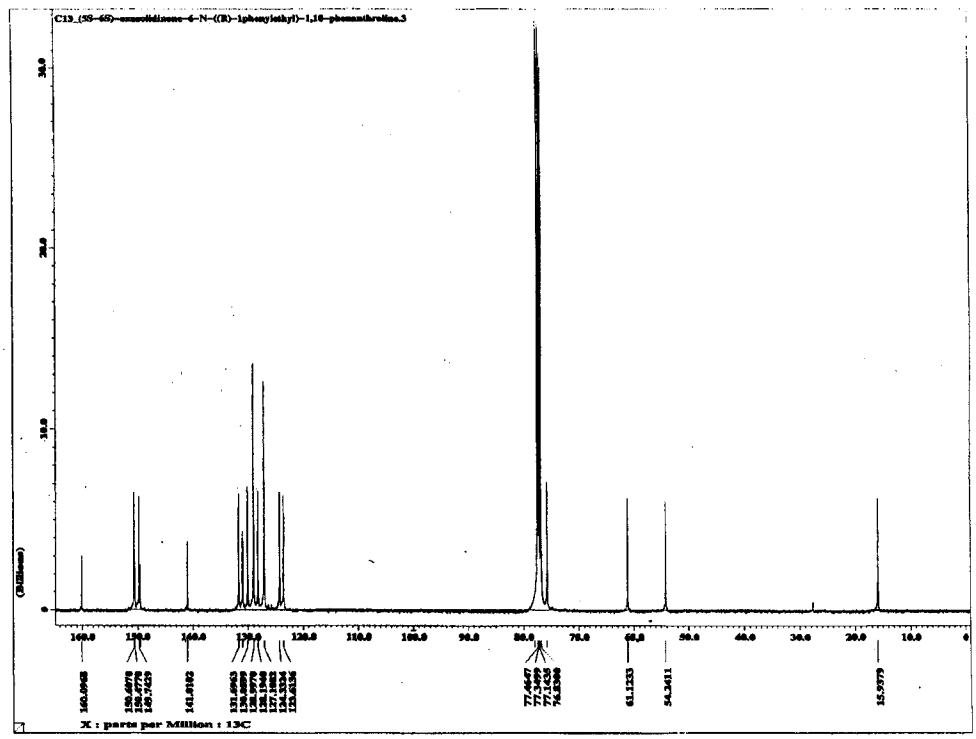


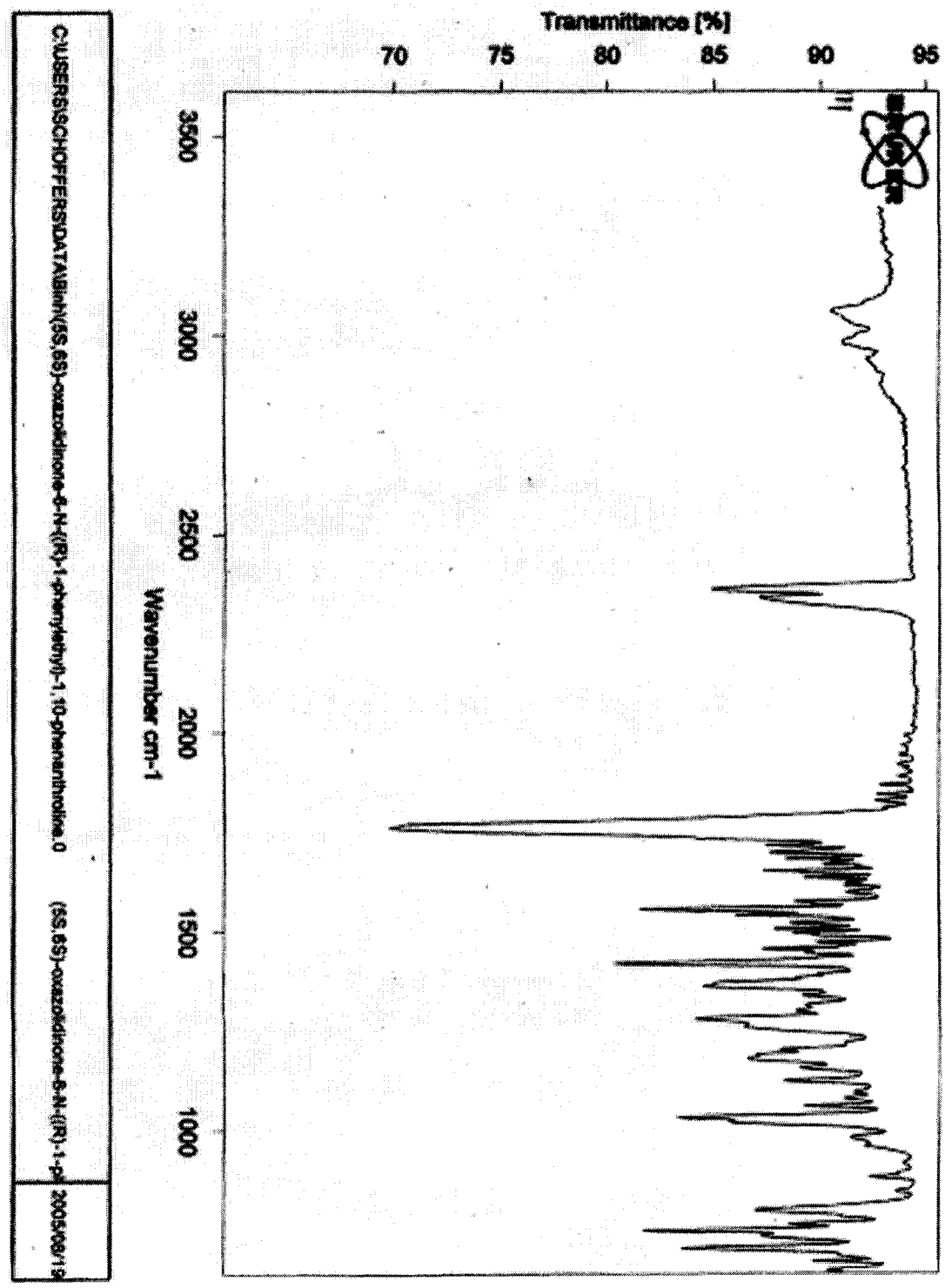


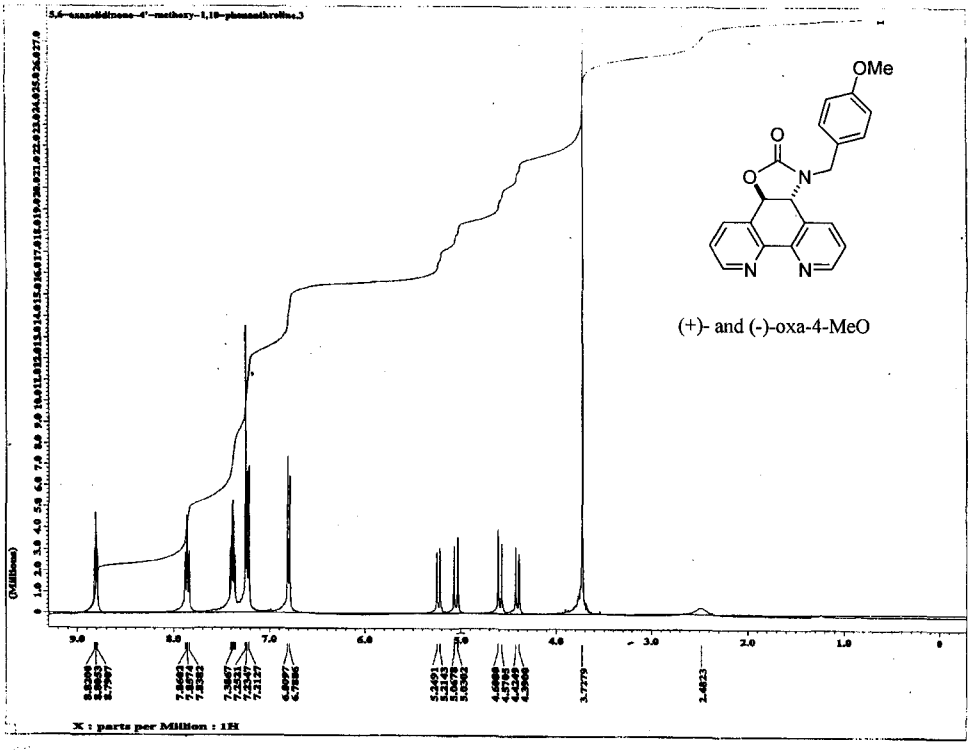


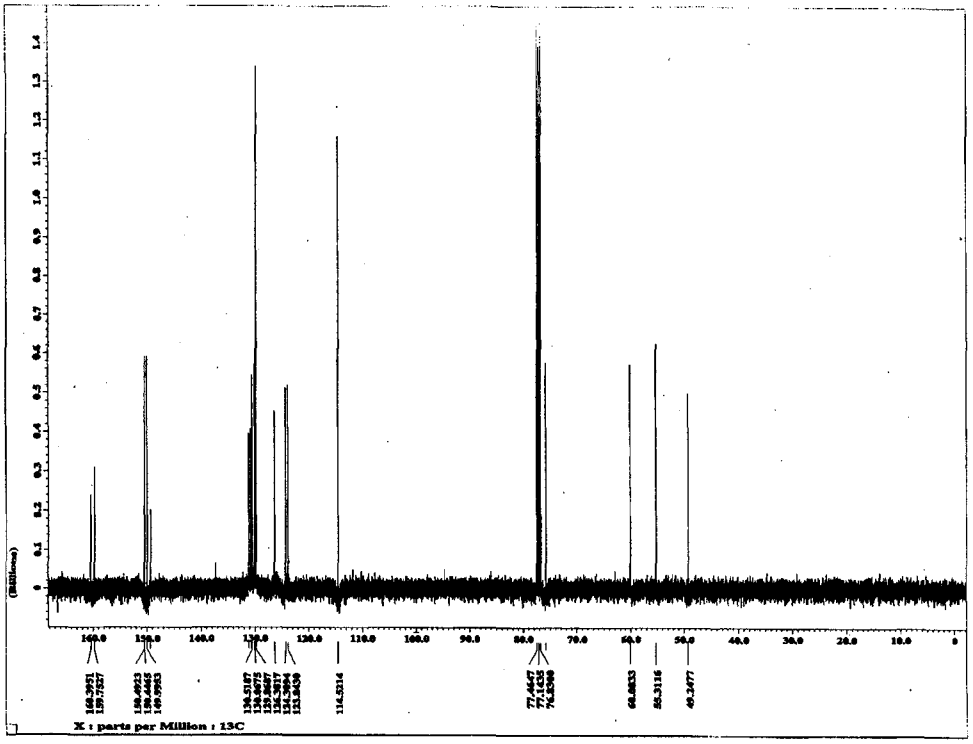


