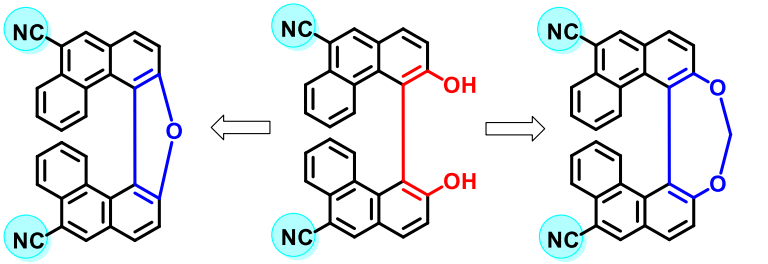
# Chapter-3

## *Synthesis & Study of optically pure 5,13-dicyano oxa[7]helicene and helicene-like molecules*




*Helicene* *Helicene-like*

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# 3.1 Introduction:

## 3.1.1 Introduction to Helicenes:

The word *'Helix'* is derived from a Greek word which translates to twisted or curved. Helix is a geometrical structure found abundantly not only in man-made structures but also in nature. Some of the popular representation of helix found in nature is the shell of a snail, spiral galaxy, petal arrangement of certain flowers, some plants that that grow spirally around their support. These examples reveal that nature utilizes "*helix*" not only as visually appealing form, but probably also to optimize the utilization of space. The DNA double helix, which forms the basis of life by storing and expressing genetic material, has a helical arrangement which greatly contributes towards its complex performance and functions.

**Figure 1 Helical structures present in nature**

Polyacenes and helicenes are similar but distinct classes of isomeric benzenoid hydrocarbons that differ in their annelation patterns. Polyacenes are linearly fused aromatics possessing translational symmetry. Helicenes, on the other hand, are analogues of phenanthrene formed as a result of *ortho* fusion of four or more aromatic systems.

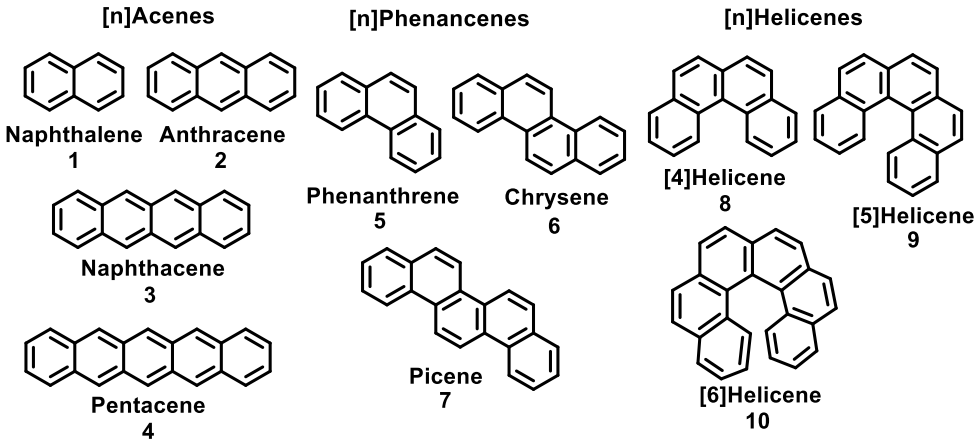



**Figure 2 Structural difference between polyacenes and helicenes**

Polyacenes and helicenes differ greatly in their physical, chemical as well as biological properties. Higher members of the polyacene family are unstable whereas the stability of

corresponding helicenes is high due to the considerable increase in their resonance energy. The steric repulsion between the terminal rings of helicene may however, affect their stability in highly fused systems. The intramolecular steric repulsion between the π-systems of the terminal rings in helicenes leads to conformational distortion causing loss of planarity rendering the molecule to adapt a helical topology. Hence, the molecule spirals upwards or downwards leading to the formation of enantiomers. If the helical twist is right handed (or clockwise) it is denoted by *P* while a left handed (anticlockwise) helical twist is denoted by *M*.[1] As a general trend of their specific optical rotations, *P* helicenes are found to be (+) or dextrorotatory whereas *M* helicenes are (–) or levorotatory.[2]

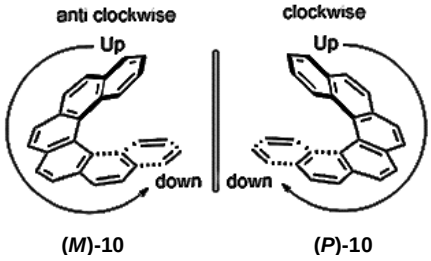



**Figure 3 Enantiomers of [6]helicene denoted as *P*- and *M*-isomers**

Helicenes are classified into different types depending upon the π-systems involved: (a) Carbohelicenes: when the helical skeleton is made up of benzene rings only (b) Heterohelicenes: when there is presence of one or more heteroaromatic ring as a part of the helical backbone (c) Double-Helicenes: when two or more independent helical units of same or opposite helicity are present in a single molecule[3] (d) Bihelicenyls: two helical units held together by a single bond.[4]

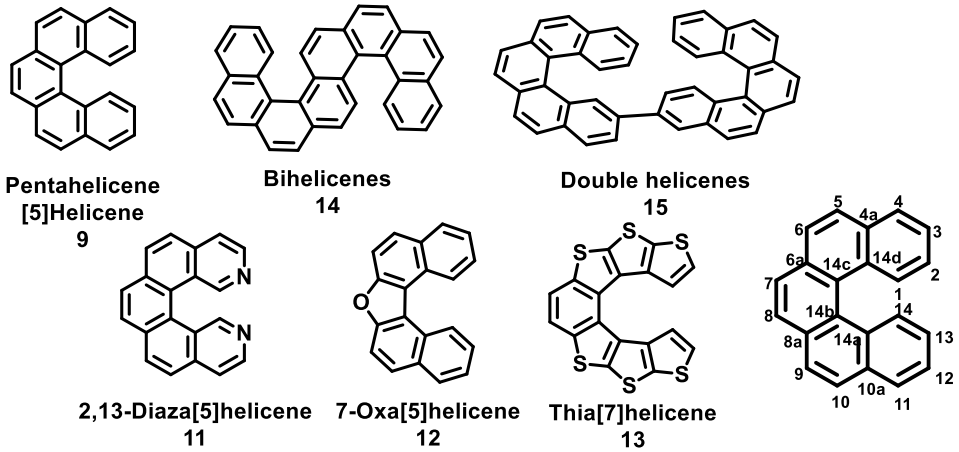



**Figure 4 Nomenclature and numbering of helicenes**

The nomenclature for such class of helical compounds was put forward by Newman and Lednicer[5] where the number of rings (n) forming the helical core is represented in square

brackets [n] with a prefix of heteroatom (oxa, aza, thia *etc*.) in case of heterohelicenes followed by the suffix "helicene". Chirality in helicenes depends on the extent of overlap of the terminal rings, which in turn depends on the number and nature of aromatic rings present in the helicene skeleton. The six-membered aromatic rings, like benzene or pyridine, have larger internal angles (about 60°) than that of five-membered rings (about 45° for thiophene, 35° for pyrrole and 32° for furan) hence more rings are required to cover a complete 360° rotation of a screw if five-membered rings are present. For example, carbo[6]helicene needs nearly six rings, whereas thia[7]helicene needs three benzene rings and four thiophene units.[6]

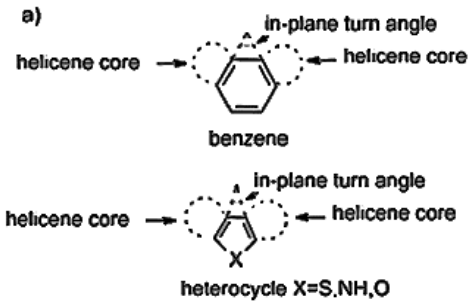


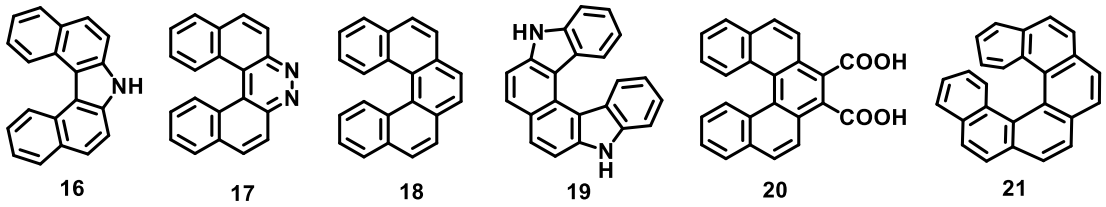

**Figure 5 Schematic representation of in-plane turn angle**

The torsional strain due to the helical topology of such molecules, causes a change in the bond lengths along inner as well as outer helical rim. The increase in the bond lengths along the inner rim (1.48Å) and its shortening along the periphery (1.36Å) with each aromatic ring of the helical skeleton being deformed to a different degree is a characteristic for this class of compounds.

The helicenes have some of the most impressive chiroptical properties of any class of molecules[7] like high specific optical rotations, circularly polarized luminescence,[8–11] circularly dichroism,[12–15] fluorescent having moderate to high quantum yields,[16–19] form π-complexes[20–22] and enhanced physical-organic properties.[23,24] These unique properties of helicenes pave a way in the development of their applications as chiro-optic materials,[25] photochromic materials,[26] sensors,[27] molecular level devices,[28] organic electronics,[29] NLO materials[30] *etc*. Their characteristic structure has a close resemblance with biological macromolecules making them ideal candidates to study selective binding to nucleic acids and influencing the biological activity in living systems. Literature reports mention the interactions of helicenes with DNA[31–33] and enzymes such as telomerase[34] or

topoisomerase-I[35] which may be useful for medicinal purposes. All these features sum up the importance of helicenes as synthetic targets.

The term '*helicene*' was first introduced in 1955 by Newman, whose pioneer work in the field of helicenes cannot be overemphasized. The word *'helicene'* itself contains a prefix *'helic-'* meaning non-planar and suffix *'–enes'* which denotes the presence of unsaturated conjugated systems. Since his landmark study on the synthesis and resolution of [6]helicene,[5,20,36] this class of compounds have emerged as a fascinating set of synthetic targets. This important discovery was possible due to prior efforts by Meisenheimer[37] who reported the first helicenes **16** and **17** in 1903 starting from 2-nitronaphthalene. In the next few decades, only a few helicene derivatives **18-21**[38–41] were synthesized leading to little contribution towards the growth in the field of helicene chemistry until Martin and co-workers developed the photodehydrocyclization of stilbene-type precursors for the synthesis of helicenes.




16 17 18 19 20 21

**Figure 6 Helicenes synthesized before 1960**

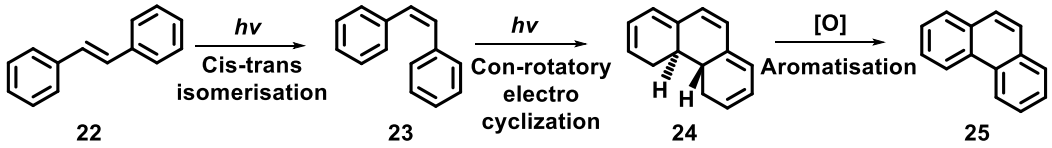
In the next three decades, Wynberg,[42–44] Martin,[45,46] Laarhoven[47–49] and Katz [50–52] carried out pioneering studies on the synthesis, spectral properties and structural aspects of helicenes. However, the smaller members of helicenes were more studied theoretically and practically during most of the five-decade lifetime of helicene chemistry. The main causes for this were: difficult synthesis of higher members of this class with $n>13$ due to the steric distortion and the absence of a more general synthetic methodology to get individual enantiomers on a preparative scale.

## 3.1.2 Photochemical Synthesis of helicenes:

The synthesis of helicenes has always been a challenging task in synthetic organic chemistry due to the steric factors involved and difficulty in controlling the regioselectivity of the reactions. Some of the classical methods for the synthesis of helical compounds include the following approaches: Diels-Alder reactions, benzylic coupling, McMurray coupling and

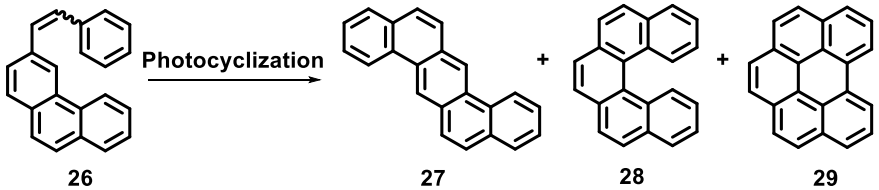
various metal-catalyzed coupling reactions. Although these non-photo-oxidative methods had various advantages, they suffered from major drawbacks like requirement of electron rich diene and electron deficient dienophile for Diels-Alder reaction which limits its scope of utility with a wide variety of functional groups, poor to moderate yields, requirement of temperatures as low as -60°C in some cases, use of expensive Pd/C for the dehydrogenation necessary for aromatization *etc*. In comparison to these methods, oxidative photocyclization has gained much support over the years, due to easily accessible starting materials, wide functional group tolerance, mild conditions and atom efficient. The only major disadvantage of this method is the use of large amounts of solvents required for dilution which limits its applicability at gram scale.

The photochemical synthesis of helicenes by irradiation of a dilute solution of 1,2-diarylethylenes in the presence of an oxidizing agent is based on the photocyclodehydrogenation of stilbene into its corresponding phenanthrene derivative. Irradiation of stilbene causes a rapid interconversion between *Z*- and *E*-isomers. *Cis*-stilbene thus formed **(23)**, undergoes a conrotatory cyclization to give *trans*-dihydrophenanthrene **(24)**, a short living intermediate. In the presence of an oxidizing species, it undergoes dehydrogenation to give phenanthrene derivative **(26)**. A small amount of the oxidizing agent is sufficient to cause dehydrogenation of **24**, but to prevent oxidation of the end product, use of stoichiometric quantity of oxidizing agent and deaeration of the solvent may be a better choice. In principle all solvents that do not absorb at the wavelength of irradiation and do not react with the helicene precursor or the oxidizing agent can be used.



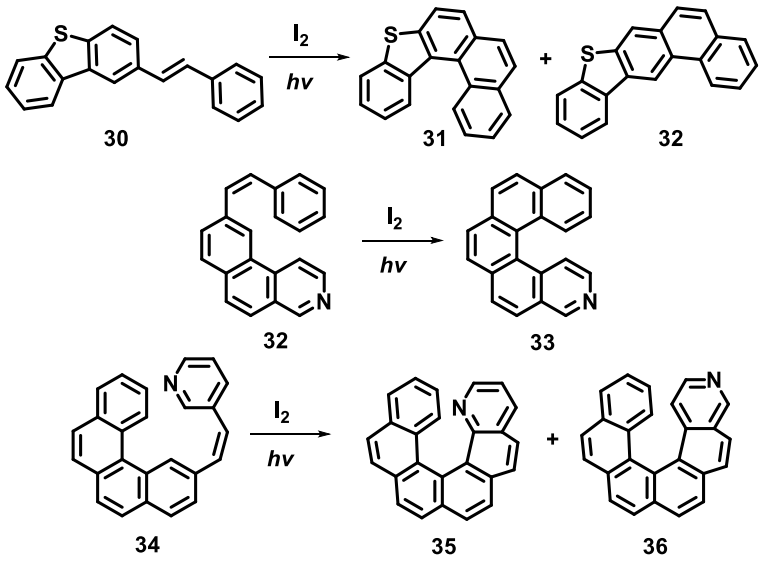

**Scheme 1 Mechanistic steps involved in photocyclization reaction**

But, during the synthesis of [5]helicene **(28)**, overoxidation of desired product was observed and undesired benzo[*ghi*]perylene **(29)** was formed during the course of photoreaction.[53]




**Scheme 2 Photochemical synthesis of [5]helicene (28)**

Similar to the synthesis of carbohelicenes, photoinduced synthetic routes can be utilized for several modified stilbene-type precursors for the synthesis of a variety of heterohelicenes.[54–57]



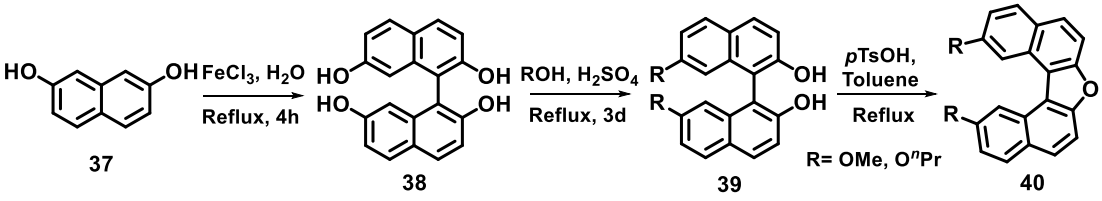

**Scheme 3 Synthesis of heterohelicenes using photocyclisation method**

## 3.1.3 Oxahelicenes:

The incorporation of heteroatoms into the helicene skeleton is a promising way to modify the electronic structure and modulate the physical properties. Since the development of the field of helicenes, a lot of focus has been given to the synthesis and study of carbohelicenes, but heterohelicenes are relatively less explored. Heterohelicenes containing oxygen atom as a part of ring system are classified as oxahelicene. The furan ring has less effective in-plane turn angle (α) and hence contributes to a lesser extent in the overall helicity of the molecule in comparison to benzene, pyridine, thiophene, and pyrrole rings present in the helicene skeleton. Considerable attention has been devoted to thiahelicenes and azahelicenes but very few oxahelicenes are synthesized and studied till date. Moreover, the synthetic methods to embed furan ring into a helicene framework has not been well explored.