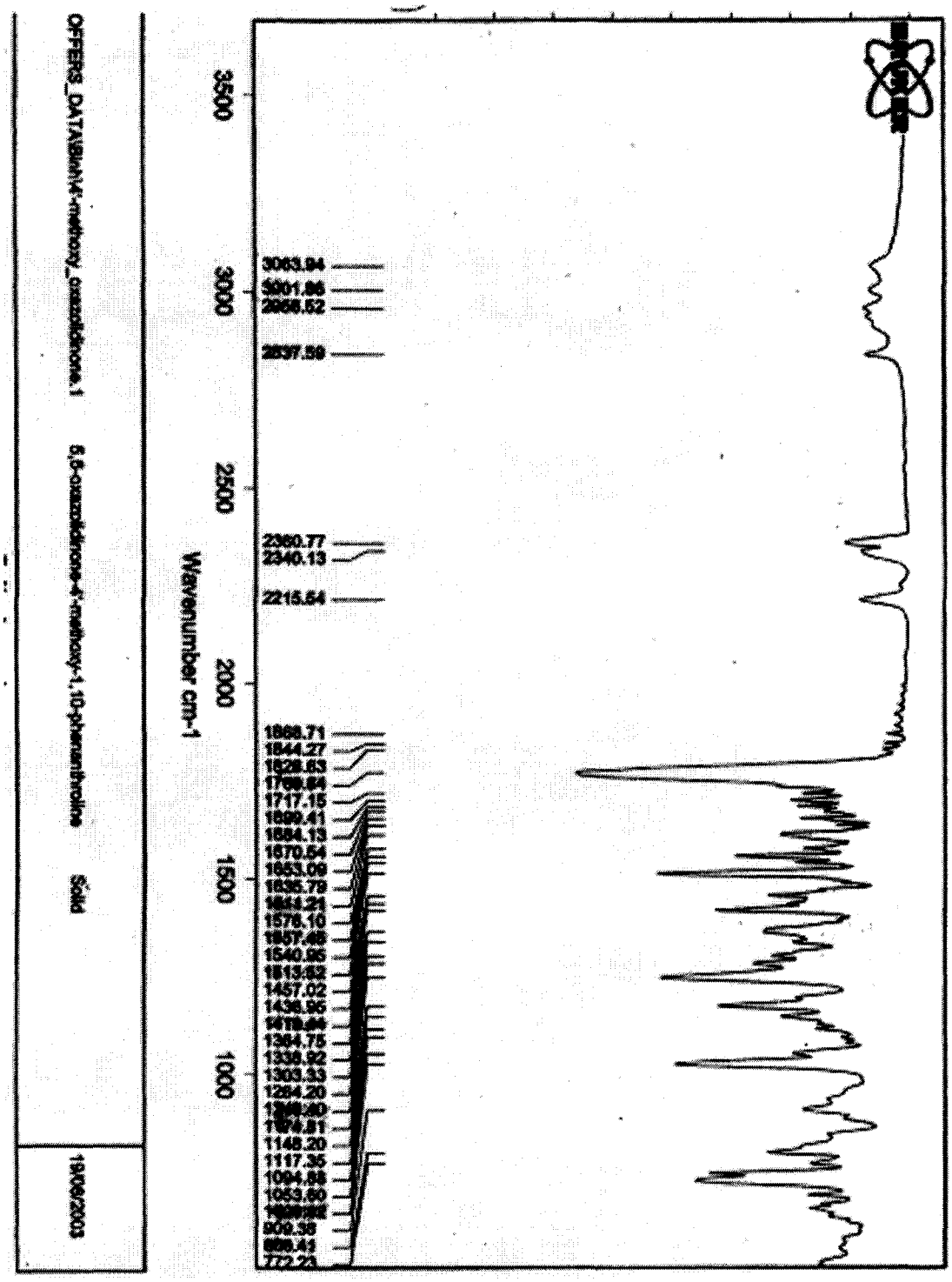


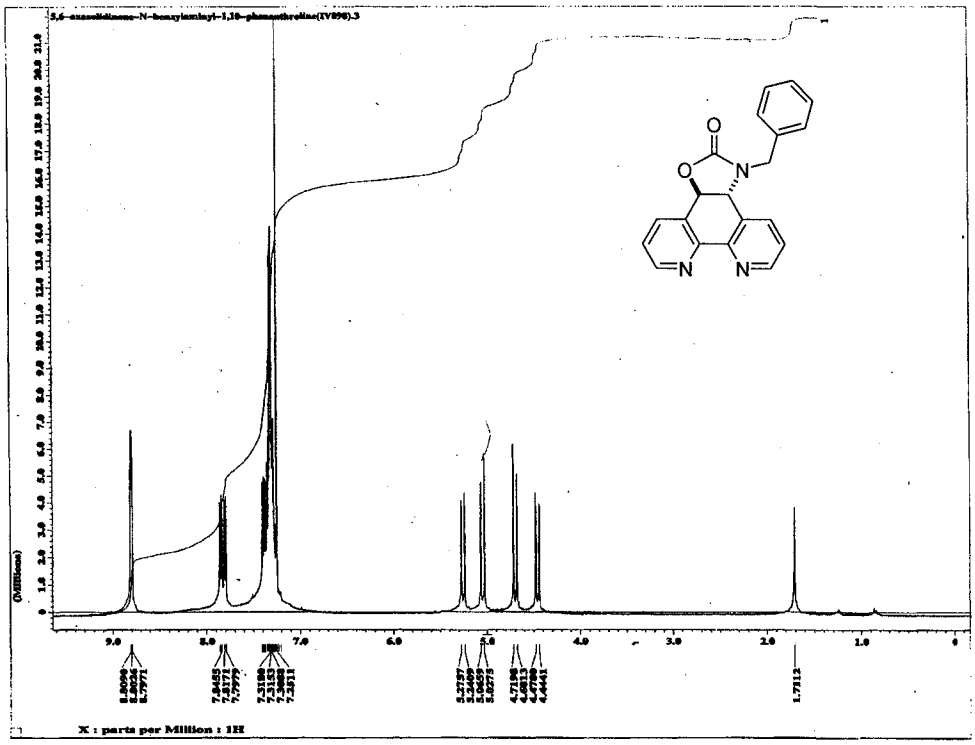


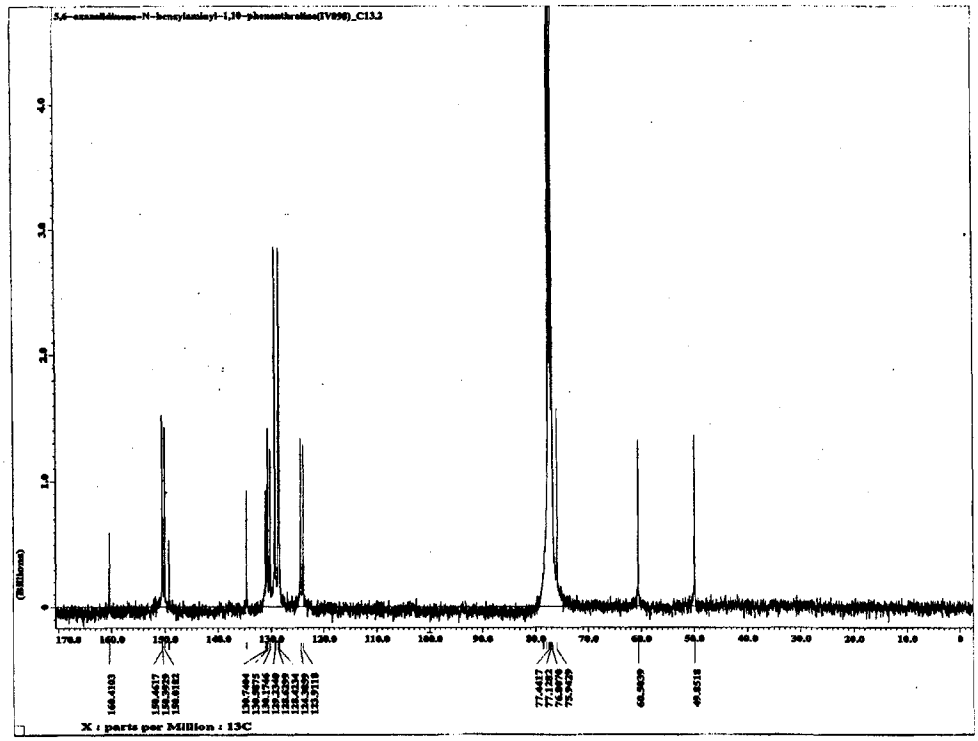


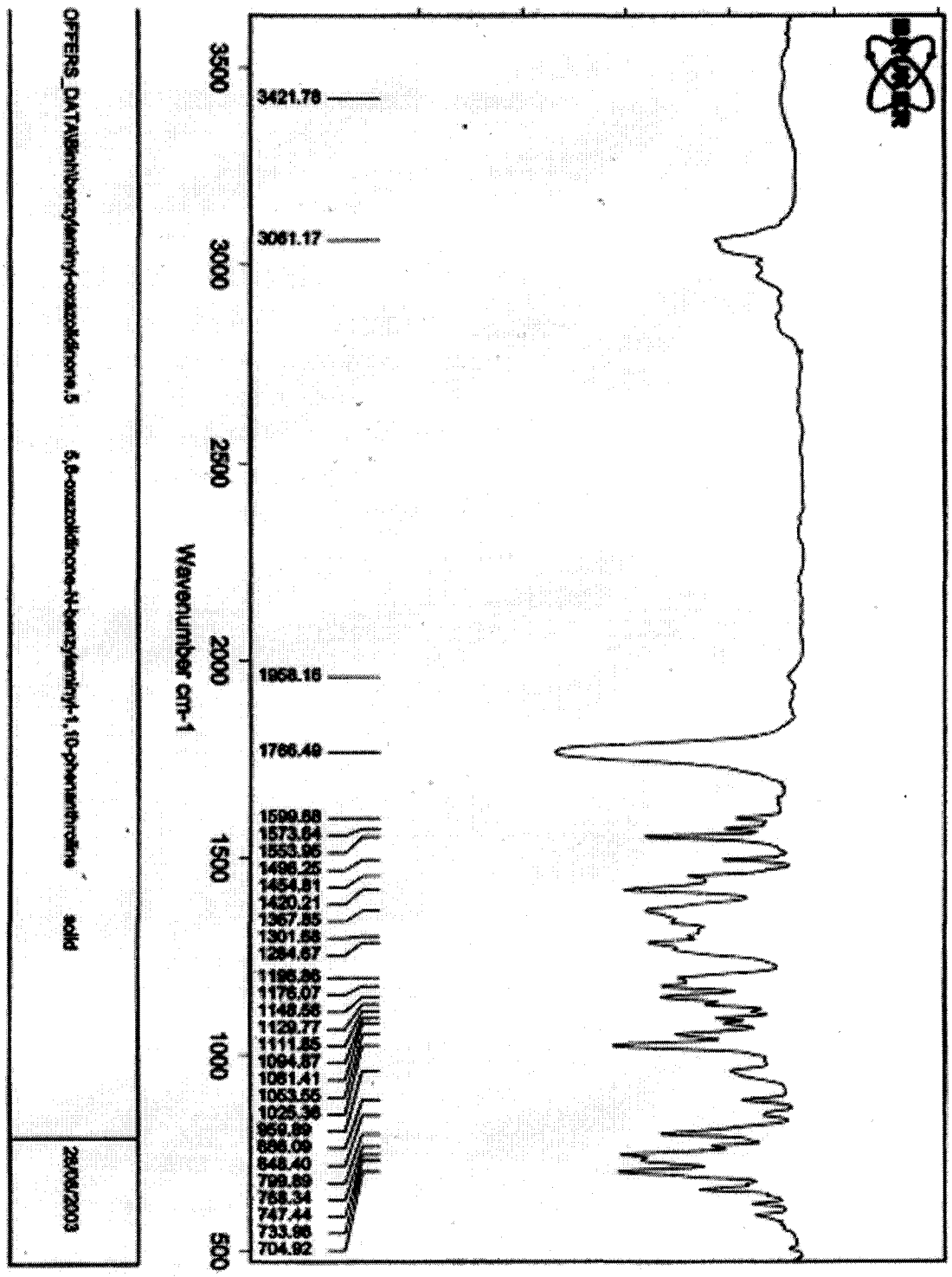