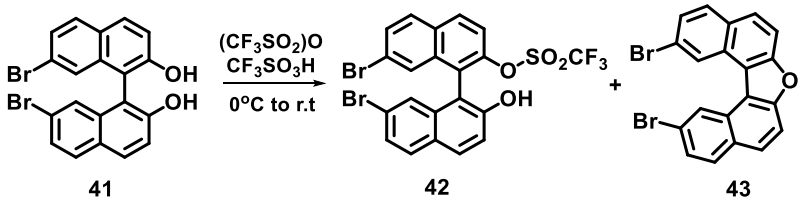
One of the most convenient strategy to construct furan ring in a helical framework is the use of BINOL based systems. Carolina *et al* synthesized 7-oxa-[5]helicerne-3,11-dicarboxylic acid from reported *rac*-6,6'-dibromo-1,1'-binaphthol, and their complexes with Co and Cu were synthesized and studied for their self-aggregation property.[58] However, the yields were extremely poor and scaling-up was a major problem. The first multigram synthesis of oxa[5]helicene derivatives was reported by Thongpanchang using 2,7-

dihydroxynaphthalene **(37)**, followed by its C-C homo coupling and subsequent dehydration**.** These oxa[5]helicene derivatives **(40)** were however, found to be planar and hence achiral.[59]

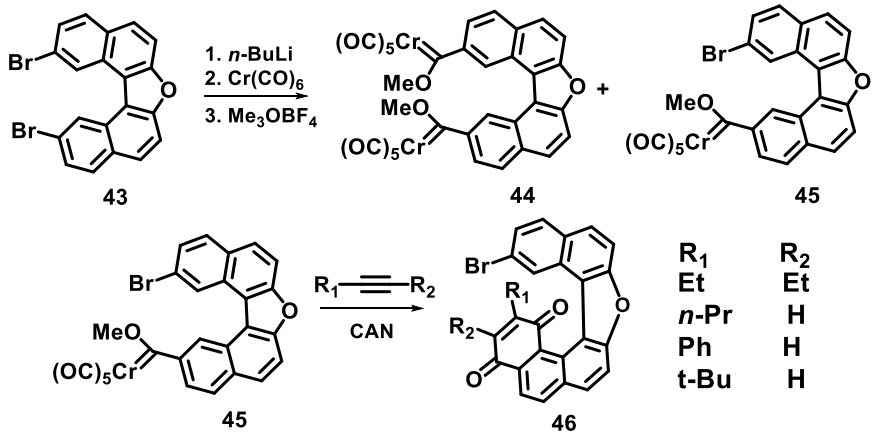



**Scheme 4 Synthesis of 2,12-disubstituted-7-oxa[5]helicenes (40)**

Using a similar strategy, Dotz and coworkers synthesized a series of [5]helicenes by activation of one of the –OH groups of 7,7'-dibromo-2,2'-dihydroxy binaphthyl, followed by intramolecular cyclization to obtain substituted [5]helicenes **(43)**. They were then subjected to chromium-templated benzannulation reaction with various alkynes to give higher members of helical mono- and bis-quinone oxahelicenes **(46)**.[60]

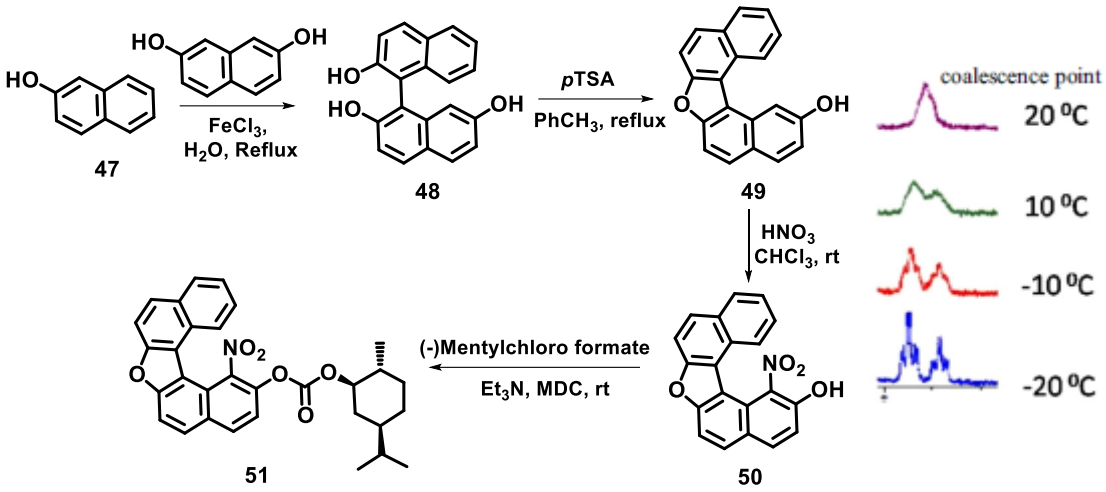



**Scheme 5 Synthesis of oxa[5]helicene (43)**



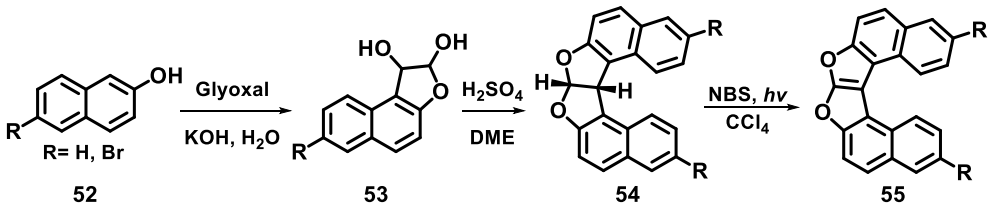

**Scheme 6 Synthesis of helical quinones using chromium carbine complexes (46)**

The relatively flat structure of oxa[5]helicene unit was established by single crystal X-ray diffraction analysis of one of its derivative 2-hydroxy-7-oxa[5]helicene **(49)** indicating the absence of stable helical enantiomers. However, the introduction of nitro group at 1-position of the oxa[5]helicene **(50)** provides sufficient steric crowding to observe the presence of two helical isomers at low temperature, as confirmed by $^{1}$H NMR at -20$^{o}$C.[61]




**Scheme 7 (a) Synthesis of 1-nitro-2-hydroxy-7-oxa[5]helicene (50) and its menthyl carbonate (51) (b) VT NMR showing the signal for proton at chiral center**

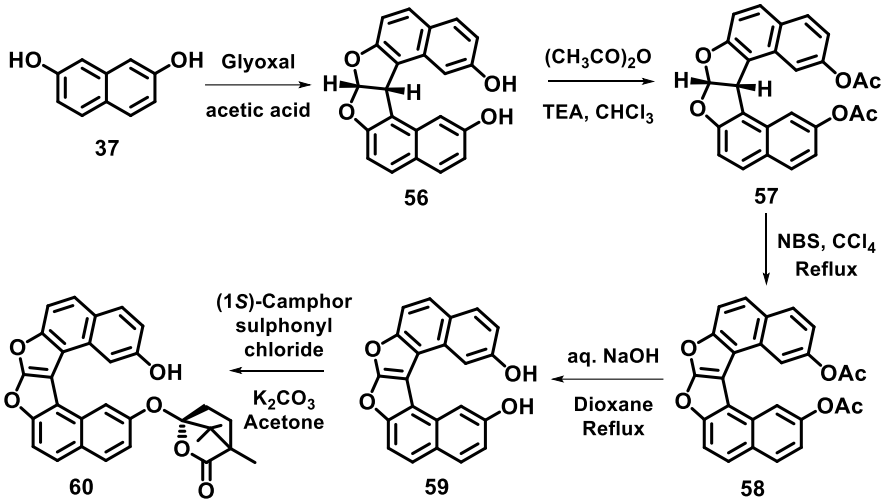
However the enantiomers of 1-substituted oxa[5]helicenes could not be resolved due to their rapid racemization at room temperatures. Hence much focus was then shifted to the synthesis of higher analogues of oxahelicenes. Bechgaad *et al* synthesized dioxa[6]helicene **(55)** which was the immediate next analogue of oxa[5]helicene having an additional furan ring instead of a benzene ring in its backbone.[62]



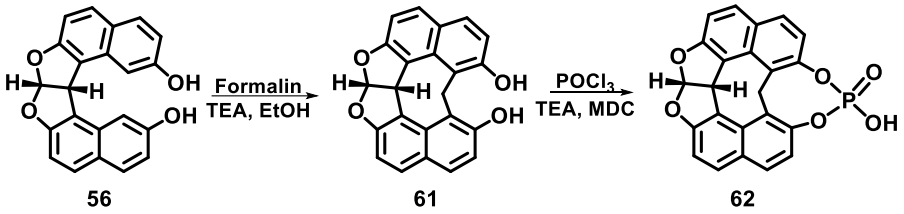

**Scheme 8 Synthesis of dioxa[6]helicene (55)**

This synthetic strategy paved a way for the synthesis of various derivatives of dioxa[6]helicene. Karnik *et. al.* reported dioxa[6]helicene diol **(59)**, using a slightly modified strategy. Dioxa[6]helicene diol **(59)** was sufficiently helical to be resolved by forming diastereomers with optically active camphor sulfonyl chloride (Scheme 9). The optically pure dioxa[6]helicene diol was utilized as a sensor for recognition of *trans*-1,2-cyclohexanediamine using various spectrophotometric techniques.[63,64]

The same group later developed C*s*-symmetric rigid achiral organophosphoric acid **(62)** from dihyrodioxa[6]helicene diol (Scheme 10) and utilized them as a chiral system for the determination of absolute configuration of 1,2-amino alcohols by induced CD (ICD) studies.[65]

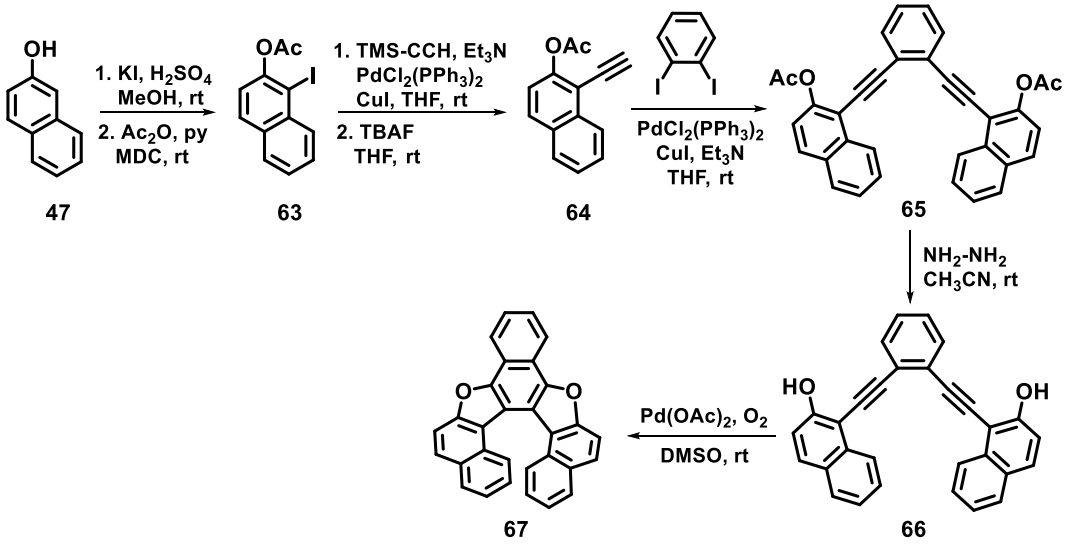



**Scheme 9** **Synthesis of dioxa[6]helicene diol (59)**



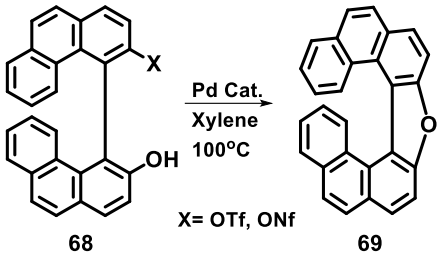

**Scheme 10** **Synthesis of phosphoric acids derived from dihyrodioxa[6]helicene**

The 5- and 6- ringed members of oxahelicenes were easy to synthesize but, oxa[7]helicene and higher members were difficult to synthesize. Dioxa[7]helicene **(67)** where two naphthafuran units are *ortho*-fused to a central benzene ring, was synthesized by oxidative tandem cyclization of the *o*-phenylene linked bis-2-naphthol.[66] It was successfully resolved using chiral HPLC but rapidly isomerize at ambient temperatures.



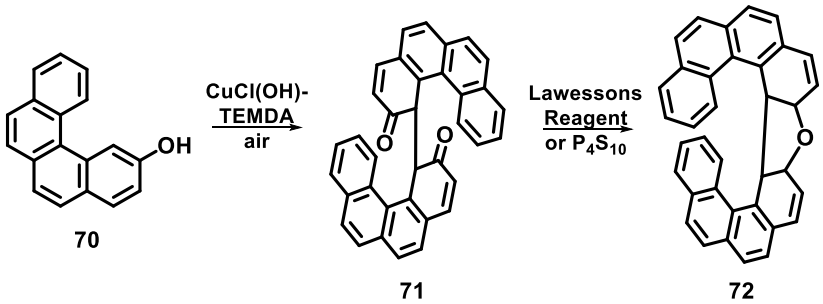

**Scheme 11** **Synthesis of naphtha fused dioxa[7]helicene (67)**

The unsuccessful resolution of dioxa[7]helicene **(67)** lead to the synthesis of oxa[7]helicene, which has the presence of a single furan moiety in the carbohelical backbone. Nozaki *et al* used a strategy similar to the Thongpanchang methodology (for the synthesis of oxa[5]helicenes from BINOL) using various analogues of BINOL and its derivatives. Pd-catalysed intramolecular *O*-arylation of mono triflates or nonaflates of the starting biaryl derivatives gave oxa[7]helicenes with excellent yield.[67] The oxahelicenes could be successfully obtained in their optically active forms by the resolution of the biaryl intermediate using commercially available camphor sulfonyl chloride. However, oxa[7]helicene **(69)** was found to racemize at a temperature of 100°C.




**Scheme 12 Synthesis of oxahelicene by Pd-catalyzed arylation of triflates/ nonaflates**

The C-C oxidative coupling of naphthols and its analogues often lead to the formation of helical quinones in considerable quantities leading to drop in the yields of the desired helicene. Salim *et.al.* treated these helical quinones with Lawesson's reagent or phosphorus pentasulfide to obtain the corresponding oxahelicene in yields ranging from 32-87%.[68–70] They successfully synthesized oxa[9]helicene **(72)** using this method.