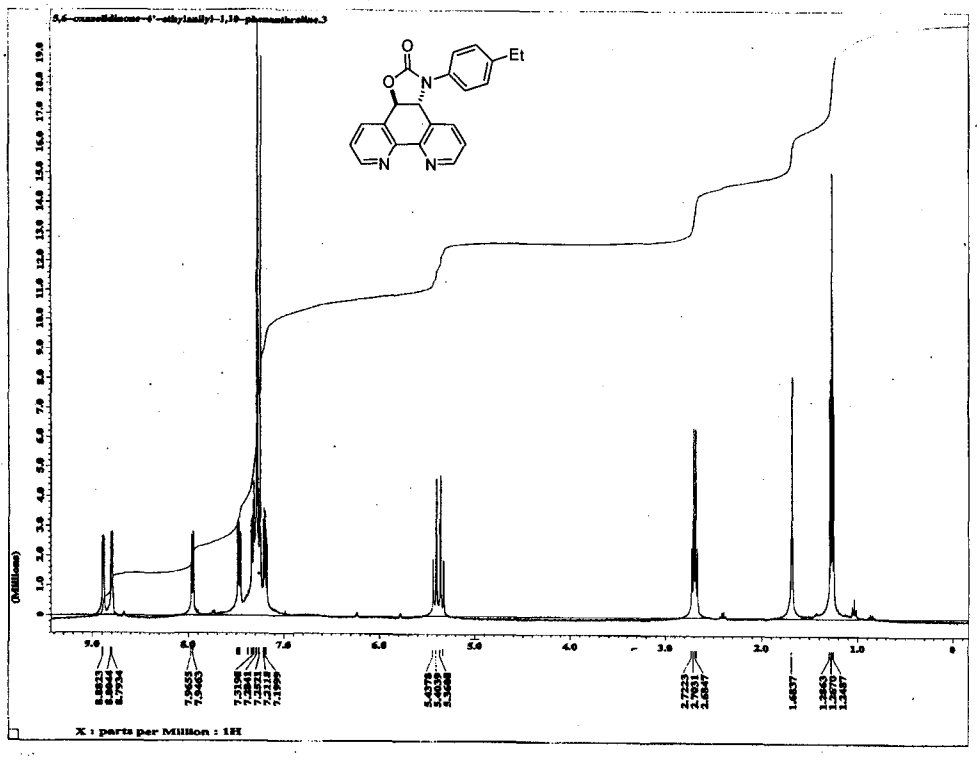


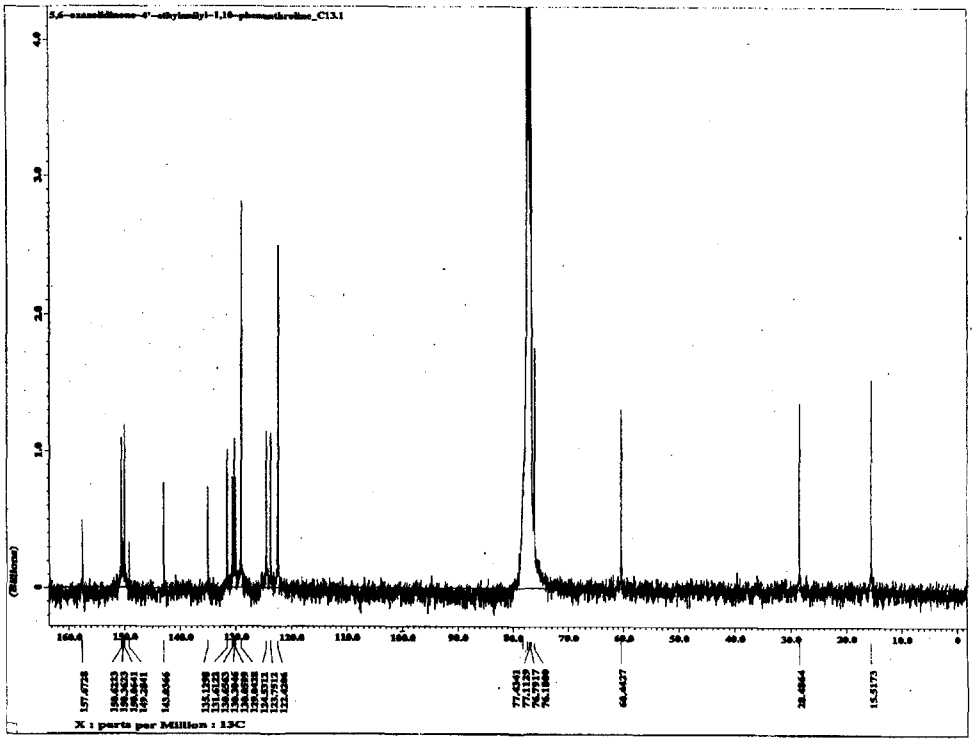


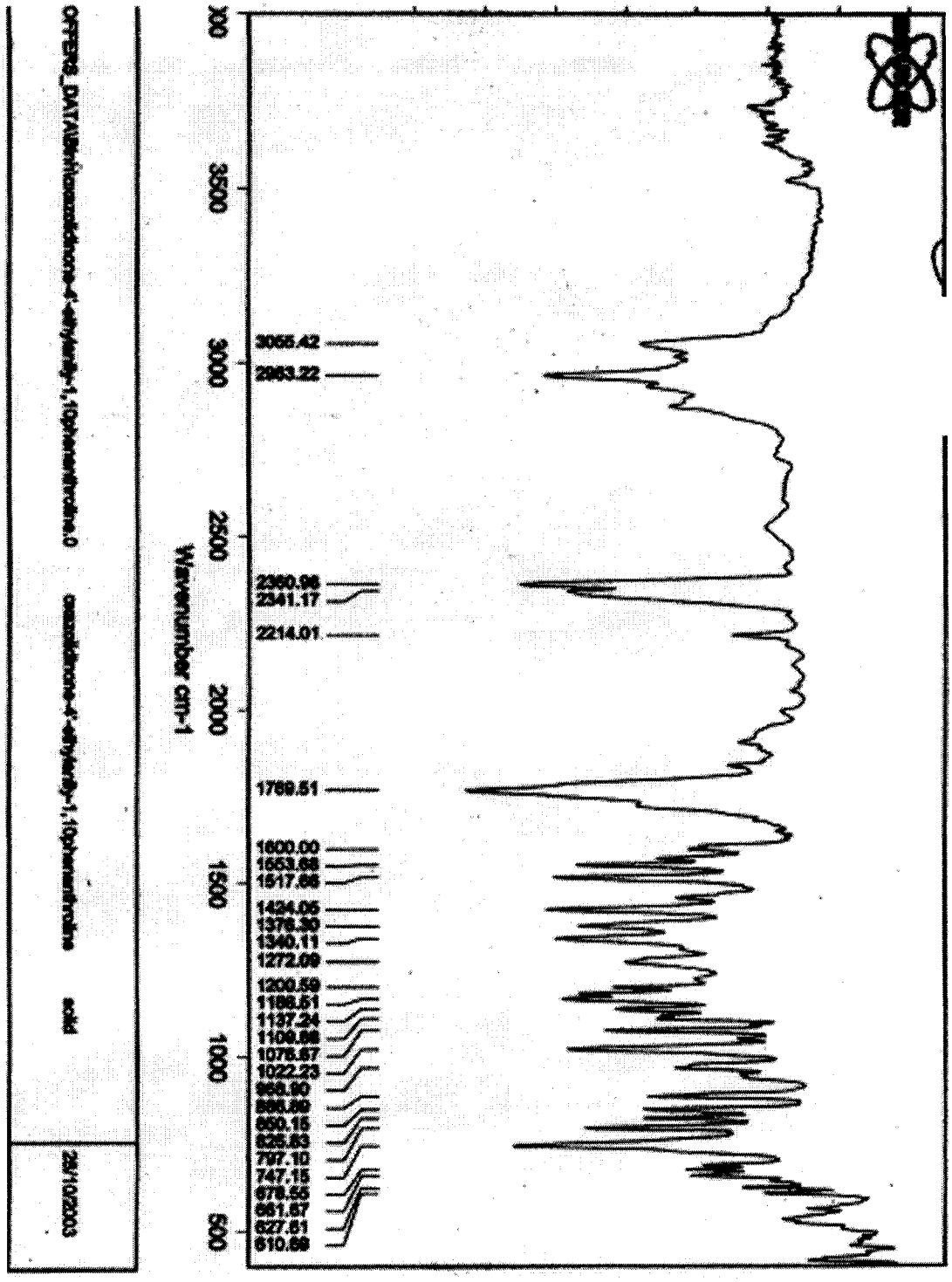


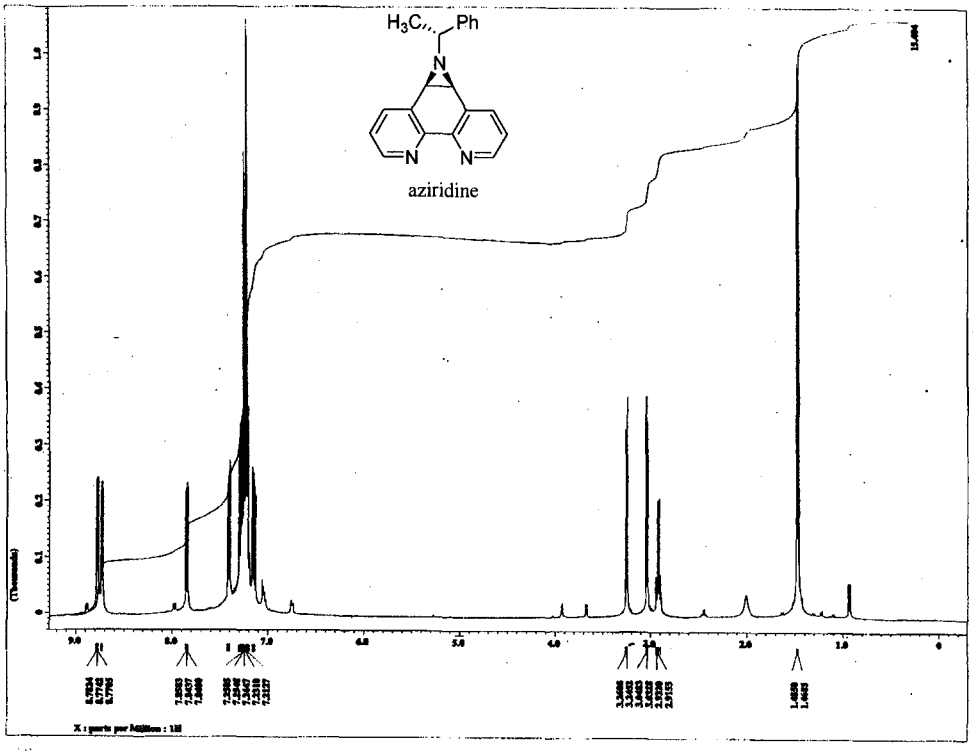


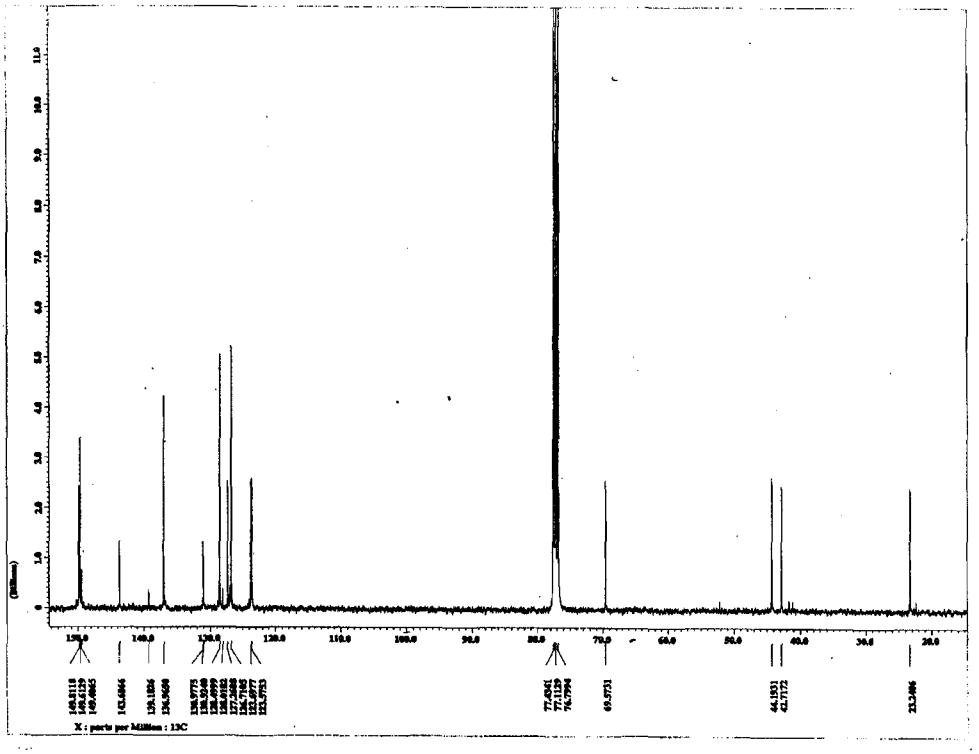