**Scheme 13 Synthesis of oxa[9]helicene (72) from helical bis-quinone (71)**

The synthesized oxa[9]helicene derivatives were then successfully resolved using chiral HPLC.[70] Various oxa[9]helicenes derivatives namely 11-oxa[9]helicene and 9-diethyleneglycoxy-11-oxa[9]helicene have been synthesized using this strategy and utilized in the preparation of thin monolayered films by the Langmuir technique.[71]

To compare the difference in the optical and electronic properties of oxahelicenes due to increasing ring number, Tsubaki *et. al.* synthesized a series of oligonaphthofurans **(73-75)** having alternating naphthalene and furan fused ring systems. Comparison between these molecules revealed that as the number of aromatic rings of the oligonaphthofurans increased, the absorption peak at the longest wavelength in the UV−Vis spectra steadily red-shifted. These molecules also showed an effective spreading of the π-electrons and were found to be more rigid. Such properties provide extremely useful information for the development of new features in 3D π-systems and their application in devices.[72]

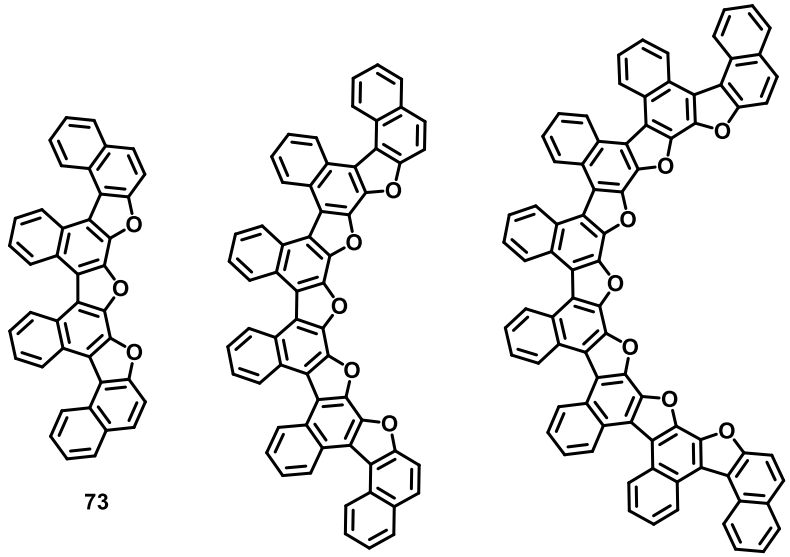
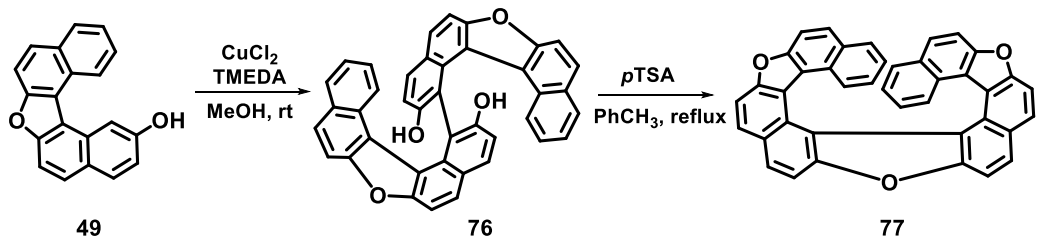



**Figure 7 Oligonaphthofurans (73-75) synthesized by Tsubaki *et. al.***

The largest oxahelicene reported in literature till present is 7,12,17-trioxa[11]helicene **(77)**. This 11-membered trioxahelicene was synthesized by a combination of oxidative coupling and dehydrative cyclization. The final helicene was characterized by single-crystal X-ray diffraction and photochemical studies showed interesting properties.[73]




**Scheme 14 Synthesis of 7,12,17-trioxa[11]helicene (77)**

## 3.1.4 Resolution of Helicenes:

The chiral resolution of helicenes into their *M* and *P* enantiomers is essential to take advantage of their chiral nature. Helicenes can be resolved if the interconversion barrier between the two enantiomers, is sufficiently high. For [3]-, [4]- and [5]helicenes, racemization occurs readily at room temperature while for [6]helicenes and higher members are configurationally more stable and hence resolvable. However, the addition of bulky substituents on the terminal rings of lower helicenes may add to the enantiomeric stability of the molecule making its resolution possible.[74] Once the helical enantiomers are separated, they must have a sufficiently high barrier of racemization so that the optical purity is not lost in the application process. To the best of our knowledge, there is a narrow range of robust methodologies for the chiral resolution of helicenes. Use of various analytical tools for such resolution has been well reported in literature. The use of chiral HPLC,[75–78] with different chiral stationary phases to obtain enantiopure helicenes from a racemic mixture is one of the most exploited method for resolution of such molecules. These chiral stationary phases are silica modified with tetranitro-9-fluorenylidene-aminooxy, substituted organic acids, amylose or cellulose derivatives.[79–81] Although this technique is quantitative, sensitive and extremely precise, it often suffers from various disadvantages like: continuous need for new stationary phases for efficient resolution of helicenes as some stationary phases are very selective towards the recognition of helicenes. Also this technique is not cost effective as it utilizes expensive chiral columns as well as it may be time consuming. Another analytical tool frequently used for the chiral separation of helicenes is Capillary Electrophoresis.[82,83] High sensitivity of this methodology towards slight changes in pH, makes this technique a lesser choice for the resolution of helicenes. Helicenes are good π-donars which has been used for the resolution of racemic non-functionalized hexahelicene by forming a charge transfer complex with electron-deficient molecule TAPA.[5,20]

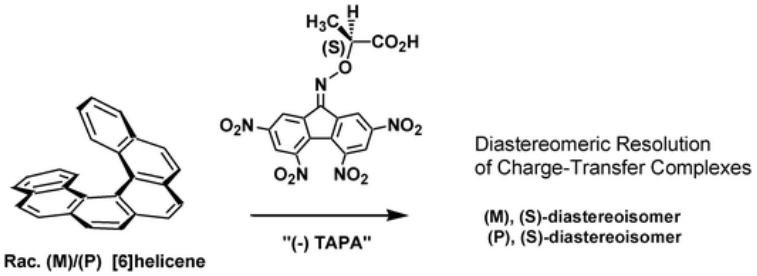
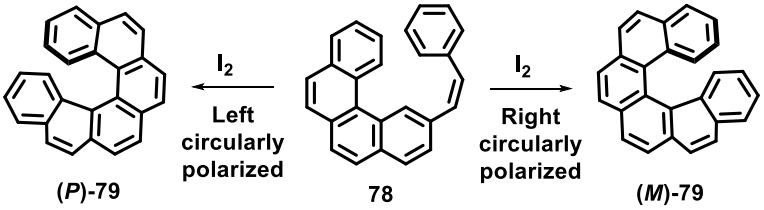


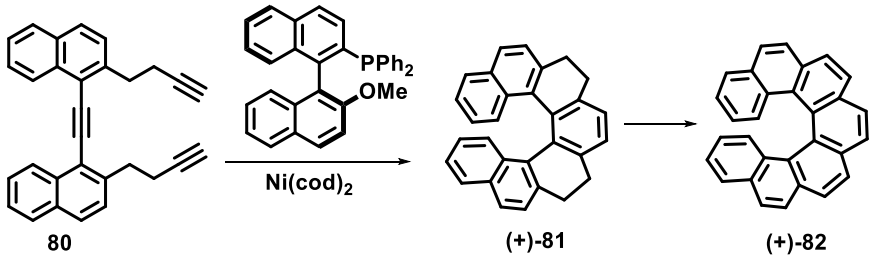

**Figure 8 Resolution of [6]helicene by charge transfer complex formation with TAPA**

Asymmetric synthesis is another strategy which uses stereochemical control to obtain non-racemic products or rarely a single enantiomer without the need of an additional step for the resolution. The first example of asymmetric synthesis for helical molecules was reported in 1971 by Kagan who synthesized hexahelicene in enantio-enriched form having 20% *ee* by using circularly polarized light.[84]



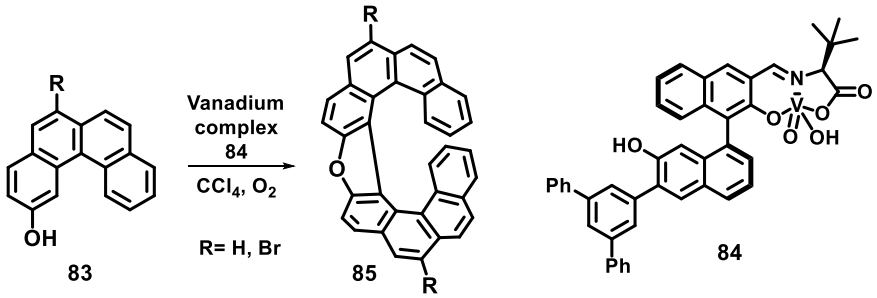

**Scheme 15 Asymmetric synthesis of hexahelicene using circularly polarized light**

Other methods for asymmetric synthesis of helicenes involve the use of Katz methodology of Diels-Alder reaction for the enantioselective synthesis of helical quinones,[85–87] diastereoselective oxy-Cope rearrangement,[88] use of an enantiopure,[89] the use of chiral phosphine ligands in palladium catalyzed cyclizations[90] *etc.* The first metal mediated enantioselective synthesis of helicene by cycloisomerization of triyne utilized $Ni^0$ catalyst with a chiral binaphthyl-derived phosphine ligand as a chiral inducer. Such enantioselective cyclization of **80** gives 40% *ee* of (+)-**81**.[91]




**Scheme 16 Nickel mediated enantioselective synthesis of heptahelicene (82)**

Sako *et. al.* successfully used BINOL-based chiral vanadium complex **(84)** for the synthesis of oxa[9]helicene **(85)** in 94% *ee* starting from polycyclic phenols. The reaction proceeds *via* oxidative coupling, followed by intramolecular cyclization.[92]

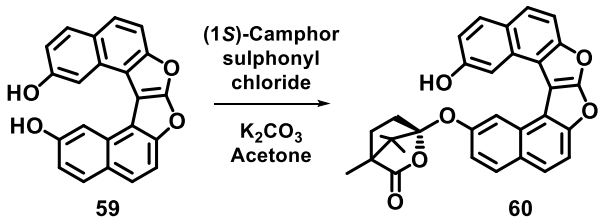



**Scheme 17 BINOL-Vanadium complex catalyzed asymmetric synthesis of 85**

Recently, [60]fullerene was used for resolution of [6]helicene by using catalytic amounts of a chiral reagent. The helicene-fullerene diastereomer was then separated efficiently using column chromatography which gave access to both the enantiomers of the helicene.[93]

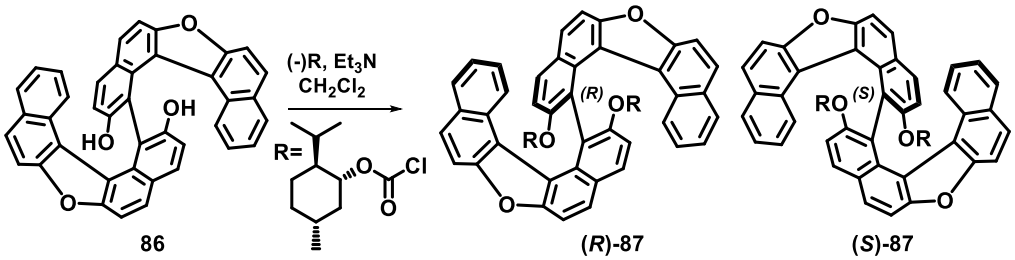
Regardless of such recent progress and intriguing past achievements, the racemate resolution dominates in attaining enantiomerically pure helicenes and its derivatives. In the case of functionalized helicenes the major methods of optical resolution are based on diastereomeric salt formation using chiral reagents,[94,95] chromatographic separation of diastereomers[96–98] or enzymatic resolution.[99,100] A conventional method involved in the resolution of helicenes comprises the use of chiral resolving agents to obtain diastereomeric species which can be easily separated. The chiral resolving agent can be regenerated after diastereomeric separation by mild cleavage leading to efficient resolution of the helicene. This can be achieved either at stages prior to the synthesis of helicene, where the chirally resolved intermediate can be converted to corresponding helicene without the loss of stereochemistry during the course of reaction, or the helicenes can be resolved after their synthesis.[101] The use of chiral resolving agents such as (*S*)-camphanic acid,[67,96,102] (*R*)-menthyl chloroformate, [61,103] derivatives of amino acids,[104] *etc.* to obtain chromatographically separable diastereomers has been well reported. This approach has a distinct advantage of attaching and detaching a chiral auxiliary before and after the diastereomeric separation, making the whole procedure recyclable, highly efficient and hence the process of choice for resolution of helicenes.

For substituted helicenes bearing free –OH group, the use of various resolving agents that for diastereomeric esters or carbonates have been reported in literature. One such example was described by Karnik *et al* who carried out selective mono esterification of dioxa[6]helicene diol **(59)** with chiral (1*S*)-camphor sulphonyl chloride in acetone afforded diastereomers **(60)** which were separated using chiral HPLC.[63]



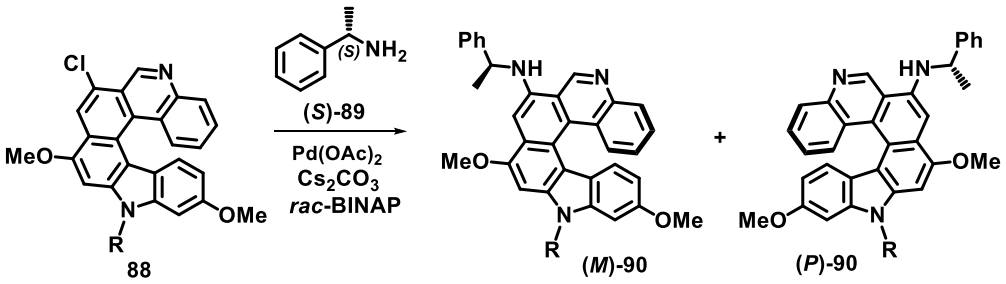

**Scheme 18 Resolution of dioxa[6]helicene (59) using camphor sulphonyl chloride**

Karikomi *et al* have used optically pure menthyl chloro formate for the resolution of atropisomeric biaryl diol (Scheme 19). The diastereomeric carbonates hence formed were resolved using HPLC, after which the pure enantiomers of biaryl diol were regenerated by mild hydrolysis.[103]




**Scheme 19 Use of menthyl chloro formate as chiral resolving agent**

The helicenes possessing halogen group can be subjected to Pd-catalyzed Buchwald–Hartwig coupling with optically pure amines giving chromatographically separable diastereomers. This approach has been used by Dehaen *et al*. utilizing *S*-(-)-α-methyl benzylamine **(*S*)-89** along with 10 mol % $Pd(OAc)_2$ to chloro substituted aza[6]helicene derivative. The diastereomers obtained **(*P*)-90** and **(*M*)-90**, were readily separated using column chromatography.[105]



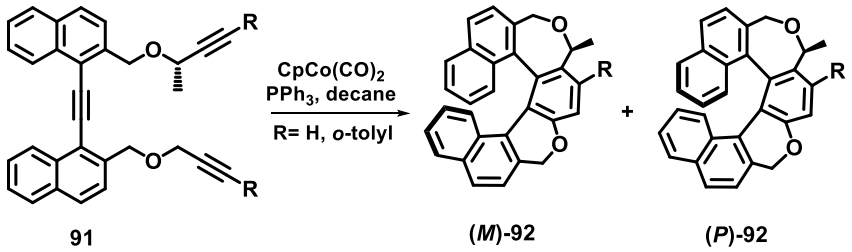

**Scheme 20 Use of (*S*)-phenyl ethyl amine as resolving agent**

## 3.1.5 Oxahelicene-like compounds:

Besides the well-defined helicenes, there are molecules having structure resembling to that of helicenes, called helicene-like molecules or helicenoids. T molecules contain at least one saturated atom as a part of the ring system of the helicene core. For example, saturated hydrocarbon-containing helicenes, which are actually dihydrohelicenes, are well documented in literature as precursors for helicene synthesis. Similarly, a series BINOL-based helical systems are referred to as oxahelicene-like, have been reported the literature. For this class of molecules, the saturated ring is not able to adopt a planar structure, resulting in the enhancement of helicity rendering them to be configurationally stable. Such

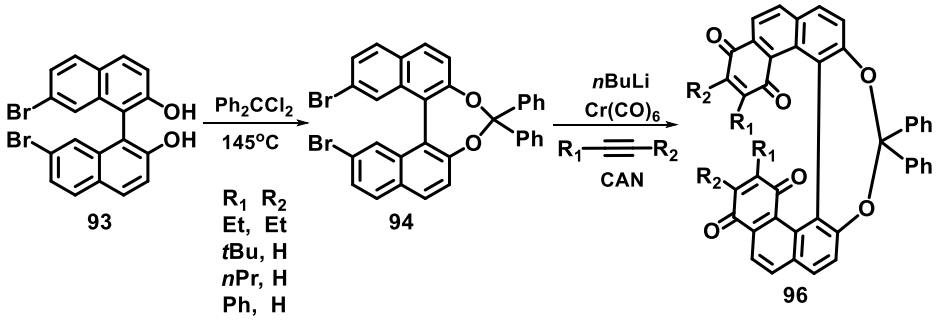
molecules play a vital role in crafting of new chiroptically active molecules which has broadened its scope of application in materials, catalysis and DNA binding.[106,107]

The first report for the synthesis of oxahelicene-like compounds was made by Stary and Stara. They developed a methodology for the synthesis of oxa[5] and oxa[7]helicene-like compounds, utilizing $CpCo(CO)_2/PPh_3$ and substituted trialkynes to give a [2+2+2] cycloisomerization with 46% *de* to 100% *de*.[108–114]



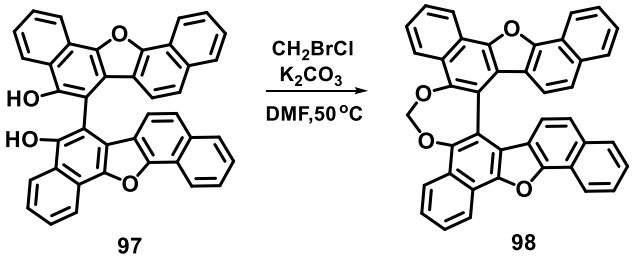

**Scheme 21 Diastereomeric synthesis of 92 using [2+2+2] cycloisomerization**

Another organometallic approach to novel, functionalised, helicene-like bisquinones **(96)** had been developed based on the chromium-templated [3+2+1] benzannulation reaction.[113]



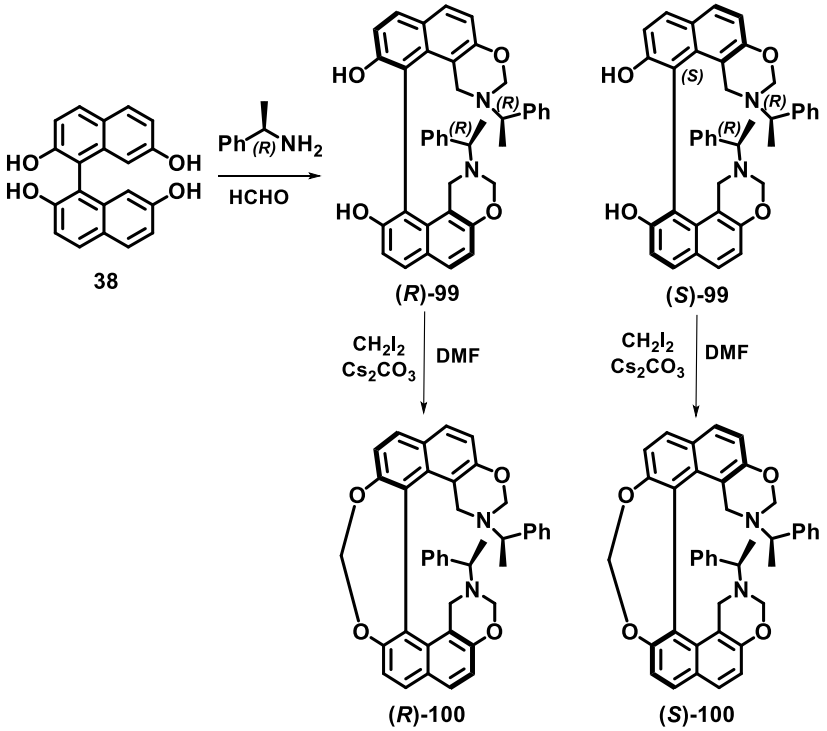

**Scheme 22 Synthesis of helicene-like bisquinones (96)**

Another synthetic target bis(dinaphthofuran)diol was synthesized by Tsubaki *et al* and successfully resolved by chiral HPLC. It was found that bis(dinaphthofuran)diol easily racemized at room temperature. On the other hand, racemization of enantiomerically pure oxahelicene-like derivative did not occur. These results indicate that the methylene bridge in helicene-like compounds, prevents racemization of the axial chirality.[115]



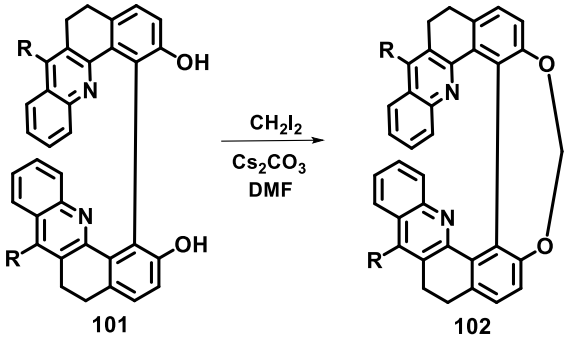

**Scheme 23 Synthesis of oxahelicene-like derivative from bis(dinaphthofuran)diol**

Another system 1,3-oxazines condensed with aromatic moiety has gained considerable attention due to their wide applicability in pharmaceutical and biological sciences as anti-cancer, anti-fungal, anti-inflammatory, and anti-bacterial agents.[116] Owing to their importance, our group has reported a series of novel 1,3-oxazines on a binaphthyl framework **(100)** which were easily separable showing good thermal stability.[114]



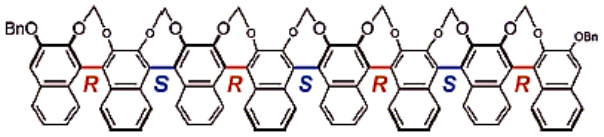

**Scheme 24 Synthesis of optically pure helicene-like oxazines (100)**

Acridine is another such motif having fluorescent nature which was exploited by Lyon *et al* by synthesizing dibenzo[*c*]acridine helicene-like compounds **(102)** on a large scale in pure enantiomeric form showing enhanced chiro-optic properties.[117]




**Scheme 25 Synthesis of helicene-like acridine derivatives (102)**

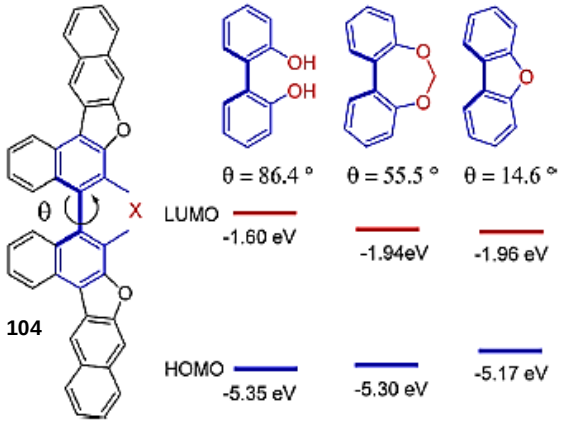
To study the effect of number of methylene bridges and naphthalene rings on the optical properties of oxahelicene-like molecules, Tsubaki *et al* synthesized axially chiral 2,2′-methylenedioxy-bridged-1,1′-binaphthyls, quaternaphthalenes, and octinaphthalenes. DFT calculations showed that the LUMO and HOMO of these bridged oligonaphthalenes were spread over a wide range which could be modulated to suit various applications.[118] The CPL and fluorescence quantum yields of these molecules both in solution as well as solid state. This is one of the highest solid-state CPL $g_{lum}$ values reported.[119]




103

**Figure 9 Bowl shaped oligonaphthalenes (103) with methylenedioxy bridges**

However, a more direct comparison of optical properties between biaryl, corresponding oxahelicene and oxahelicene-like was reported by the same authors. A close correlation between the dihedral angle formed by adjacent dinaphthofuran rings and/or the sizes of the fused aromatic rings on the optical band gap and other properties was determined.[120]




104

**Figure 10 HOMO-LUMO levels of biaryl, helicene-like and helical derivatives**

## 3.2 Results and Discussion:

### 3.2.1 Synthesis of optically pure oxa[7]helicene and helicene-like molecules:

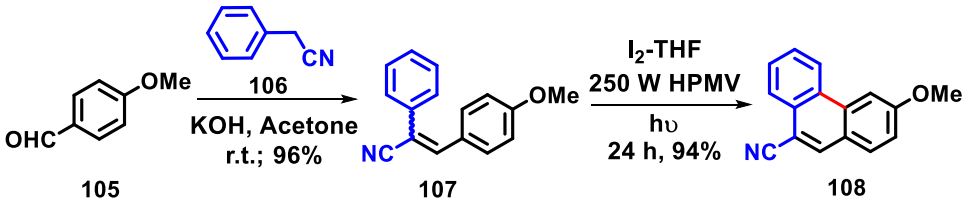
Our group has been actively involved in the synthesis of oxygen containing helicenes and their helicene-like analogues due to their applications in various fields of chemistry as well as material sciences. The smallest member of oxahelicene family is [5]oxahelicene. Various literature reports on unsubstituted oxa[5]helicenes and 1-substituted oxa[5]helicenes have led to a generalization that oxa[5]helicenes are incapable of showing enantiomerism at room temperature. The two enantiomers are conformationally labile undergoing rapid flipping leading to racemization, thus making the isolation of oxa[5]helicenes in their optically pure form difficult.[121] To overcome this problem, we planned to introduced additional aromatic rings at both the termini of oxa[5]helicene which would provide sufficient bulk to the helicene skeleton to render enantiomers stable at room temperature.

In the present work, we have synthesized oxa[7]helicene bearing cyano functionality symmetrically positioned on the helicene core in their enantiomerically pure forms. The -CN functionality is not only a known precursor for various functional group interconversions, but also influences the photophysical response by changing the energy levels of the HOMO and LUMO orbitals. In some cases it assists in the formation of supramolecular assemblies due to its ability to undergo various non-covalent interactions.[122–124] Literature reports show that the presence of electron withdrawing groups favours the stability of the furan moiety and hence, we expected cyano group will prove to be useful in stabilizing the target oxa[7]helicene. These benefits encouraged us to synthesize symmetrical oxa[7]helicene and helicene-like compounds bearing cyano groups and compare their optical properties.

Since the introduction of furan ring in the early stages of synthesis is not feasible due to its labile nature and tendency to undergo ring opening even under mild conditions, we designed the retrosynthetic scheme such that the furan moiety is introduced in the last step. The target compound could be obtained by cyclodehydration of the corresponding bis-phenanthrol which is a BINOL analogue. The bis-phenanthrol can in turn be obtained from C-C oxidative homocoupling of phenanthrol derivative. As phenanthrene motifs are easy to synthesize on a multi-gram scale using various techniques, this retrosynthetic scheme

proved to be ideal for the synthesis of target molecules. We utilized the photodehydrogenative method for the synthesis of phenanthrene skeleton due to the presence of a library of methodologies available for the synthesis of stilbenes. The multi-gram synthesis of stilbenes from commercially available starting material, proves to be beneficial as they serve as precursors for the synthesis of phenanthrenes.

The Knoevenagel reaction is one for the most explored and widely used methods for the synthesis of olefins. This reaction is very efficient with aldehydes and reactants possessing active methylene group. Benzyl cyanide and methoxy substituted benzaldehyde were the reagents of choice. The advantage of using benzyl cyanide was the enhanced activation of benzylic methylene group due to the presence of cyano functionality and the introduction of –CN in the preliminary step itself. Methoxy substituted aldehyde was used as the condensation partner to make the aldehyde more reactive and also the need for accessing a handle for C-C oxidative coupling during later stages of synthesis. Knoevenagel condensation between benzyl cyanide **(106)** and *p*-anisaldehyde **(105)** in presence of potassium hydroxide in acetone at room temperature gave us the desired stilbene precursor **(107)** in almost quantitative yield. This stilbene derivative was then subjected to dehydrogenative photocyclization using stoichiometric iodine as the oxidizing agent and tetrahydrofuran as HI scavenger in toluene.[125] The solution was irradiated by a 250W HPMVL for 24 hours giving our desired phenanthrene **(108)** as the only product with good conversion.

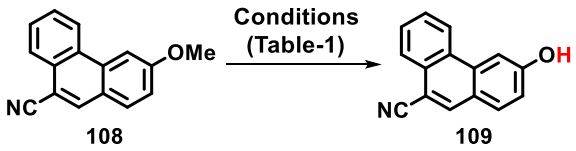



**Scheme 26 Synthesis of 3-methoxyphenanthrene-9-carbonitrile (108)**

Both the functional groups –CN and $–OCH_3$ which are sensitive in nature, remained intact during the photocyclization which was confirmed by various spectroscopic tools like $^1H$ NMR, $^{13}C$ NMR and IR spectroscopy. $^1H$ NMR of **108** showed the disappearance of olefinic proton and appearance of a sharp singlet in the downfield region at **δ** 8.21 which corresponds to the proton *ortho* to –CN group and a signal for three protons at **δ** 4.07 which proves that $–OCH_3$ group has not been affected during the reaction. The presence of –CN group was proved using $^{13}C$ NMR where signal at **δ** 160.96 corresponds to the carbon atom of the –

CN group which was also confirmed by IR spectroscopy which showed a sharp band at ν 2217 $cm^{-1}$ characteristic to the –C≡N stretching frequency.

To generate free –OH from the protected precursor required neutral condition due to the fact that the –CN group present on the phenanthrene core may undergo hydrolysis, both in acidic as well as basic conditions. Utilizing $BBr_3$ or HBr-Acetic acid[126] are known to hydrolyze cyano group during deprotection of –OMe.[127] Hence a method was developed utilizing mild Lewis acid (lithium and sodium halide salts) and heating at high temperatures.[128] A comparison of individual reactions with NaBr, NaI, LiCl and LiBr showed us that LiBr[129] showed better conversion as compared to other salts where the conversions were poor and starting material was recovered. We also studied the effect of certain additives like TBAB which acts as a phase transfer catalyst and Montmorillonite K10 which is weakly acidic in nature, expecting them to promote the reaction in the forward direction. It was found that there was an increase in the yield of the desired product, but the best condition involved the use of 100% w/w 4Å MS in refluxing in AR grade DMF and excess of LiBr (2 eq.).




108 109

**Scheme 27 Synthesis of 3-hydroxyphenanthrene-9-carbonitrile**

**Table 1 Conditions studied for cleavage of methoxy group of 108[a]**

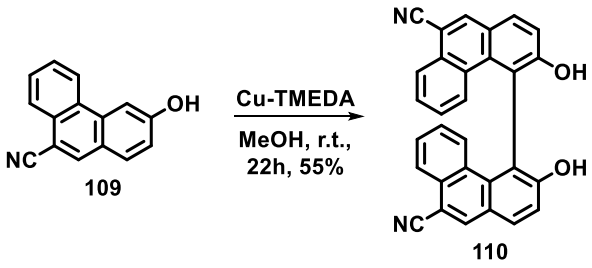
| No | Additive | **109** (% Y) | **108** (% Y) |
|---|---|---|---|
| 1 | -- | 37 | 63 |
| 2 | TBAB (0.1 eq.) | 51 | 49 |
| 3 | Mont-K10 (40 % w/w) | 73 | 25 |
| 4 | Mont-K10 (100 % w/w) | 82 | 16 |
| 5 | 4A MS (40 % w/w) | 65 | 32 |
| 6 | 4A MS (100 % w/w) | 85 | 12 |

[a]LiBr (2 eq.), DMF, 180°C, 24 h.

The structure of 3-hydroxyphenanthrene-9-carbonitrile **(109)** was confirmed by disappearance of the signal for –OC*H*$_3$ protons and appearance of a broad singlet at **δ** 5.69 in $^1$H NMR. The IR spectra clearly showed a broad peak at ν 3404 $cm^{-1}$ which is characteristic O-H stretching frequency and a sharp band at ν 2216 $cm^{-1}$ showing that the

cyano group is not cleaved during this deprotection step. Hence a practical method was developed for the synthesis of 3-hydroxyphenanthrene-9-carbonitrile **(109)** in good yields.

Considerable attention has been devoted to oxidative biaryl coupling of phenols due to its wide utility in synthetic reactions and its involvement in the biosynthesis of many natural products containing biaryl motif. The most straightforward approach for the synthesis of biaryls is by coupling two aromatic partners to generate a stereogenic axis. Transition metal salts or complexes are often employed either in stoichiometric or catalytic amounts for such coupling reactions as they can undergo single electron transfer and promote keto-enol tautomerism which are essential for such reactions. Some of the well documented transition metal systems used in the formation of C-C bonds are Fe(III),[73][130] Mn(III),[131] Cu(II)-amine,[132] CuCl(OH)-TMEDA/$O_2$,[133] V complexes[134] *etc.* The advantage of constructing biaryl motif is their atropismomeric nature which renders them as chiral. These compounds can be resolved, providing access to enantiomerically pure biaryls, which act as a source of chirality and can be used in building other chiral motifs. BINOL, VANOL and VAPOL are some of the important biaryl systems which are used profusely in asymmetric catalysis, chiral recognition and optics.[135,136] Due to their wide applicability, the synthesis of BINOL and its derivatives from corresponding naphthols has been well documented in the literature. Utilizing a similar strategy of oxidative coupling using Cu·TMEDA[133,137] in methanol at ambient conditions, the synthesized precursor, 3-hydroxyphenanthrene-9-carbonitrile **(109)** was subjected to C-C homocoupling reaction to afford (±)-**110** in moderate yield.

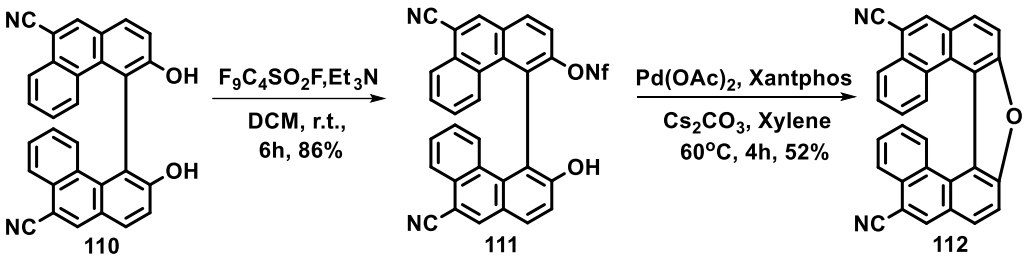



**Scheme 28 Synthesis of bis-phenanthrol (110)**

The mechanism for such C-C oxidative coupling often produces a mixture of regioisomers where coupling can occur at C1 or C3 at both the positions are activated by the presence of neighboring –OH group. The coupling reaction proceeds regioselectively at C1 position of 3-hydroxyphenanthrene-9-carbonitrile **(109)**. The reaction involves the formation of keto dimer intermediate which maybe is highly unstable and hence readily undergoes keto-enol tautomerism to give the corresponding bis-phenanthrol derivative as the only product. $^1$H

NMR for this compound showed half the number of expected signals owing to its symmetrical nature. The signal for the proton next to –CN is shifted further downfield to δ 8.69 along with the disappearance of the signal for proton at 4$^{th}$ position. HRMS for this compound showed [M+Na] peak and the exact mass *m/z* 459.1109 is in accordance with the structure.

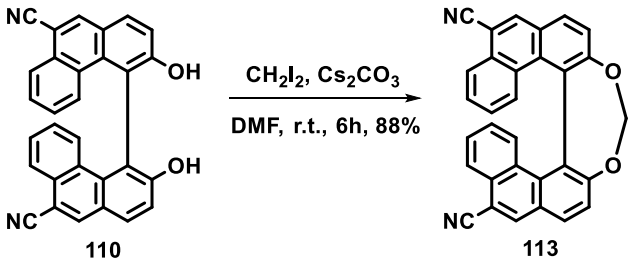
Attempts to perform acid catalyzed dehydration reaction of this diol with *p*TSA, conc. $H_2SO_4$ and using solid acidic catalysts like Montmorillonite K10 resulted in either no reaction or decomposition of the starting material. Hence, we resorted to palladium catalyzed cyclization after due activation of the diol.[67] The activation of one of the –OH groups to facilitate nucleophilic attack was necessary for intramolecular cyclization to form the furan ring. Hence, **110** was converted to its mono nonafluoro sulfonate **111** by the known procedure and subjected to cyclization with palladium acetate-xantphos catalyst system.