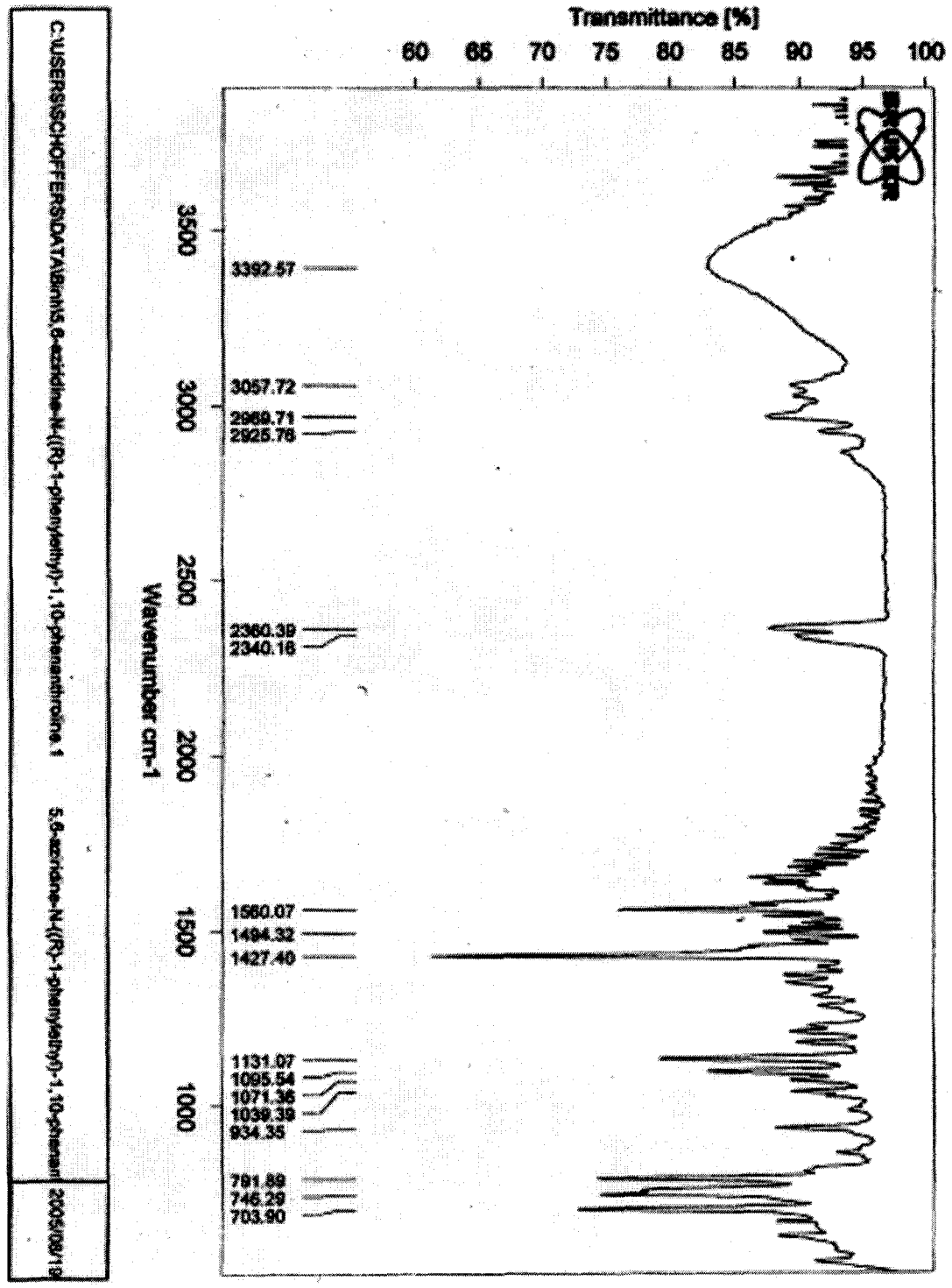


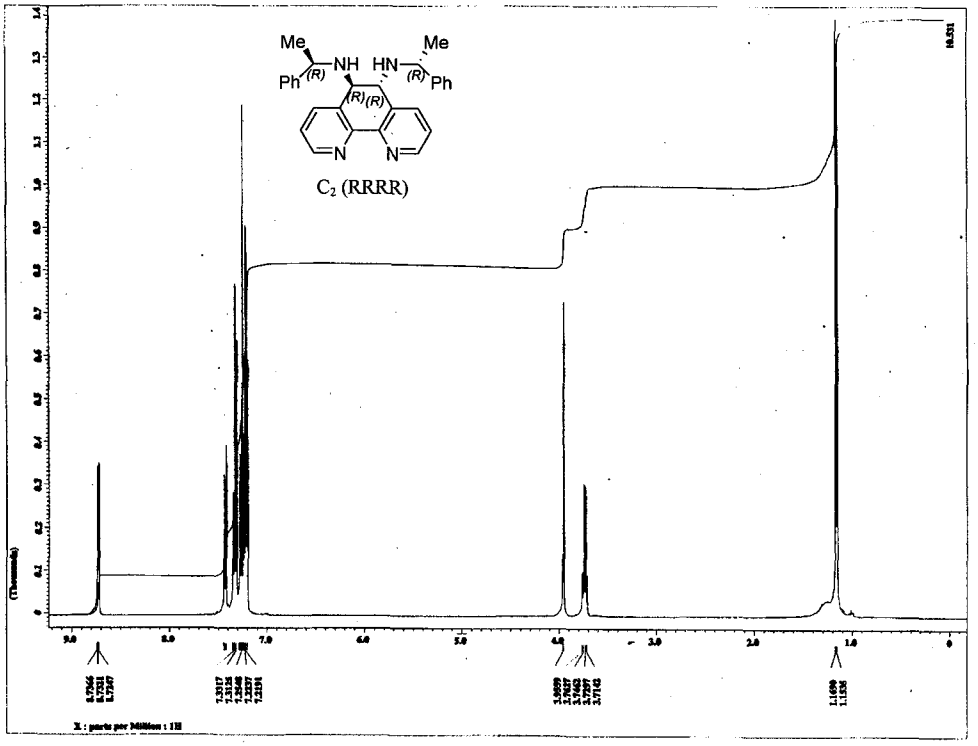


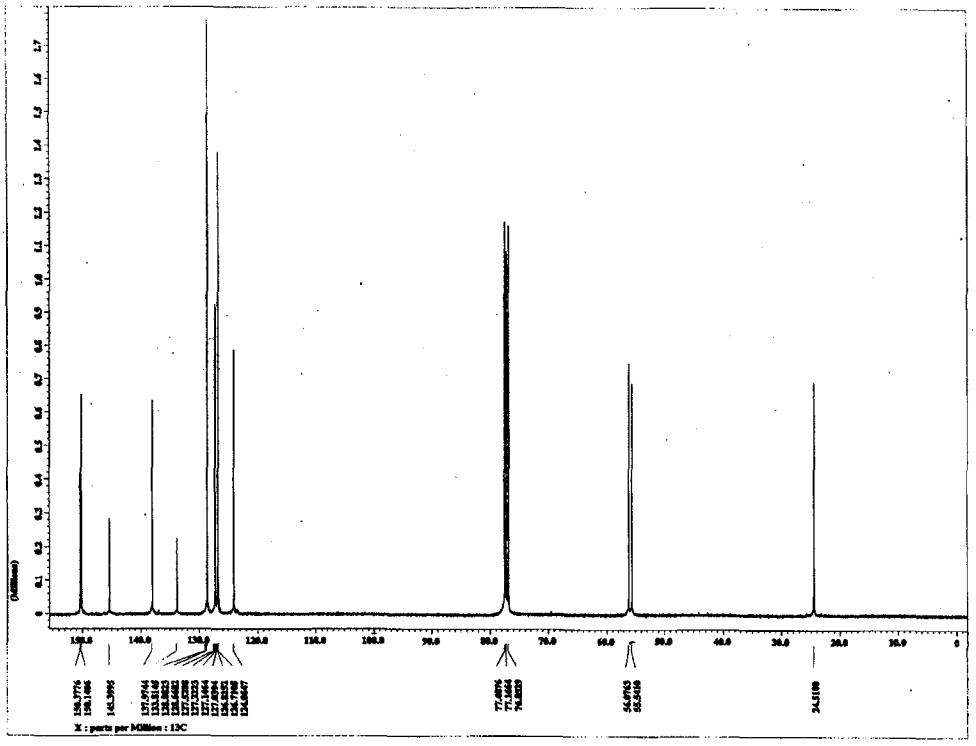


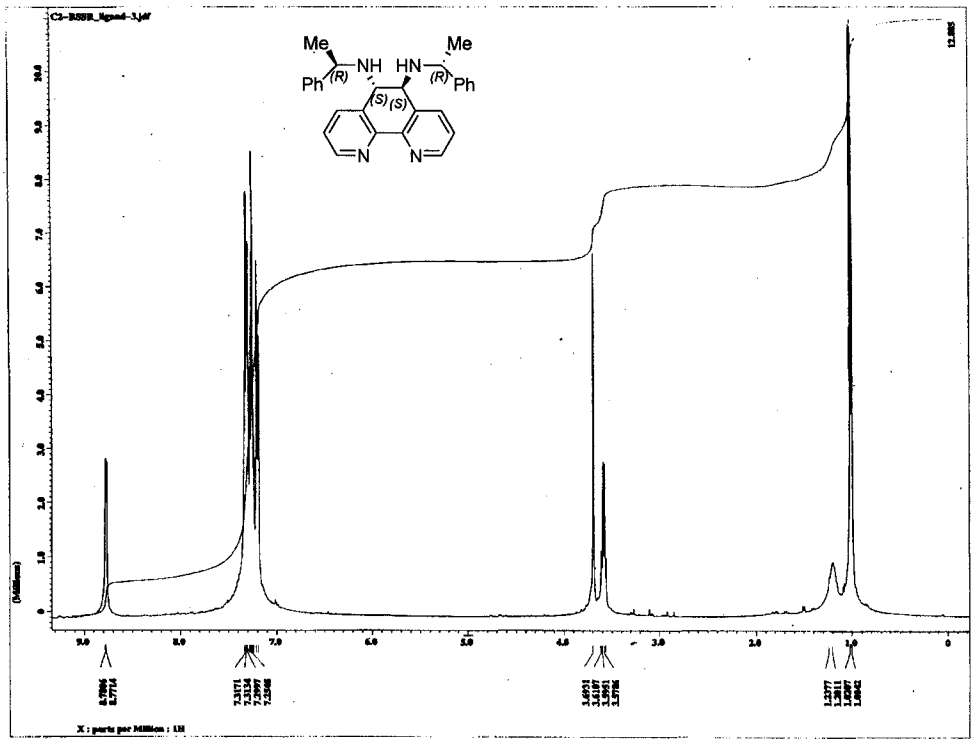


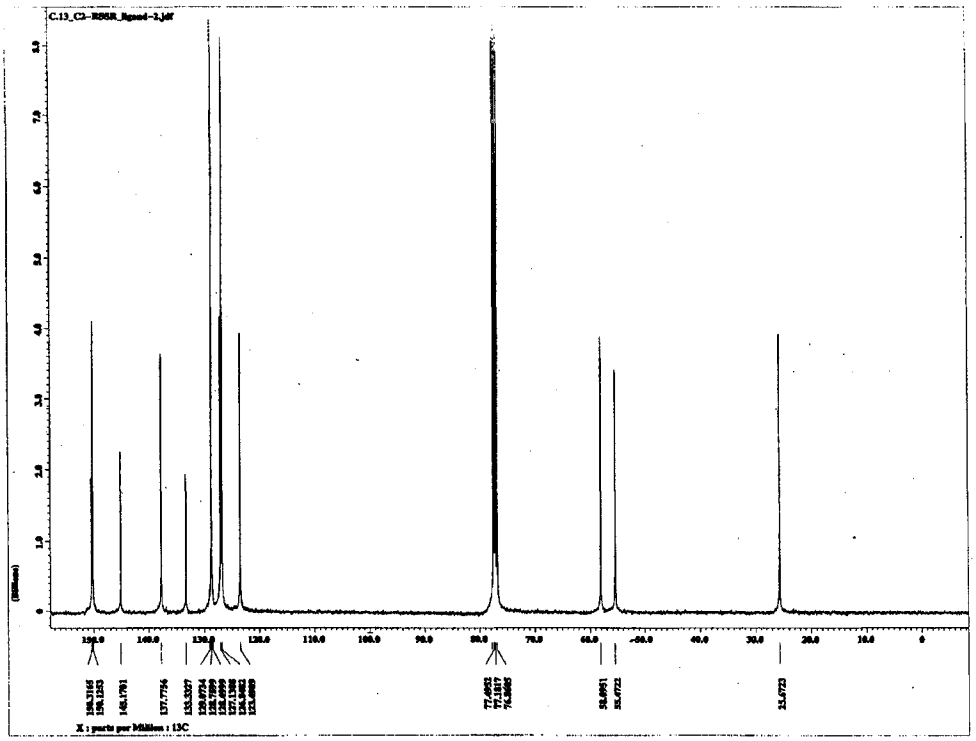


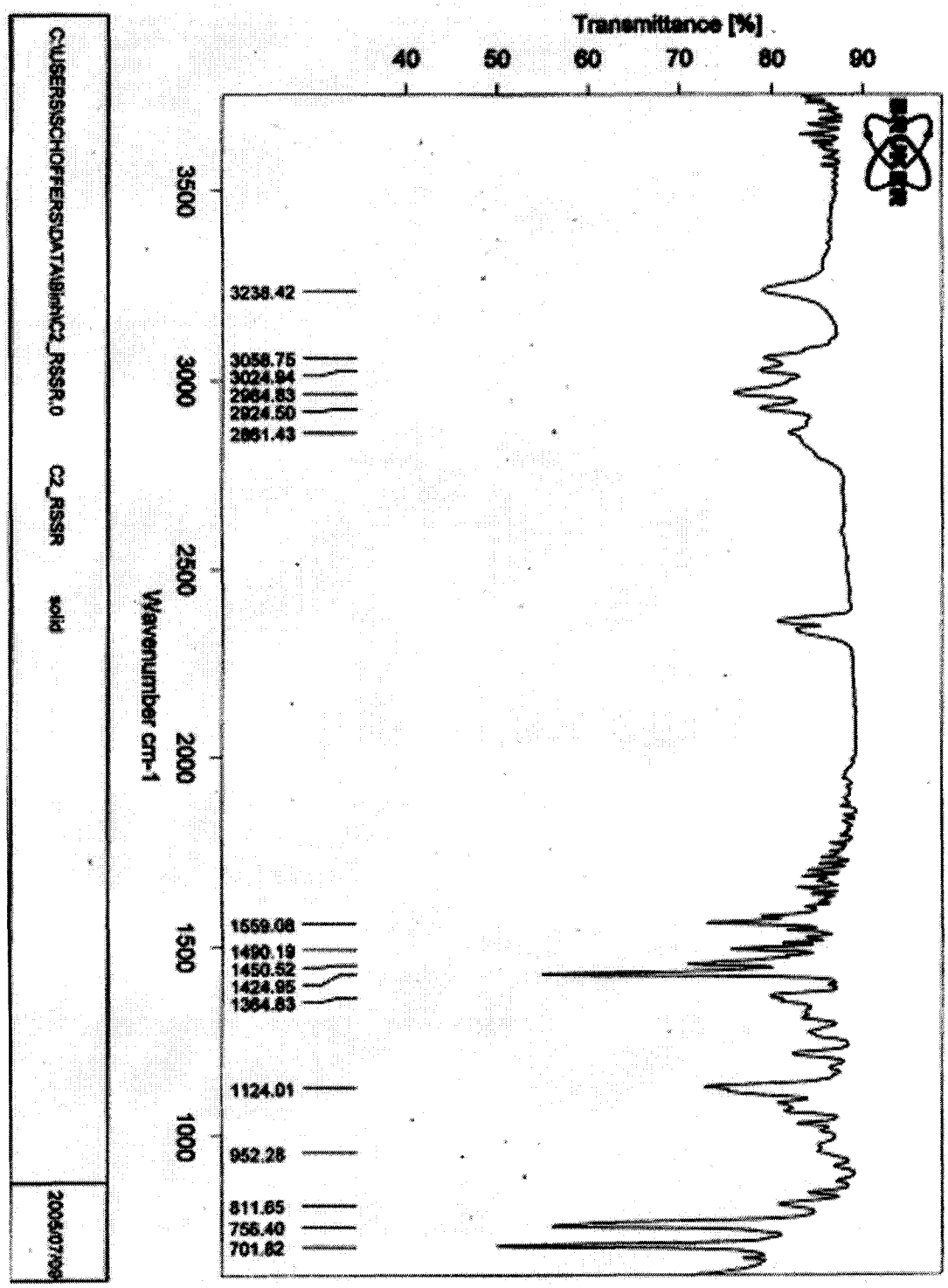


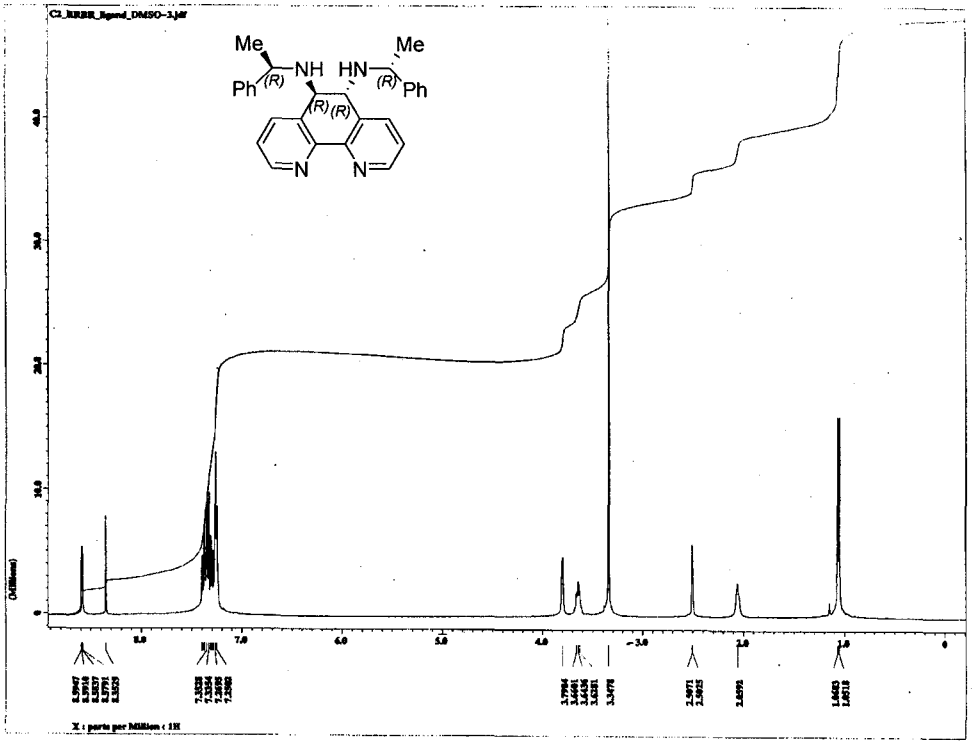


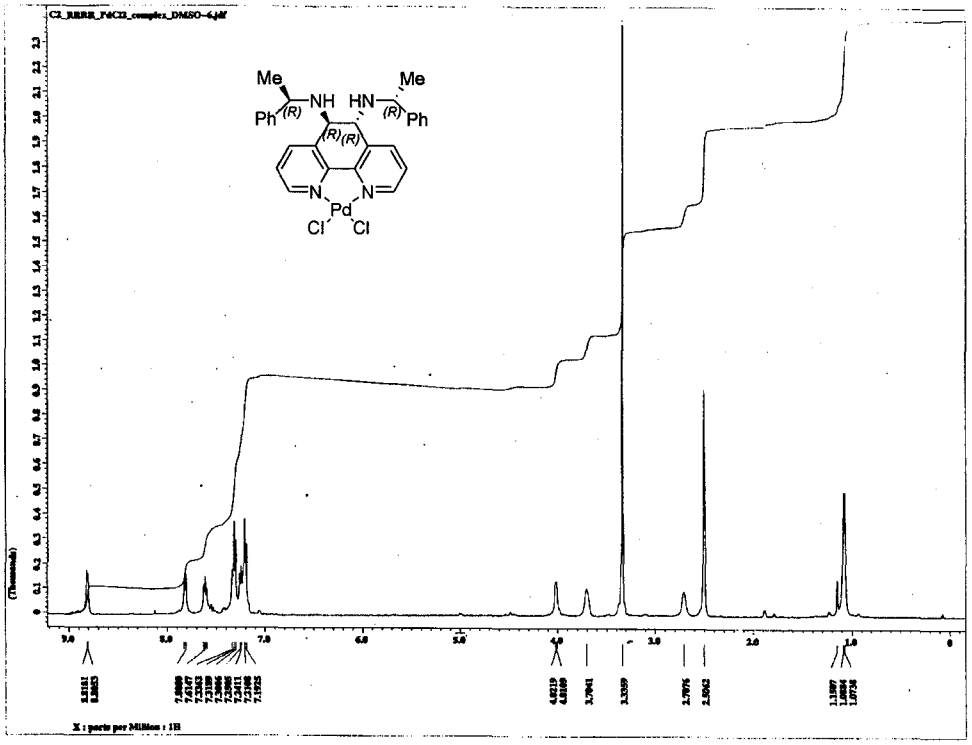