**Scheme 29 Synthesis of (±)-5,13-dicyano-9-oxa[7]helicene (112)**

The cyclized product, 5,13-dicyano-9-oxa[7]helicene **112** was isolated in moderate yield. The structure was established by usual spectral analysis, particularly by $^1$H NMR which showed signals typical for helicenes. Protons attached to C1 and C17 fall underneath the terminal aromatic rings and hence shielded due to anisotropy, shifting upfield to **δ** 6.47.

The other class of helicene-like compounds diarylated[*d*,*f*][1,3]dioxepine analogues are also subject of the present study. Thus, the diol **110** were subjected to ether formation with diiodomethane and $Cs_2CO_3$ as base. The resultant dioxepine derivative **113** were obtained in good yields.

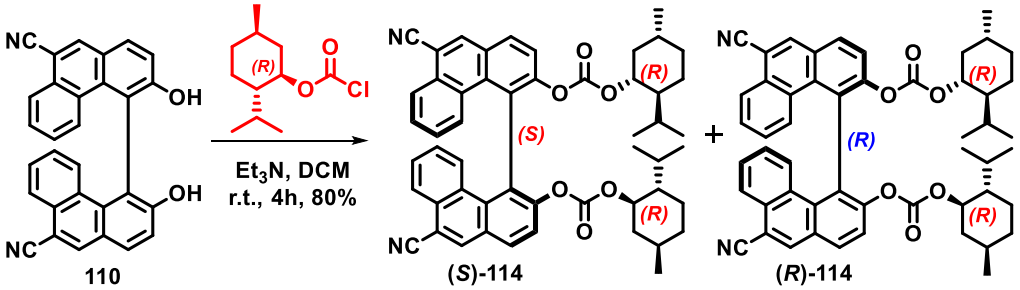



**Scheme 30 Synthesis of diarylated[d,f][1,3]dioxepine (113)**

## 3.2.2 Resolution of 3,3'-dihydroxybiphenanthrene dicarbonitrile:

The resolution of atropisomeric compounds is a challenging task in synthetic organic chemistry. The simplest way to resolve them involves the formation of diastereomers either by chemical bond formation or cocrystallization using an optically pure species called auxiliary. The diastereomers hence formed, can be efficiently separated using physical or chemical tools, yielding optically pure compound and regenerating the auxiliary. The synthesized 3,3'-dihydroxy[4,4'-biphenanthrene]-9,9'-dicarbonitrile **(110)** is one such example of atropisomeric molecules where enantiomerism arises due to the restricted rotation around the C-C bond between the two bulky units.

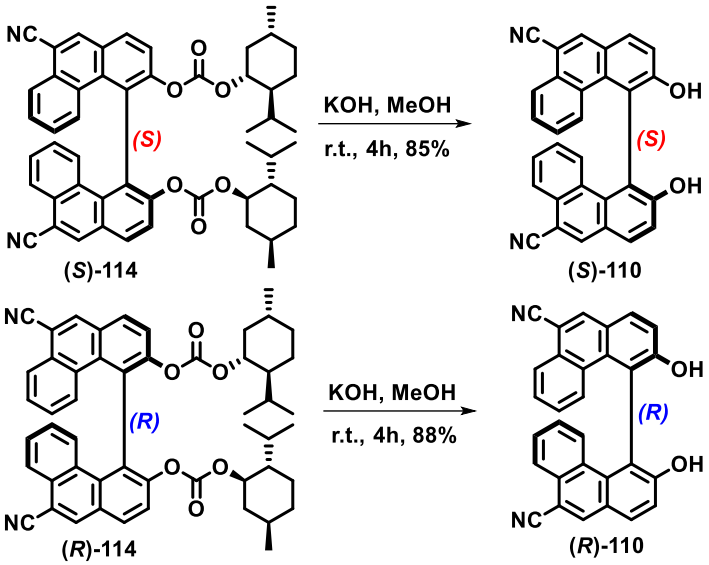
Utilizing the free –OH groups in 3,3'-dihydroxy[4,4'-biphenanthrene]-9,9'-dicarbonitrile **(110)**, it was subjected to biscarbonate formation with optically pure (-)-menthyl chloroformate[138] as the resolving agent (Scheme 31).




**Scheme 31 Synthesis of diastereomeric bis-carbonate using chiral auxiliary**

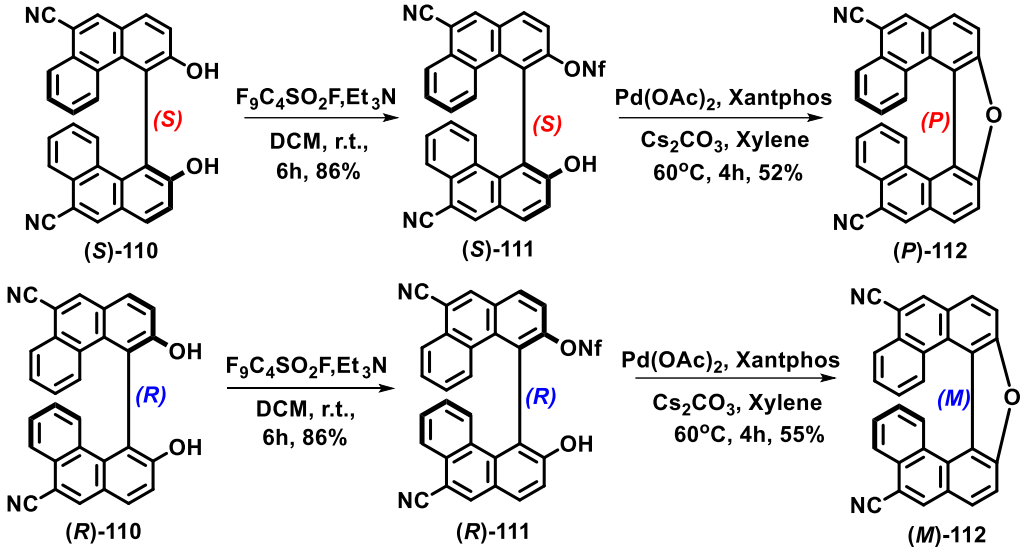
The diastereomeric bis-carbonate **(114)**, was subjected to crystallization in 30% chloroform in hexane giving transparent clear crystals. $^{1}$H NMR spectra for these crystals showed the presence of a single diastereomer which could be easily determined by analyzing the signal for the proton attached to the chiral center of menthyl moiety and comparing it with that of the racemic sample. Its $^{1}$H NMR spectra showed a single set of signal at **δ** 4.02 whereas for the other diastereomer obtained from concentrating the mother liquor showed the same signal at **δ** 4.07 proving that effective separation of diastereomers by simple crystallization.

The separated diastereomers were then subjected to mild basic hydrolysis to access both the enantiomers of 3,3'-dihydroxy[4,4'-biphenanthrene]-9,9'-dicarbonitrile **(110)**. The purity of these enantiomers was later determined using chiral HPLC.

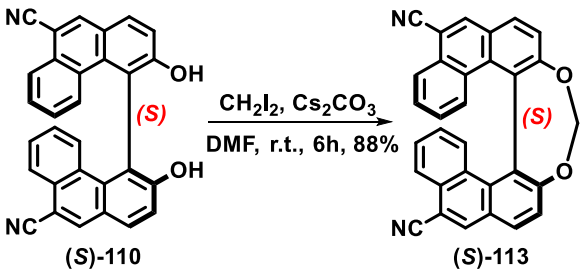



**Scheme 32** **Regeneration of bis-phenanthrol (110)**

Each enantiomer of **110** was subjected to same reaction conditions to obtain our target 5,13-dicyano-9-oxa[7]helicene **(112)** and helicene-like **(113)** in enantiomerically pure form without any racemization.




**Scheme 33** **Synthesis of optically pure oxa[7]helicene (112)**




**Scheme 34** **Synthesis of helicene-like dioxepine (113) as pure enantiomers**

## 3.2.3 Determination of Absolute Configuration:

The absolute configuration of 3,3'-dihydroxy[4,4'-biphenanthrene]-9,9'-dicarbonitrile **(110)** was determined by carrying out SCXRD of the diastereomeric carbonate **(114)** that crystallized out from slow evaporation of its solution in chloroform in hexane was determined by carrying out SCXRD of the crystallized bis-carbonate derivative which was established to be (*S*).

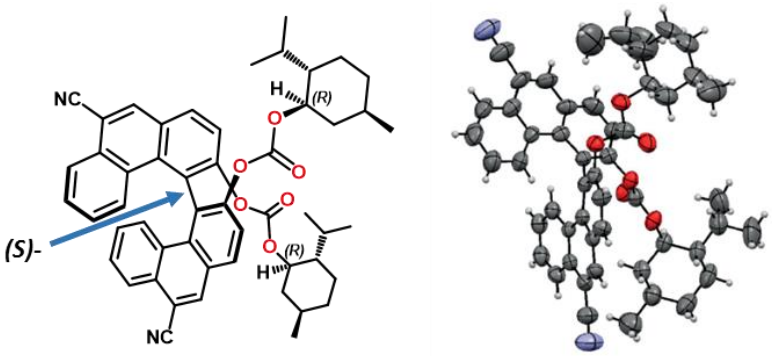



**Figure 11 ORTEP diagram of bis-carbonate derivative for determination of absolute configuration and its diagrammatic representation**

Hence the hydrolysis of **(*S,R,R*)-114** gave (*S*)-3,3'-dihydroxy[4,4'-biphenanthrene]-9,9'-dicarbonitrile **(*S*)-110** and **(*R,R,R*)-114** obtained from mother liquor gave **(*R*)-110.**

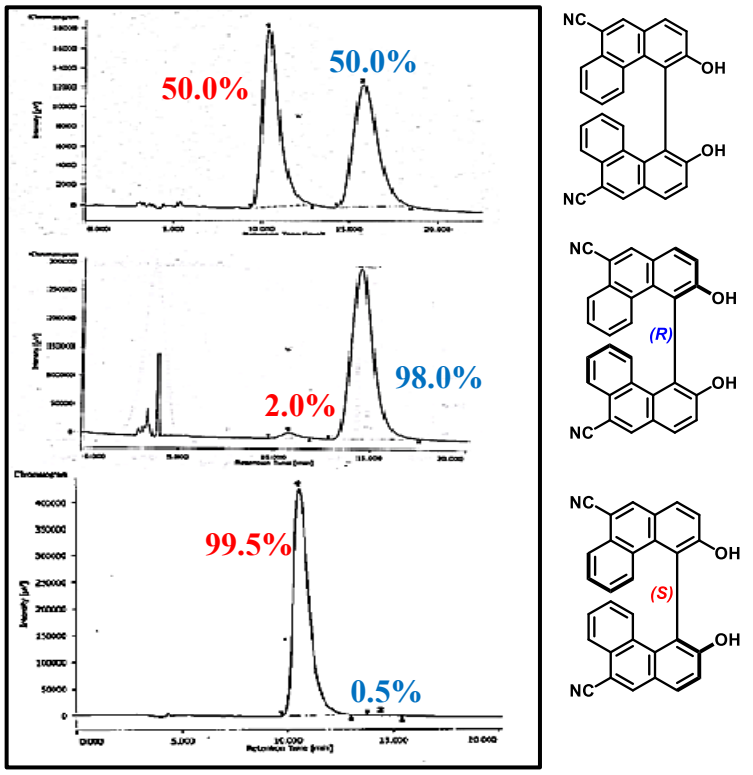



**Figure 12 HPLC chromatogram of bis-phenanthrol (110) after hydrolysis**

The enantiomeric purity was accurately determined by carrying out chiral HPLC of the hydrolysed 3,3'-dihydroxy[4,4'-biphenanthrene]-9,9'-dicarbonitrile **(110)** on chiralpak OD-H, showing that crystals were >99% enantiomerically pure whereas the mother liquor had 96%*ee* and there is no loss in optical purity during hydrolysis.

As the oxa[7]helicene and dioxapine helicene-like molecular skeleton was built on 3,3'-dihydroxy[4,4'-biphenanthrene]-9,9'-dicarbonitrile unit, the stereochemistry was retained in the target molecule *i.e.* (*R*)-3,3'-dihydroxy[4,4'-biphenanthrene]-9,9'-dicarbonitrile **(*R*)-110** gave (*R*)-diphenanthro[3,4-d:4',3'-f][1,3]dioxepine-5,15-dicarbonitrile **(*R*)-113** and (*M*)-5,13-dicyano-9-oxa[7]helicene **(*M*)-112** whereas (*S*)-3,3'-dihydroxy[4,4'-biphenanthrene]-9,9'-dicarbonitrile **(*S*)-110** gave (*S*)-diphenanthro[3,4-d:4',3'-f][1,3]dioxepine-5,15-dicarbonitrile **(*S*)-113** and (*P*)-5,13-dicyano-9-oxa[7]helicene **(*P*)-112**. This was also supported by the SOR and CD measurements stated later.

### 3.2.4 Single Crystal XRD of racemic 5,13-dicyano-9-oxa[7]helicene:

The solid state structure was revealed by carrying out SCXRD for 5,13-dicyano-9-oxa[7]helicene **(112)** which showed characteristic lowering of C-C bond lengths at outer rim of the helical core, while that on the inside rim were found to be slightly elongated in comparison to normal aromatic system. A close comparison of the crystal structures of **112** with unsubstituted oxa[7]helicene was made to determine the role of –CN in crystal packing. Along with the CH–π and π–π interactions, an additional C–N···H–Ar interaction (2.74 Å) was observed. The study of such interactions can be helpful not only in providing a deeper insight into understanding them, but also the energy trends and variation in structural properties. The extent of helicity is determined in terms of the dihedral angles and interplanar angle formed between the terminal rings. This depends not only on the number and type of aromatic rings that make up the helicene skeleton, but also on the substituents present. The sum of five dihedral angles on the inner helical rim was reduced by 2.1° (in case of oxa[7]helicene: 78.9°), to 76.8° in **112**. The angle between the planes passing through the two terminal rings in oxa[7]helicene is reported to be 33.63°, whereas it was found to be 39.64° in **112** which attributes to the higher tolerance of **112** towards racemization as compared to unsubstituted oxa[7]helicene. Hence, the addition of –CN group lead to substantial increase in the interplanar angle of the helicene which is a key aspect in its potential application in various fields of chemistry.

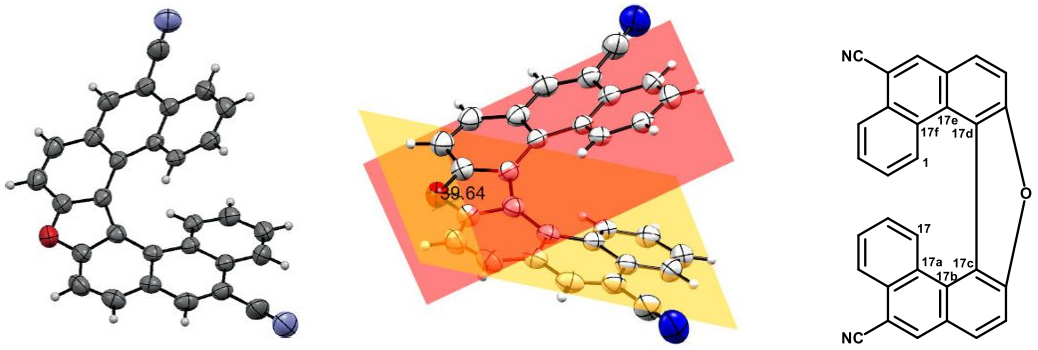



**Figure 13 ORTEP diagram of dicyano oxa[7]helicene showing interplanar angle**

The helical topology of these class of compounds along with the π-delocalization is a typical characteristic and an intrinsic property of such molecules which renders these compounds with unique chiroptic properties. The UV-Vis and CD spectra for heterohelicenes are better resolved as compared to their corresponding carbohelicene analogue which allows one to gather more information related to their electronic features. A direct correlation between the degree of delocalization and chiroptic properties can assist in the modulation of helicenes and related compounds to give desired properties.

## 3.2.5 Comparision of Chiroptic properties of helicene and helicene-like molecules:

### 3.2.5.1 Specific and Molecular Optical Rotation:

One of the important properties of optically pure helical compounds is their high optical rotation ($[\alpha]_D$) and molecular optical rotation ($[\varphi]_D$). Since several years, specific optical rotation (SOR) and circular dichroism (CD) were only utilized to assign absolute configuration of helicenes. Over many years of helicene study, it was concluded that a general relationship between the absolute configuration and the chirality exists *ie.* (*P*)-helicenes are dextrorotatory, while (*M*)-helicenes are levorotatory. The observed values for **112** derived from (*S*)-**110** is positive whereas for that from (*R*)-**110** it is negative leading to the assignment of absolute configuration of **112**. The enantiomer obtained from intramolecular cyclization of (*S*)-**110** is (*P*)-**112** that obtained from (*R*)-**110** is (*M*)-**112**. With the recent progress in this field, SOR is not only used for determination of absolute configuration of helicenes, but it has also gained tremendous importance in the study of helicenes as chiral sensors. However, the primary requirement for making such sensory devices is to access materials which can show high degree of specific optical rotation. It is

known that chiral compounds with chiral centre or chiral axis tend to have much lower optical rotations, which increases drastically when converted to helical compounds attributed to their continuous delocalization of electrons and high conjugation. The comparison of the present set of compounds also indicates that both the isomers of chirally pure **110** showed much less rotation, which changed considerably when converted to helicene-like compound **113**. When the helical compound was synthesized, there was considerable increase in the value of optical rotation as well as molecular rotation. The sample of (*S*)-**110** with OR of +157 and molecular OR of +685 was converted to (*P*)-**112**, the values changed to +790 and +3306, respectively.