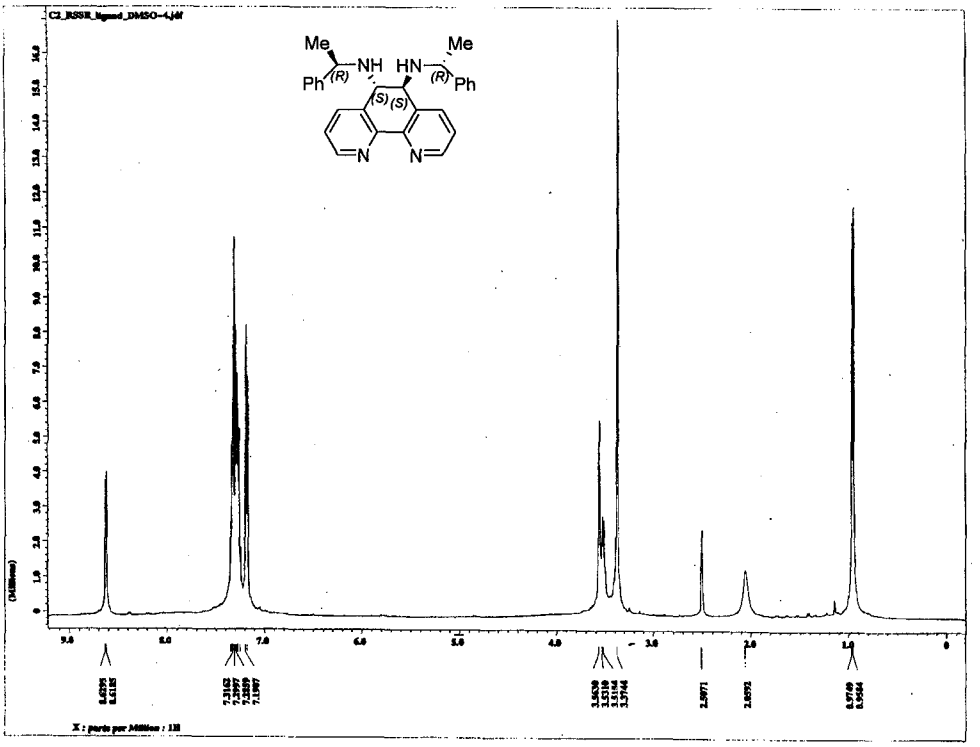


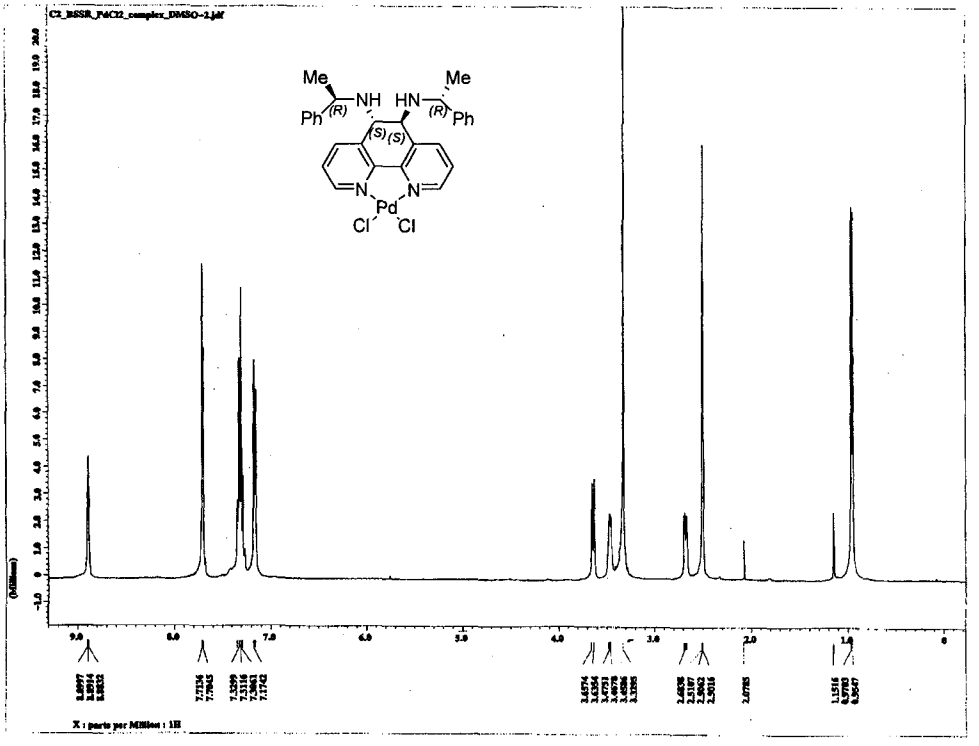


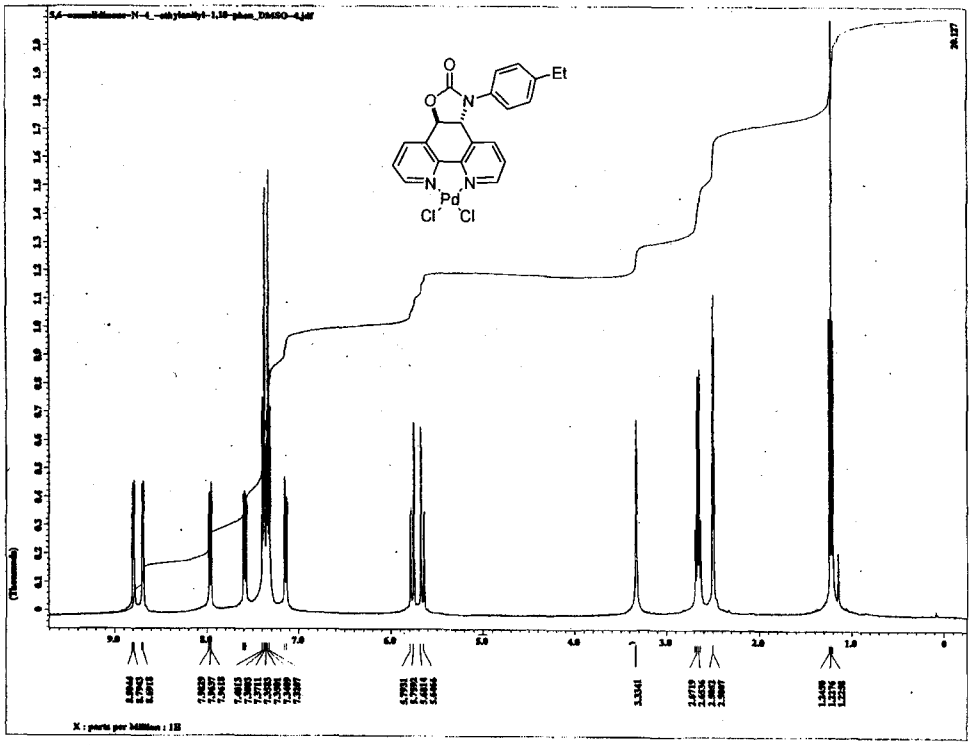


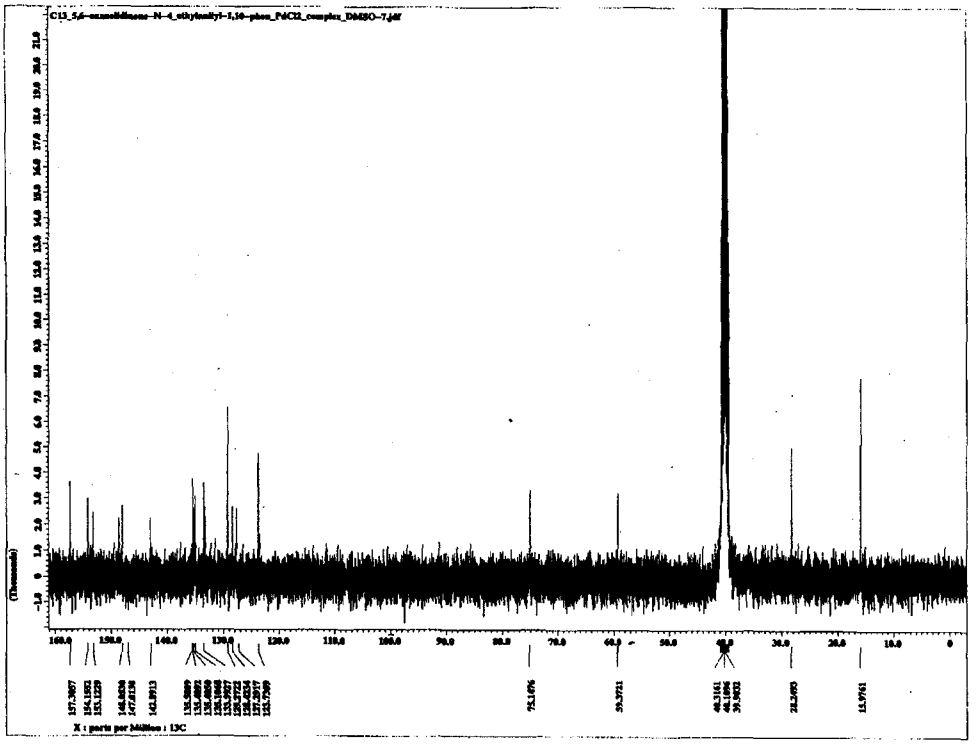


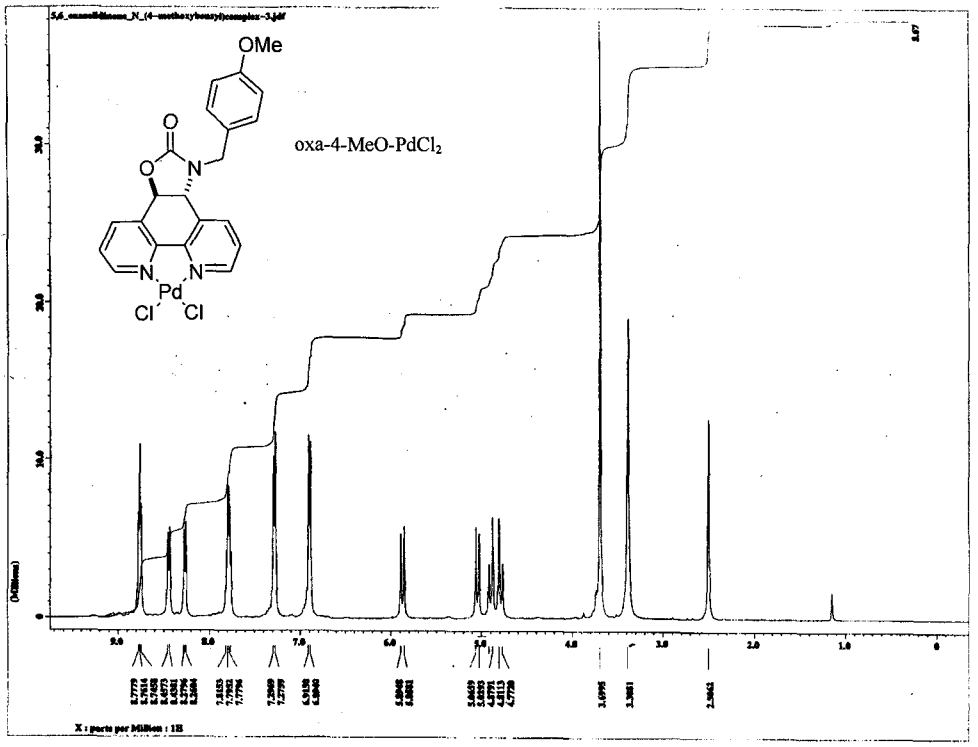


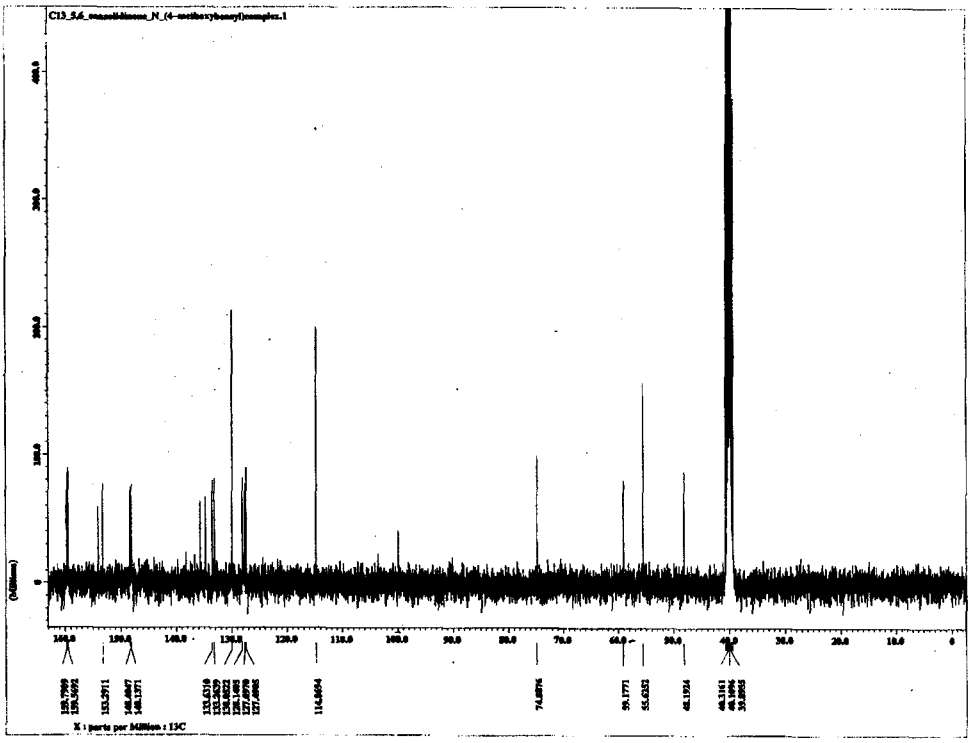


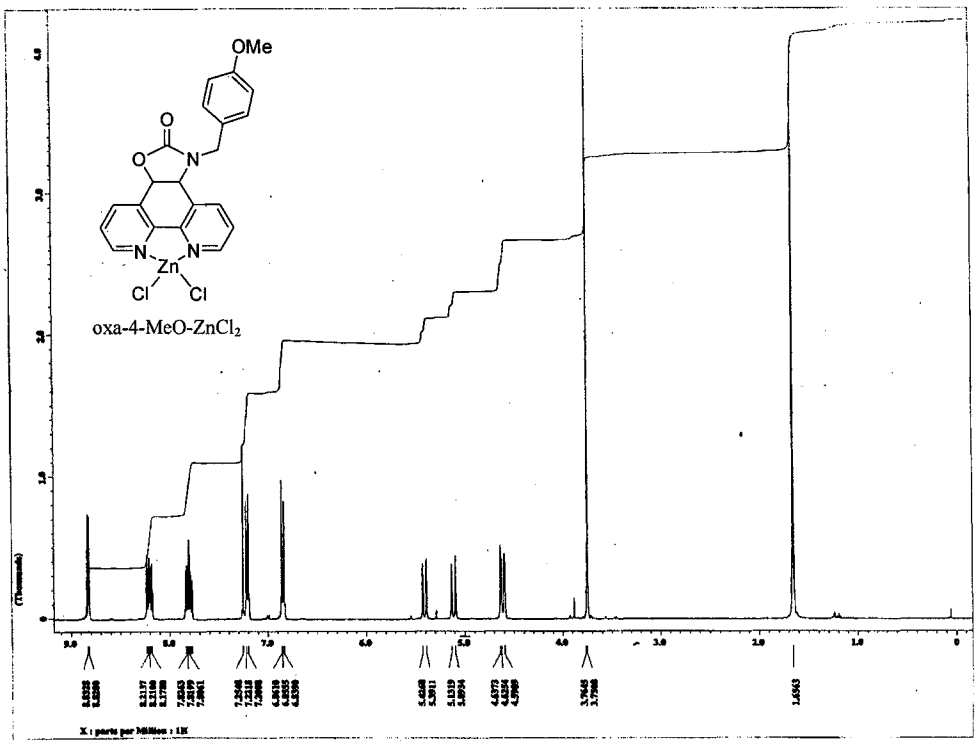


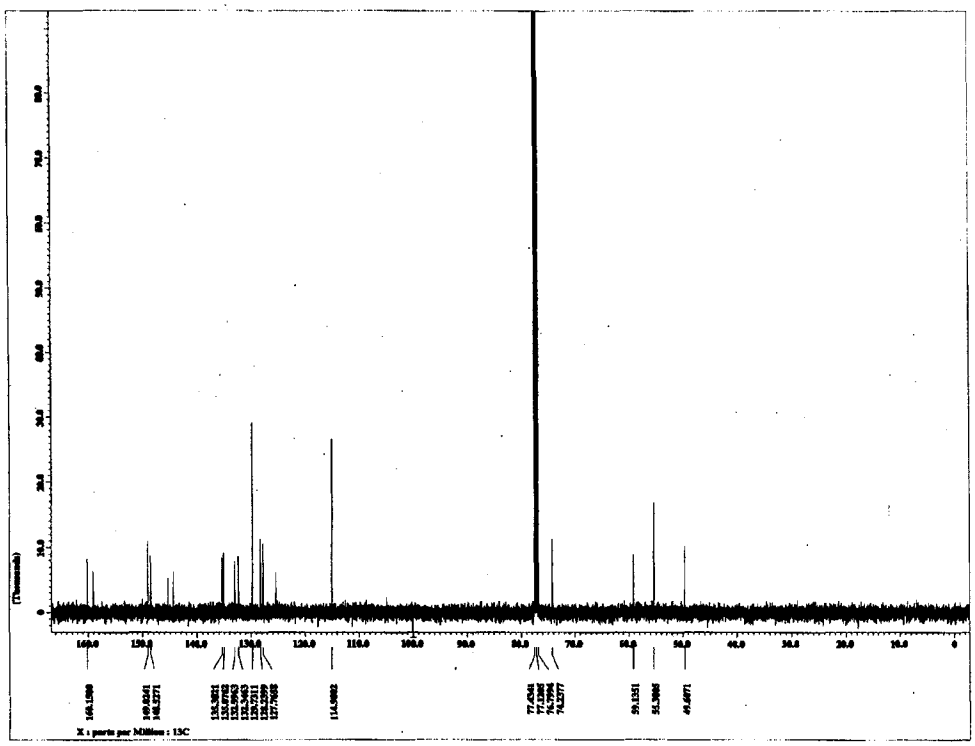