**Table 2 Chiroptical properties of isomers of 110, 112 and 113**

| | (*R*)-**110** | (*S*)-**110** | ($R_a$)-**113** | ($S_a$)-**113** | (*M*)-**112** | (*P*)-**112** |
|---|---|---|---|---|---|---|
| $[\alpha]^a$ | -150 | +157 | -515 | +543 | -755 | +790 |
| $[\Phi]^b$ | -655 | +685 | -2310 | +2433 | -3160 | +3306 |

[a]Specific optical rotation, c = 0.1, in DMSO; [b]Molecular optical rotation;

(*R*)-**110**, ($R_a$)-**113** and (*M*)-**112** = 96% *ee*; (*S*)-**110**, ($S_a$)-**113** and (*P*)-**112** = 99% *ee*

### 3.2.5.2 UV-Vis and Fluorescence spectroscopy:

With an aim to compare the chiroptic properties of helicene and helicene-like molecules, the synthesized compounds **112** and **113**, were studied for their optical properties using UV-Vis and fluorescence spectroscopy (Table 3). The observed values of absorption-emission bands and Stokes shift were in the expected range for such type of compounds. The longest absorption maxima for **112** and **113** were observed at 323 and 310 nm respectively.

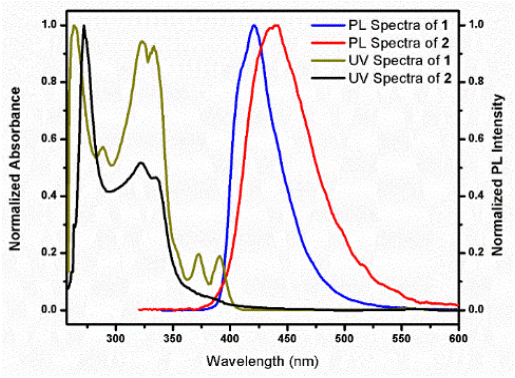



**Figure 14 Absorption and Emission Spectra of 112 and 113 in DMSO (abs 1.5X10$^{-6}$ M; ems 1X10$^{-4}$ M)**

The replacement of furan unit with dioxapine unit in the helical skeleton lead to a blue shift of 13 nm which may be attributed to the break in effective conjugation of the molecule due

to the presence of an $sp^2$ carbon bridge. A similar trend was observed for their absorption edges.

**Table 3 Photophysical properties of 112 and 113**

| Compound | $\lambda_{abs}$ (nm) | $\lambda_{ems}$ (nm) | Stokes Shift (nm) |
|---|---|---|---|
| **1** | 323 | 421 | 98 |
| **2** | 310 | 439 | 129 |

A comparison of the PL spectra for **112** and **113** showed that the emission maxima for helicene-like compound **113** (439 nm) was marginal red shifted (18 nm) to that of **112** (421 nm). The lower value of the emission maxima and Strokes shift in helicenes is probably attributed to loss in energy due to more facile intersystem crossing in such molecules.[139]

### 3.2.5.3 Circular Dichroism:

Circular dichrism (CD) is a spectroscopic tool to analyze the difference in the interaction of enantiomers with circularly polarized light. Circularly polarized light can be considered as chiral as it is obtained in two forms: left and right circularly polarized components which are non-superimposable mirror images of each other. A chiral molecule can discriminate between the two forms of circularly polarized light. The CD is used not only as a supporting tool for assignment on absolute configuration, but also widely explored for the study of conformational features of chiral molecules which cannot be determined by normal absorption spectra. The separated isomers of **112** and **113** were further analyzed by circular dichroism (Figure 15), where two opposite bisignate couplets showing opposite cotton effects, were observed. The absolute configuration of the helicenes was assigned based on CD spectra. The isomer of helical compound **112** showing a positive curve at the higher wavelength (Figure 15b) was assigned (*P*) and that with a negative curve was assigned as (*M*) configuration.

A comparison of the CD spectra of **112** and **113** helps us to correlate the dihedral angle to position of CD band. It has been reported in the literature that as value of dihedral angle θ increases, the CD band undergoes blue shift. Hence for **112**, the CD band appears at a wavelength of 340 nm and that for **113** is 260 nm. This is an evidence that for helicene **112**, the dihedral angle is less due to its rigid structure as compared to helicene-like **113** which has a larger dihedral angle due to presence of chiral axis and a saturated $sp^3$ hybridized

carbon atom. The significantly less intensity of the CD curve for **112** is attributed to its less solubility in commonly used organic solvents.

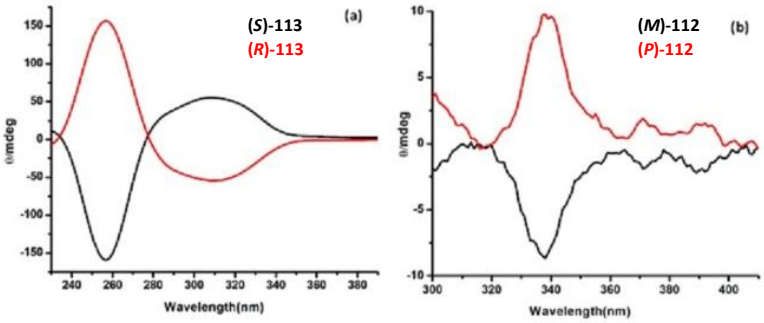



**Figure 15 CD spectra of pure (a) (Black Line) (*S*)-113 and (Red Line) (*R*)-113 at a concentration of 2.4 X $10^{-4}$ in chloroform at 25°C (b) (Red Line) (*P*)-112 and (Black Line) (*M*)-112 at a concentration of 2.1 X $10^{-4}$ in DMSO at 25°C**

### 3.2.5.4 Circularly Polarized Luminescence:

The differential absorption of left and right circularly polarized light is called CD whereas its emission is called Circularly Polarized Emission (CPE) or Circularly polarized Luminescene (CPL). The growing interest in CPL is due to the application of CPL active molecules in photonic materials in developing technologies related to 3D-display, storage of information *etc.* The CD is used to gain information about configuration and conformation of chiral molecules in their ground state while CPL is used for studying them in their excited state. It allows to further investigate the influence of the structure of the compounds on the chiroptical properties. The extent of CPL is quantified by the luminescence dissymmetry factor, ($g_{lum}$) which is given by the equation $g_{lum} = 2(I_L - I_R)/(I_L + I_R)$, where $I_L$ and $I_R$ are the intensities of the left- and right-handed circularly polarized emissions, respectively and the values of which fall between −2 and +2. The highest level of CPL has been reported for lanthanide metal complexes having a $g_{lum}$ value in the range of 0.05-0.5 but only a few organic molecules are known to show high CPL activity.

The helical topology and extended π-conjugation make helicenes a class of chromophoric compounds suitable for the study of their CPL activity. The CPL activity was considered for the synthesized optically pure helicene **112** and its helicene-like analogue **113**. The CPL spectra measured for the two sets of enantiomers (*P*)-/(*M*)-**112** and (*R*)-/(*S*)-**113** in DMSO solutions at 295 K. Both sets of enantiomers, (*P*)-/(*M*)-**112** and (*R*)-/(*S*)-**113**, showed a somewhat mirror-like CPL signal with opposite $g_{lum}$ values around the emission maximum

(+0.003/–0.002 and +0.005/–0.002, respectively) which is in the typical range of $g_{lum}$ values for most chiral organic molecules.[19] It is worth noting that **112** and **113** give a relatively similar CPL response, which is in accordance with the slight structural variation between these two compounds.

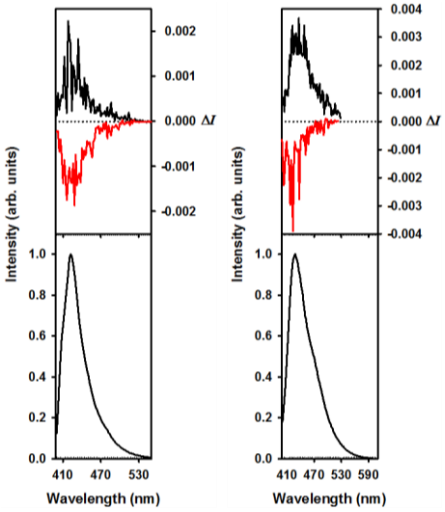


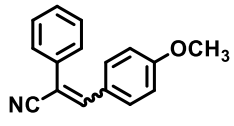

**Figure 16 CPL (upper curve) and total luminescence (lower curve) spectra of (*P*)-/(*M*)-112 (left) and (*R*)-/(*S*)-113 (right)**

## 3.3 Conclusion:

In summary, dicyano substituted derivatives of oxa[7]helicenes and helicene-like compounds have been synthesized. During the synthesis, a mild and effective method to cleave aryl methyl ether, in presence of acid sensitive cyano group is also developed. The enantiomers of these compounds were accessed by making physically separable diastereomers of phenolic intermediate, by forming its carbonate with (*l*)-menthyl chloroformate. The separated enantiomers were characterized by optical rotation, fluorescence, CD spectra and circularly polarized luminescence. Both sets of enantiomers, (*P*)-/(*M*)-**112** and (*R*)-/(*S*)-**113**, showed a mirror-like CPL signal with opposite $g_{lum}$ values around the emission maximum, which correspond to the typical range of similar chiral molecules. Such molecules having unique structure and properties due to their helical morphology are opening the door to a new world. The synthesis and resolution of helicenes mentioned in this work, could also be a contributing guideline and projection of helicenes in future. In concrete terms, the presence of –CN group on the helical skeleton or introduction of a saturated atom to give helicene-like compounds, are powerful approaches to changing the electronic structure and modulating physical properties. The usefulness of the synthesized targets underlies in the interdisciplinarity applications of such molecules in various fields. With more and more attention and efforts, we believe that new kinds of helicenes with novel and brilliant properties, is springing up and the development of helicenes is spiraling.

## 3.4 Experimental Data:

**Synthesis of 3-(4-Methoxyphenyl)-2-phenylacrylonitrile [107]:**




A mixture of benzyl cyanide **106** (1.17 g; 10 mmol), finely ground solid KOH (0.65 g; 10 mmol) and 4-methoxybenzaldehyde **105** (0.68 g; 10 mmol) in methanol (30 mL) was stirred at room temperature for 6 hours. The resultant reaction mixture was concentrated under reduced pressure, poured into water and extracted using ethyl acetate (3X50 mL). The combined organic layer was dried over sodium sulfate and concentrated to give crude **107** as pale yellow solid (2.23 g, 96%; M.P.: 96°C) which is recrystallized from ethyl acetate-petroleum ether.

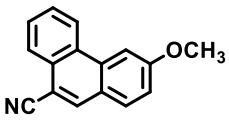
**$^{1}$H NMR (400MHz, $CDCl_3$): δ** 3.87 (s, 3H), 6.99 (d, *J*=8.8 Hz, 2H), 7.37-7.41 (m, 1H), 7.44 (d, *J*=7.6 Hz, 2H), 7.48 (s, 1H), 7.67 (d, *J*=7.6 Hz, 2H), 7.91 (d, *J*=8.8 Hz, 2H)

**$^{13}$C NMR (100MHz, $CDCl_3$): δ** 55.5, 108.5, 114.4 (2C), 118.6, 125.8 (2C), 126.5, 128.8, 129.1 (2C), 131.2 (2C), 134.8, 141.9, 161.4

**MS (DIP-EI): *m/z*** 235 ($M^+$, 21%), 234 (17%), 190 (100%), 165 (91%), 164 (57%), 139 (25%).

**IR (KBr): υ** 3013, 2844, 2207, 1596, 1507, 1448, 1304, 1250, 1179, 1026, 905, 828, 756, 693, 533 $cm.^{-1}$

**Synthesis of 3-Methoxyphenanthrene-9-carbonitrile [108]:**




A solution of **107** (0.1 g, 0.42 mmol) and iodine (0.12 g, 0.47 mmol) in toluene (425 mL) and tetrahydrofuran (1.7 mL, 21.3 mmol, 50 equivalent) was irradiated in a standard immersion well photoreactor with 250W high pressure mercury vapour lamp for 24 hours. The reaction mixture was then washed with aqueous sodium thiosulfate and dried over anhydrous sodium sulfate. The concentrated mixture was purified on silica gel column using ethyl acetate and petroleum ether (1:4) to afford **6** as pale yellow solid (0.093 g, 94%; M.P.: 118°C).

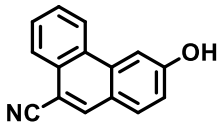
**$^{1}$H NMR (400MHz, $CDCl_3$): δ** 4.07 (s, 3H), 7.325 (dd, *J*=8.8 Hz, 2.4 Hz, 1H), 7.75-7.79 (m, 2H), 7.87 (d, *J*=8.8 Hz, 1H), 8.035 (d, *J*=2.0 Hz, 1H), 8.21 (s, 1H), 8.29-8.32 (m, 1H), 8.63-8.66 (m, 1H)

**$^{13}$C NMR (100MHz, $CDCl_3$): δ** 55.6, 104.1, 106.6, 117.9, 118.4, 123.1, 124.5, 126.1, 127.7, 128.2, 129.3, 129.4, 131.2, 133.6, 135.5, 160.9

**MS (DIP-EI):** ***m/z*** 233 ($M^+$, 100%), 232 (61%), 190 (39%), 189 (77%), 166 (14%), 81 (38%), 69 (40%), 57 (27%).

**IR (KBr):** **υ** 3022, 2966, 2935, 2845, 2217, 1618, 1503, 1453, 1372, 1232, 1144, 1030, 897, 835, 816, 721, 620, 565, 490, 427 $cm.^{-1}$

**Synthesis of 3-Hydroxyphenanthrene-9-carbonitrile [109]**:




To a round bottom flask, was added **108** (0.5 g, 2.15 mmol), lithium bromide (0.37g, 4.30 mmol) in dimethylformamide (30 mL). To this solution was added 4Å molecular sieves (100% w/w) and stirred at room temperature for 15 mins, followed by heating in an oil bath to 180°C for 22 hours. The reaction mixture was then allowed to cool to room temperature and filtered to remove molecular sieves. Water was added to the reaction mixture and it was allowed to stir till solution becomes clear. It was extracted using ethyl acetate (3X50 mL). The combined organic layer was dried over sodium sulfate and concentrated under reduced pressure. The concentrated mixture was purified on silica gel column using ethyl acetate and petroleum ether (2:3) to afford **7** as pale yellow solid (0.39 g, 85%; M.P.: >220° C)

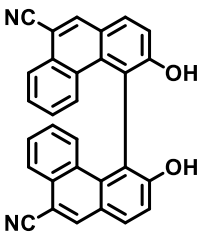
**$^1$H NMR (400MHz, $CDCl_3$): δ** 5.91 (s, 1H), 7.265 (dd, *J*=8.8 Hz, 2.0 Hz, 1H), 7.73-7.79 (m, 2H), 7.87 (d, *J*=8.8 Hz, 1H), 8.055 (d, *J*=2.0 Hz, 1H), 8.22 (s, 1H), 8.28-8.32 (m, 1H), 8.58-8.62 (m, 1H)

**$^{13}$C NMR (100MHz, $CDCl_3$): δ** 107.2, 117.9, 118.3, 123.2, 124.6, 126.1, 127.8, 128.4, 129.2, 129.3, 131.6, 133.9, 135.4, 157.1

**MS (DIP-EI):** ***m/z*** 219 ($M^+$, 59%), 218 (100%), 201 (23%), 190 (49%), 165 (16%), 163 (21%).

**IR (KBr):** **υ** 3404, 2217, 1628, 1575, 1507, 1450, 1342, 1245, 1203, 899, 856, 810, 753, 621, 564 $cm.^{-1}$

**Synthesis of 3,3'-Dihydroxy-[4,4'-biphenanthrene]-9,9'-dicarbonitrile [(±)110]:**




In a 50mL round bottom flask, a mixture of **109** (0.2 g, 0.9 mmol), $CuCl(OH)[(Me_2N)_2CH_2CH_2(NMe_2)_2]$ (0.21 g, 0.9 mmol) in methanol (25 mL) was placed and was sonicated for 10 mins. The reaction mixture was stirred at room temperature for 4.5 h under oxygen atmosphere (1 atm). The reaction mixture was concentrated to remove methanol and 1 *M* aqueous HCl was added. The resulting mixture was extracted with ethyl acetate (3X40 mL). The organic layer was dried over anhydrous $Na_2SO_4$, filtered, and concentrated under

reduced pressure. Purification of the crude residue by silica gel column chromatography with petroleum ether/ethyl acetate (1:1) as an eluent gave the ***rac*-110** as a colorless solid (0.11 g, 55 %; M.P.: >220° C) Chiral HPLC was performed on Chiralpak OD-H in 30% Isopropanol-hexane, at a flowrate of 1 mL/min and UV 254 nm, $t_R$ 10.4 and 15.8 min.