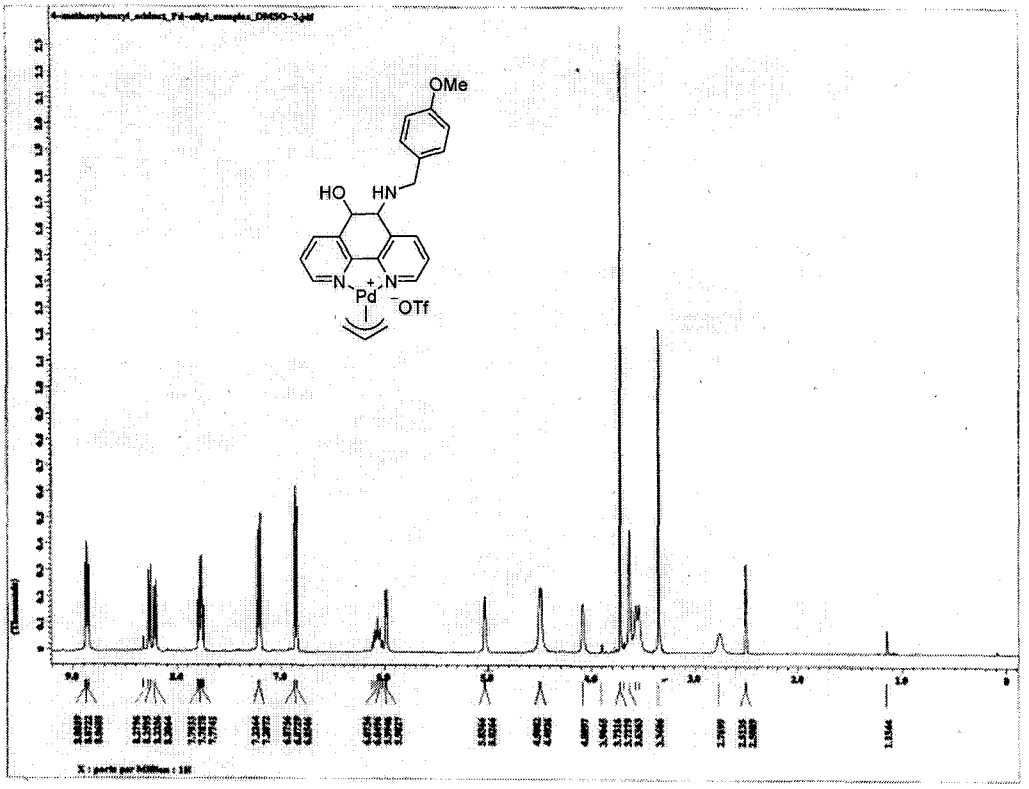


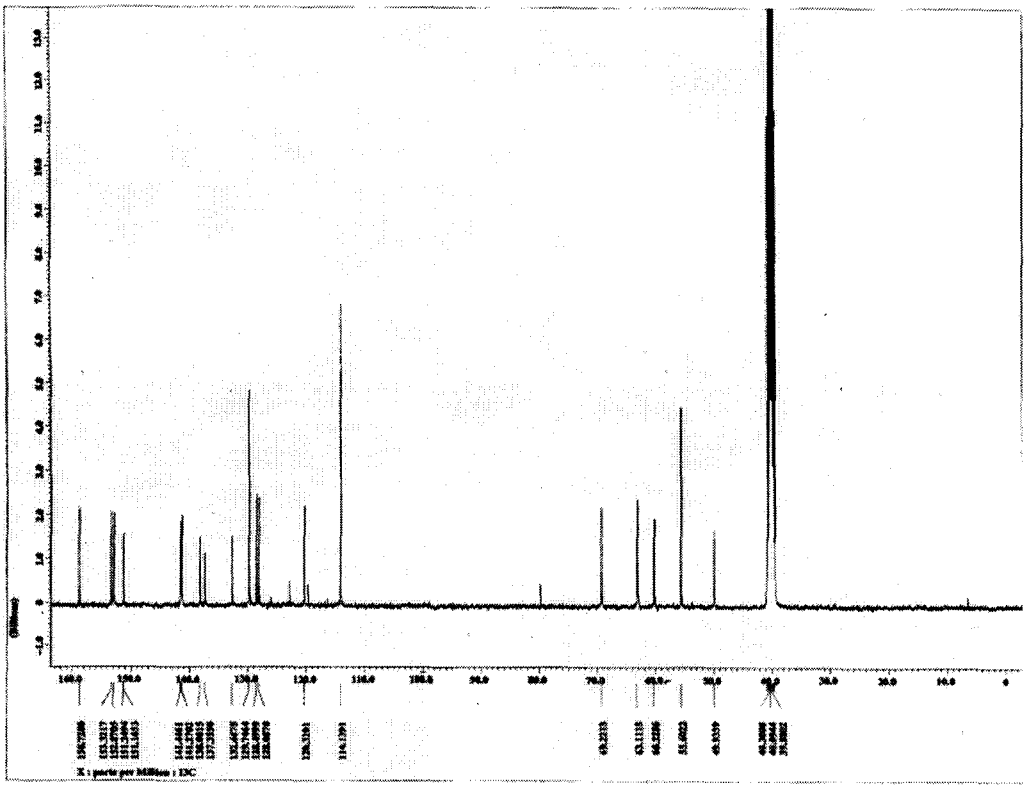


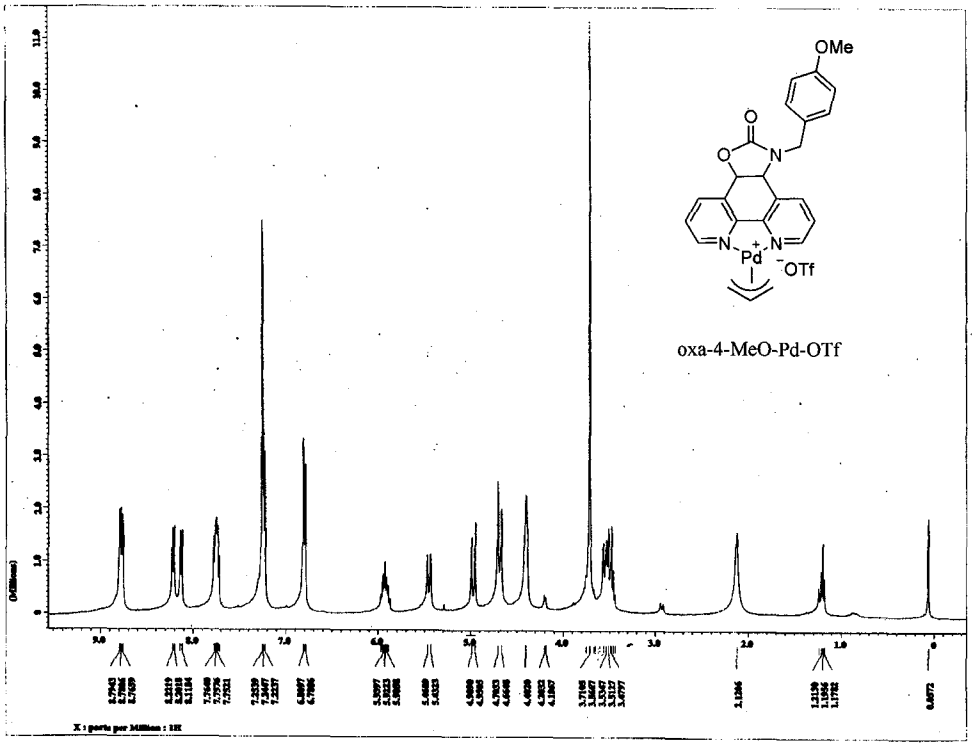












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