**$^1$H NMR (400MHz, *d*$_6$-DMSO): δ** 7.03-7.07 (m, 1H), 7.44 (d, *J*=8.4 Hz, 1H), 7.54-7.58 (m, 1H), 8.07 (d, *J*=8.0 Hz, 1H), 8.11 (d, *J*=8.8 Hz, 1H), 8.17 (d, *J*=8.8 Hz, 1H), 8.71 (s, 1H), 10.01 (bs, 1H)

**$^{13}$C NMR (100MHz, *d*$_6$-DMSO): δ** 104.9, 118.7, 118.9, 122.2, 125.5 (2C), 125.8, 127.3, 128.4, 129.9, 130.8, 132.4, 132.8, 137.9, 157.3

**MS (DIP-EI): *m/z*** 436 ($M^+$, 70%), 435 (100%), 367 (27%), 313 (33%), 312 (56%), 220 (30%), 218 (20%).

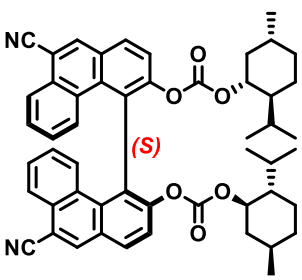
**IR (KBr): υ** 3355, 2926, 2221, 1600, 1569, 1493, 1443, 1395, 1250, 1222, 1084, 898, 762, 661, 629, 569 cm.$^{-1}$

**HRMS (ESI) *m/z*** calcd. for $C_{30}H_{16}N_2O_2Na$ [M+Na] 459.1104, found 459.1109.

**Synthesis of 9,9'-Dicyano-(4,4'-biphenanthrene)-3,3'-diyl(1*R*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl biscarbonate [(±)114]:**

To a solution of **(±)-110** (0.20 g, 0.45 mmol) and triethylamine (0.16 mL, 1.15 mmol) in dichloromethane was added (1*R*,2*S*,5*R*)-(-)-menthyl chloroformate (0.22 mL, 1.01 mmol) drop wise at 0°C under $N_2$ atmosphere. After completion of the reaction (TLC), the reaction mixture was poured in ice cold water. The aqueous layer was extracted with dichloromethane (2X50 mL), the extracts were combined and the organic layer was dried over $Na_2SO_4$ and evaporated to obtain a crude solid. The crude product was purified by column chromatography over silica gel using petroleum ether/ethyl acetate as eluent (13:1) furnishing a pale yellow solid (0.30 g, 80%).

**(*S*)-9,9'-dicyano-(4,4'-biphenanthrene)-3,3'-diyl-bis((1*R*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl)biscarbonate [(*S*)-114]:**




Melting Point: >220° C; $[\alpha]_D$: +48° (*c*=1.0, $CHCl_3$, 99% *ee*).

**$^1$H NMR (400MHz, $CDCl_3$): δ** 0.36-0.45 (m, 1H), 0.585 (d, *J*=6.8 Hz, 3H), 0.70-0.74 (m, 1H), 0.78 (d, *J*=7.2 Hz, 3H), 0.80-0.84 (m, 1H), 0.88 (d, *J*=6.4 Hz, 3H), 1.04-1.23 (m, 3H), 1.45-1.58 (m, 3H), 4.02 (dt, *J*=10.8 Hz, 4.4 Hz, 1H), 7.14-7.16 (m,

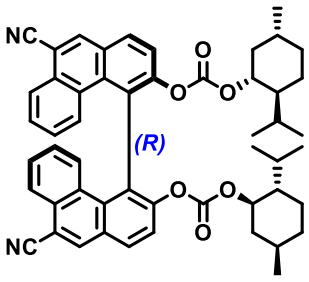
1H), 7.61-7.65 (m, 1H), 7.85 (d, *J*=8.0 Hz, 1H), 8.14 (d, *J*=8.8 Hz, 1H), 8.18 (d, *J*=8.8 Hz, 1H), 8.325 (dd, *J*=8.0 Hz, 0.8 Hz, 1H), 8.44 (s, 1H)

**$^{13}$C NMR (100MHz, $CDCl_3$): δ** 16.2, 20.6, 21.9, 23.1, 25.7, 31.1, 33.8, 39.5, 46.2, 79.3, 110.4, 117.6, 123.6, 126.1, 126.3, 127.3, 127.9, 128.6, 129.2, 129.9, 130.1, 131.6, 132.1, 135.7, 149.2, 151.6

**IR (KBr): υ** 2956, 2926, 2869, 2223, 1750, 1597, 1491, 1453, 1370, 1270, 1231, 1086, 1030, 954, 759 $cm.^{-1}$

**HRMS (ESI) *m/z*** calcd. for $C_{52}H_{52}N_2O_6Na$ [M+Na] 823.3718, found 823.3708.

**(*R*)-9,9'-dicyano-(4,4'-biphenanthrene)-3,3'-diyl-bis((1*R*,2*R*,5*S*)-2-isopropyl-5-methylcyclohexyl)biscarbonate [(*R*)-114]:**




Melting Point: 98°C; $[\alpha]_D$ : -175° (*c*=1.0, $CHCl_3$, 96%*ee*).

**$^1$H NMR (400MHz, $CDCl_3$): δ** 0.16 (d, *J*=7.2 Hz, 3H), 0.60 (d, *J*=7.2 Hz, 3H), 0.70-0.84 (m, 1H), 0.865 (d, *J*=6.4 Hz, 3H), 0.96-0.99 (m, 1H), 1.04-1.09 (m, 1H), 1.27-1.28 (m, 2H), 1.44-1.62 (m, 3H), 1.72-1.75 (m, 1H), 4.07 (dt, *J*=11.2 Hz, 4.4 Hz, 1H), 7.01-7.05 (m, 1H), 7.51-7.55 (m, 1H), 7.77 (d, *J*=8.8 Hz, 1H), 7.78 (d, *J*=8.4 Hz, 1H), 8.215 (d, *J*=8.8 Hz, 1H), 8.245 (dd, *J*=8.0 Hz, 0.8 Hz, 1H), 8.42 (s, 1H);

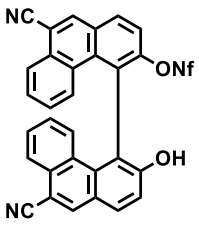
**$^{13}$C NMR (100MHz, $CDCl_3$): δ** 15.9, 20.3, 21.9, 23.2, 23.9, 25.9, 31.2, 33.8, 46.3, 79.4, 110.5, 117.6, 123.5, 126.1, 126.2, 127.3, 127.8, 128.4, 129.5, 129.8, 129.9, 131.7, 131.8, 135.5, 149.7, 151.9

**Regeneration of chiral diol [*(S)*-110]:**

To solution of KOH (0.042 g, 0.75 mmol) in degassed methanol (20 mL), 0.5 g of ***(S)*-114** (0.63 mmol) was added and the mixture was allowed to stir at room temperature for 4 h after which no starting material remained (TLC). The mixture was concentrated and to it was added 20mL of water. The aqueous layer was separated and acidified with 6M HCl, producing a white precipitate that was extracted with ethyl acetate (2X30 mL). The ether layer was dried over $Na_2SO_4$, filtered off and the solvent evaporated in vacuum to give ***(S)*-110** as white solid (0.27 g, 86%) $[\alpha]_D$ : +157° (c=0.1, DMSO, 99 %*ee*);

Similar hydrolysis treatment of ***(R)*-114** gave ***(R)*-110** $[\alpha]_D$ : -150° (c=0.1, DMSO, 96 %*ee*).

**Synthesis of 9,9'-Dicyano-3'-hydroxy-[4,4'-biphenanthren]-3-yl-1,1,2,2,3,3,4,4,4-nonafluorobutane-1-sulfonate [(±)-111]:**




A mixture of **(±)-110** (0.1 g, 2.3 mmol) and triethylamine (0.035 mL, 2.5 mmol) in $CH_2Cl_2$ (10 mL) was placed in a round bottom flask. To this solution was slowly added nonafluorobutanesulfonyl fluoride (0.045 mL, 2.5 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 6 hours and then concentrated to remove $CH_2Cl_2$. The resulting mixture was extracted with ethyl acetate (40 mLX3). The organic layer was dried over anhydrous $Na_2SO_4$, filtered and concentrated under reduced pressure. Purification of the crude residue by silica gel column chromatography with petroleum ether/ethyl acetate (70:30) as an eluent gave **(±)-111** as a pale yellow solid (0.14 g, 86%); Melting Point: 106ºC; ***(S)*-111** $[\alpha]_D$ : +59º (*c*=1.0, $CHCl_3$, 99%*ee*); ***(R)*-111** $[\alpha]_D$ : -56º (*c*=1.0, $CHCl_3$, 96%*ee*).

**$^1$H NMR (400MHz, $CDCl_3$): δ** 5.61 (bs, 1H), 7.04-7.08 (m, 1H), 7.20-7.25 (m, 1H), 7.39 (d, *J*=8.8 Hz, 1H), 7.57-7.61 (m, 1H), 7.68-7.72 (m, 1H), 7.77 (dd, *J*=8.8 Hz, 1.2 H, 2H), 8.12 (d, *J*=8.4 Hz, 1H), 8.28 (d, *J*=8.8 Hz, 1H), 8.32 (dd, *J*=8.4 Hz, 1.2 Hz, 1H), 8.37-8.40 (m, 2H); 8.38 (s, 1H), 8.48 (s, 1H)

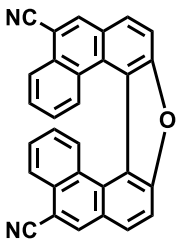
**$^{13}$C NMR (100MHz, $CDCl_3$): δ** 107.9, 112.2, 117.2, 117.9, 118.1, 118.5, 121.9, 125.3, 125.4, 126.4, 126.6(2C), 127.4, 128.2, 128.7, 129.3, 129.7, 129.9, 130.0, 130.5, 130.6, 131.0, 132.3, 132.6, 132.8, 133.3, 135.4, 136.1, 147.9, 154.7

**MS (DIP-EI): *m/z*** 734 ($M^+$, 39%); 590 (39%), 577 (43%), 433 (55%), 406 (100%), 392 (56%), 379 (69%), 378 (95%).

**IR (KBr): υ** 3334, 3076, 2226, 1663, 1607, 1574, 1526, 1498, 1423, 1351, 1239, 1035, 1009, 907, 792, 734, 693, 530, 488 $cm.^{-1}$

**HRMS (ESI) *m/z*** calcd. for $C_{34}H_{15}N_2O_4F_9SNa$ [M+Na] 741.0501, found 741.0502.

**Synthesis of Diphenanthro[3,4-b:4',3'-d]furan-5,13-dicarbonitrile [(±)112]:**




A mixture of **(±)-111** (0.17g, 0.23 mmol), $Pd(OAc)_2$ (2.6 mg, 0.012 mmol), xantphos (27 mg, 0.046 mmol), anhydrous $Cs_2CO_3$ (0.16 g, 0.46 mmol) in xylene (10 mL) was placed in a 50 mL round bottom flask and degassed by sonicating for 10 mins. The reaction mixture was stirred at 60 °C for 4 hours under nitrogen atmosphere. The reaction mixture was cooled down to ambient temperature and was then diluted with toluene (10 mL). The resulting mixture was washed with water, extracted with toluene, dried over anhydrous $Na_2SO_4$, filtered and concentrated under reduced pressure. The resulting crude residue was purified by silica gel column chromatography with petroleum ether/ethyl acetate (90:10) as an eluent to give

**(±)112** as a pale yellow solid (50 mg, 52%). Melting Point: >220°C; ***(P)*-112** $[\alpha]_D$ : +790° (*c*=0.1, DMSO, 99%*ee*); ***(M)*-112** $[\alpha]_D$ : -755° (*c*=0.1, DMSO, 96% *ee*).

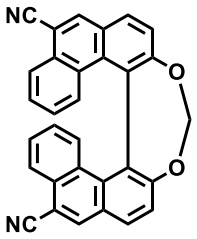
**$^1$H NMR (400MHz, $d_6$-DMSO): δ** 6.45-6.48 (m, 1H), 7.25 (d, *J*=8.4 Hz, 1H), 7.50-7.54 (m, 1H), 8.17 (d, *J*=8.4 Hz, 1H), 8.48 (d, *J*=8.8 Hz, 1H), 8.55 (d, *J*=8.8 Hz, 1H), 9.03 (s, 1H)

**MS (DIP-EI): *m/z*** 418 ($M^+$, 45%), 410 (59%), 312 (100%), 256 (64%), 236 (72%), 199 (63%), 155 (73%), 140 (53%).

**IR (KBr): υ** 2220, 1584, 1519, 1486, 1446, 1347, 1320, 1271, 1225, 1106, 922, 898, 772, 644 $cm.^{-1}$

**HRMS (ESI) *m/z*** calcd. for $C_{30}H_{14}N_2ONa$ [M+Na] 441.0998, found 441.0995.

**Synthesis of Diphenanthro[3,4-d:4',3'-f][1,3]dioxepine-5,15-dicarbonitrile [(±)113]:**




A solution of **(±)-110** (0.10 g, 0.23 mmol) and anhydrous $Cs_2CO_3$ (0.29 g, 1.15 mmol) in dry DMF (5 mL), $CH_2I_2$ (0.028 mL, 0.34 mmol) was added and the mixture was stirred for 6 hours at room temperature under nitrogen atmosphere. After the completion of the reaction (TLC) the reaction mixture was poured in ice cold water. The aqueous layer was extracted with ethyl acetate (3X50 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure to obtained crude solid. The crude product was purified by column chromatography over silica gel using petroleum ether/ethyl acetate as eluent (80:20) furnishing **(±)-113** as white solid (0.09 g, 88%). Melting Point: >220°C; ***(S)*-113** $[\alpha]_D$ : +543° (*c*=0.1, DMSO, 99%*ee*); ***(R)*-113** $[\alpha]_D$ : -515° (*c*=0.1, DMSO, 96%*ee*).

**$^1$H NMR (400MHz, $CDCl_3$): δ** 5.89 (s, 1H), 6.58-6.59 (m, 2H), 7.19-7.23 (m, 1H), 7.78 (d, *J*=8.4 Hz, 1H), 7.83 (d, *J*=8.0 Hz, 1H), 8.14 (d, *J*=8.8 Hz, 1H), 8.24 (s, 1H);

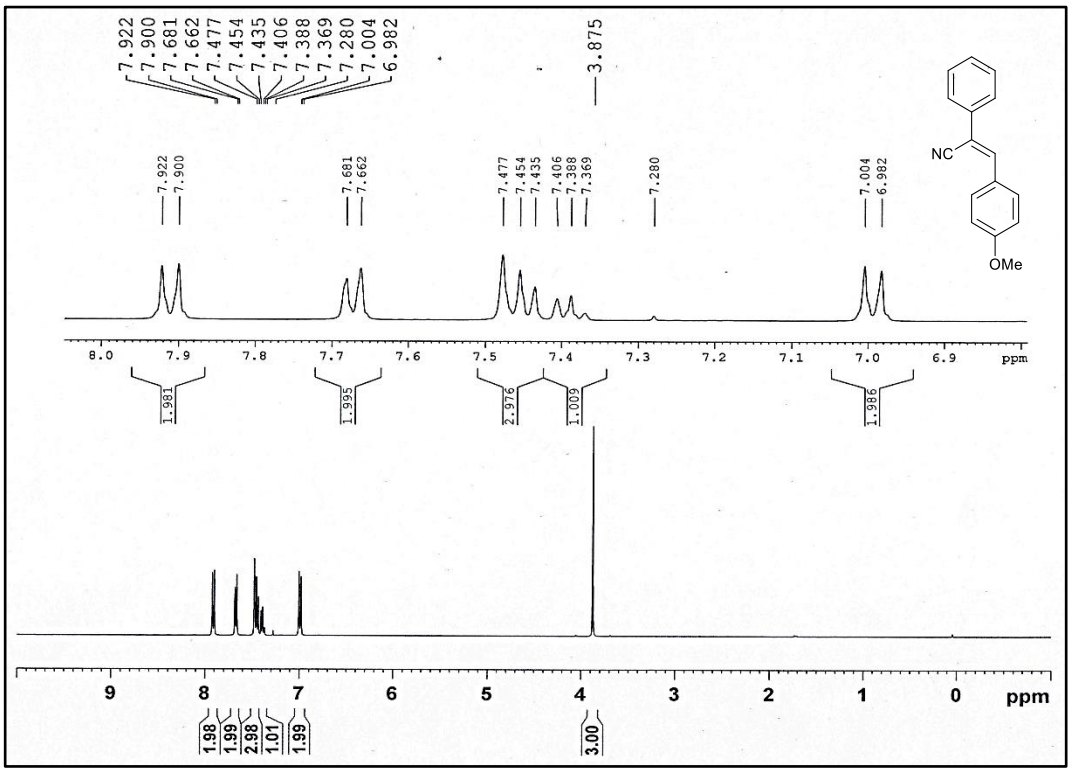
**$^{13}$C NMR (100MHz, $CDCl_3$): δ** 102.1, 109.1, 117.6, 122.2, 124.9, 125.8, 126.1, 127.9, 128.9, 129.0, 129.1(2C), 131.8, 131.9, 135.0, 153.5

**MS (DIP-EI): *m/z*** 448 ($M^+$, 100%), 447 (41%), 368 (99%), 313 (50%), 236 (81%), 152 (62%), 111 (80%).

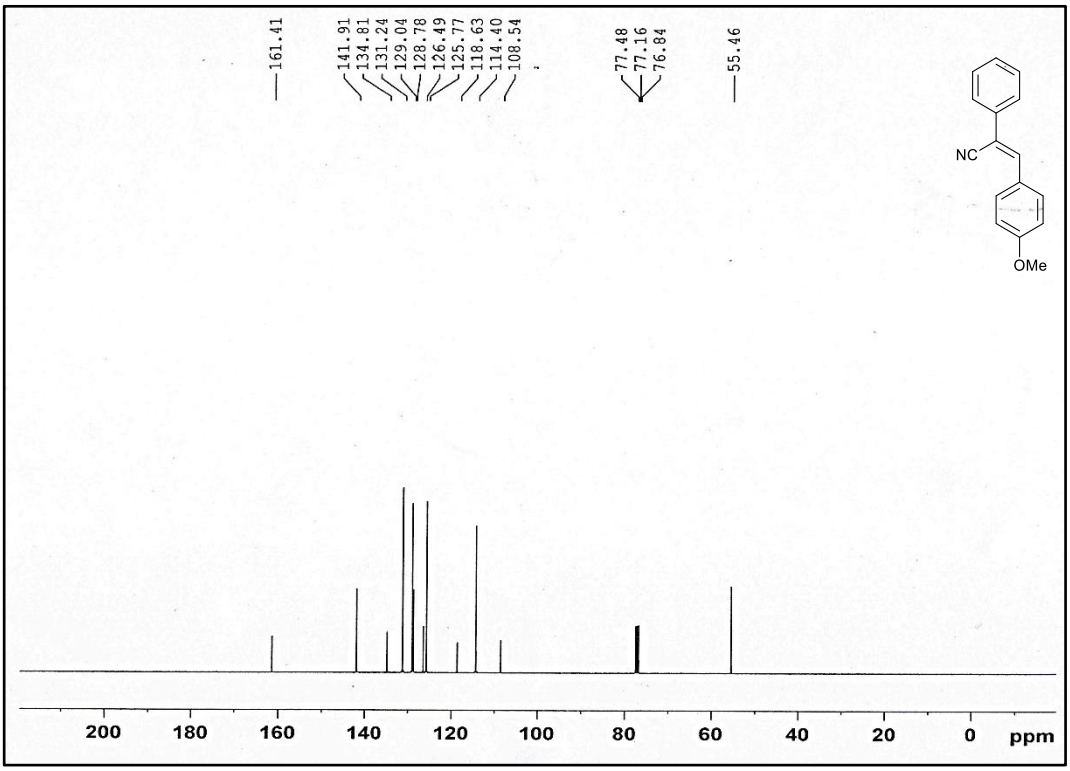
**IR (KBr): υ** 3061, 2922, 2853, 2226, 1586, 1519, 1494, 1444, 1391, 1320, 1270, 1198, 1018, 973, 895, 767, 642, 554, 448 $cm.^{-1}$

**HRMS (TOF MS EI+) *m/z*** calcd. for $C_{31}H_{16}N_2O_2$ [$M^+$] 448.1212, found 448.1207.

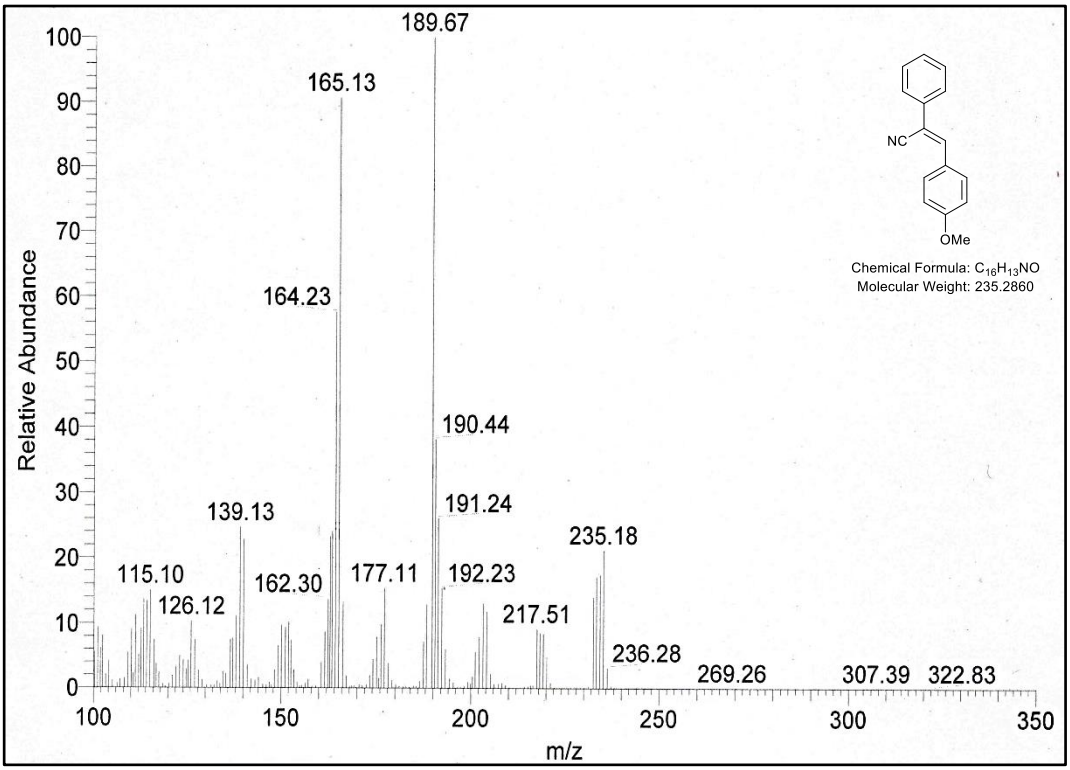
## 3.5 Spectral Data:



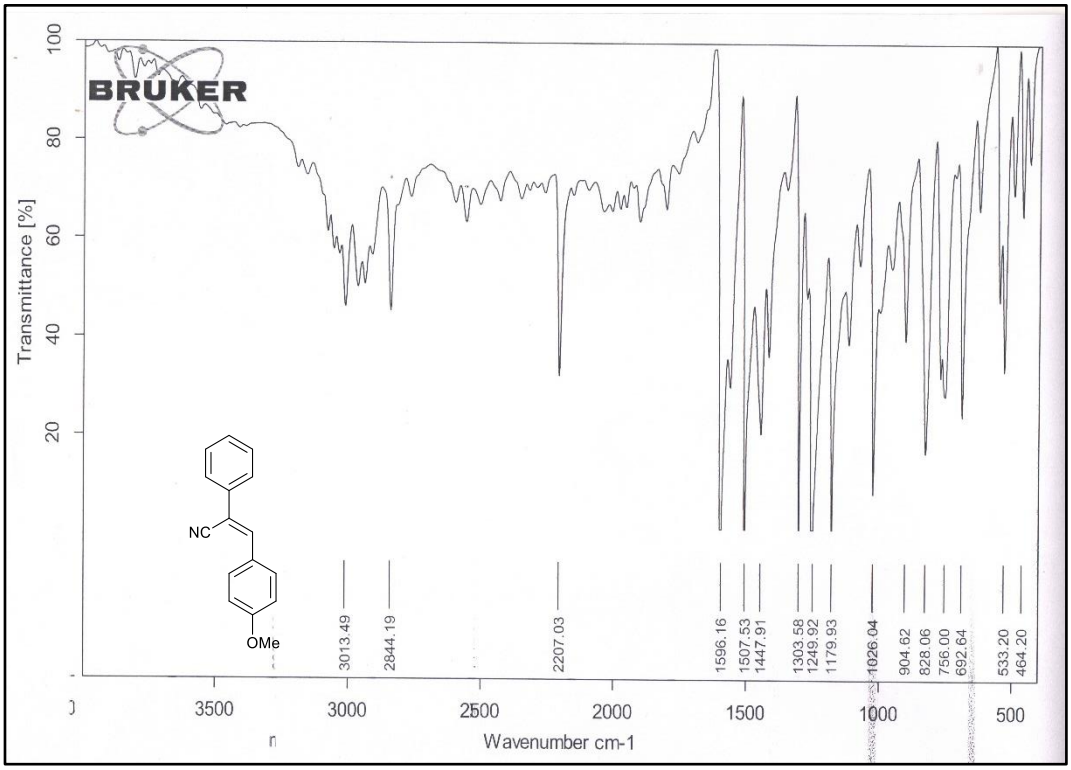

**$^{1}$H NMR Spectra of compound 107 ($CDCl_3$, 400MHz)**



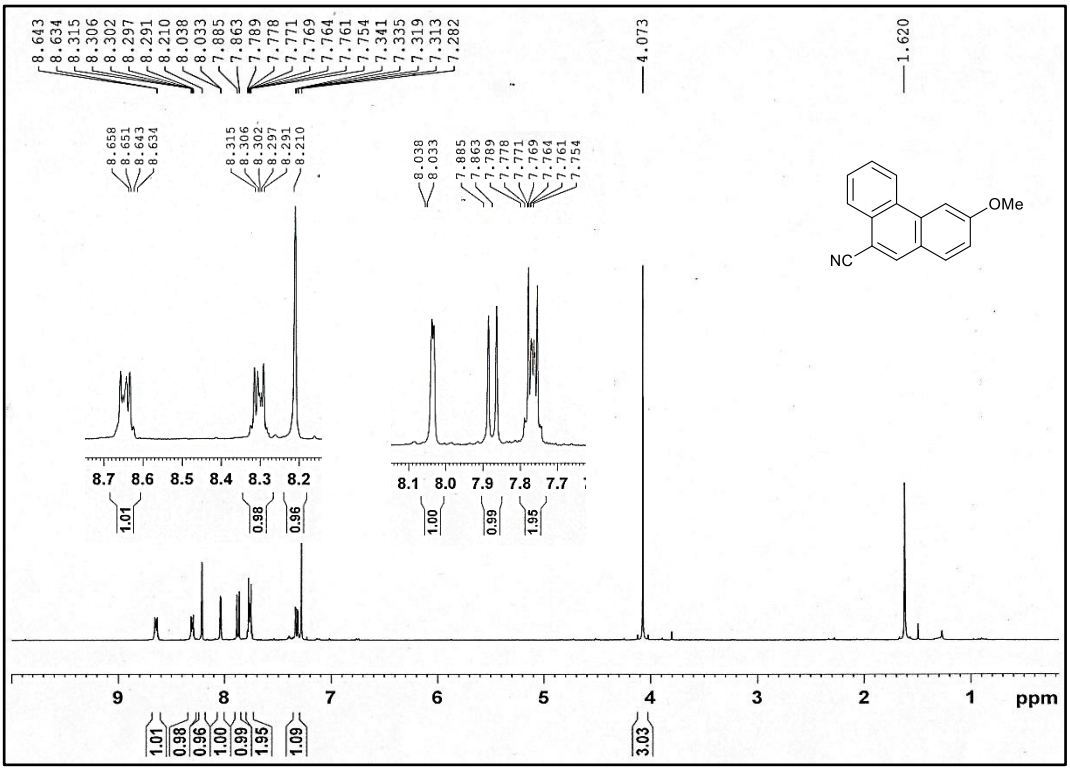

**$^{13}$C NMR Spectra of compound 107 ($CDCl_3$, 100MHz)**



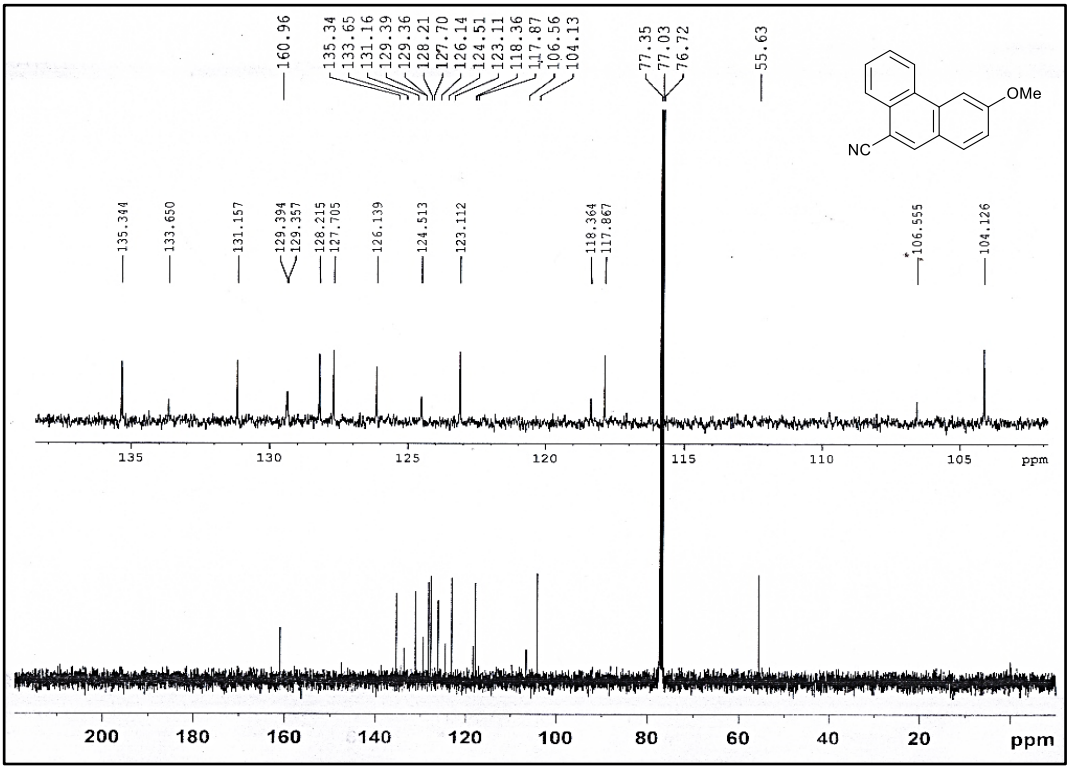

**Mass Spectra of compound 107**



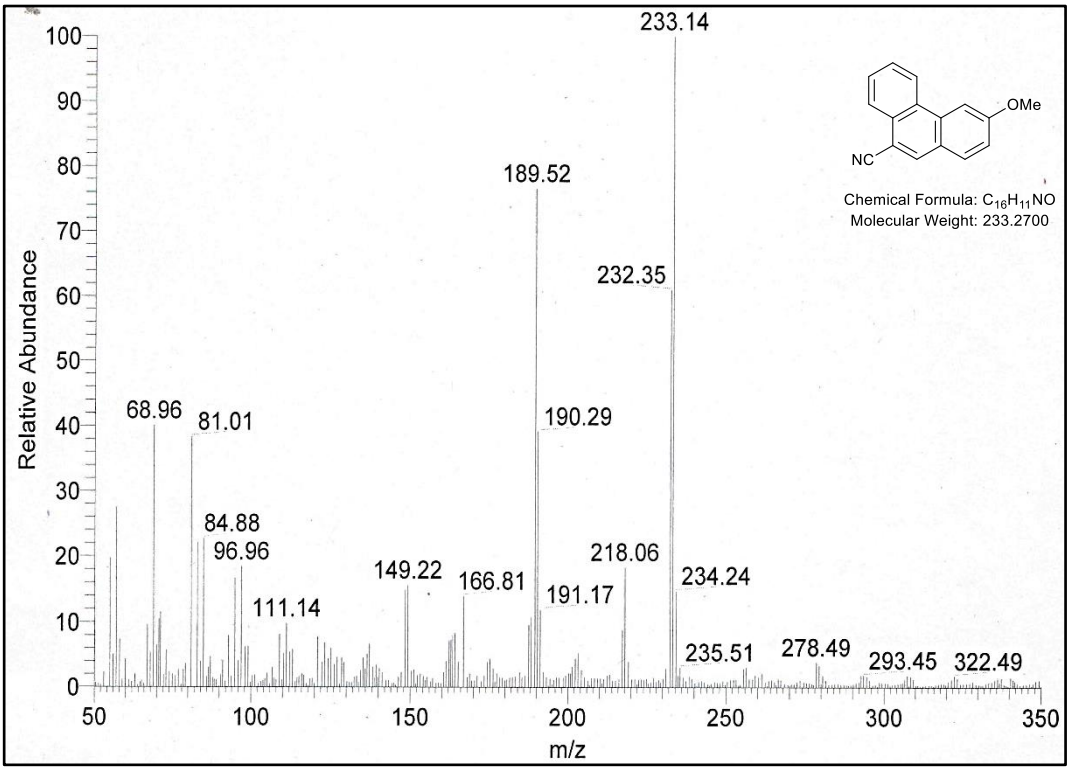

**IR Spectra of compound 107**



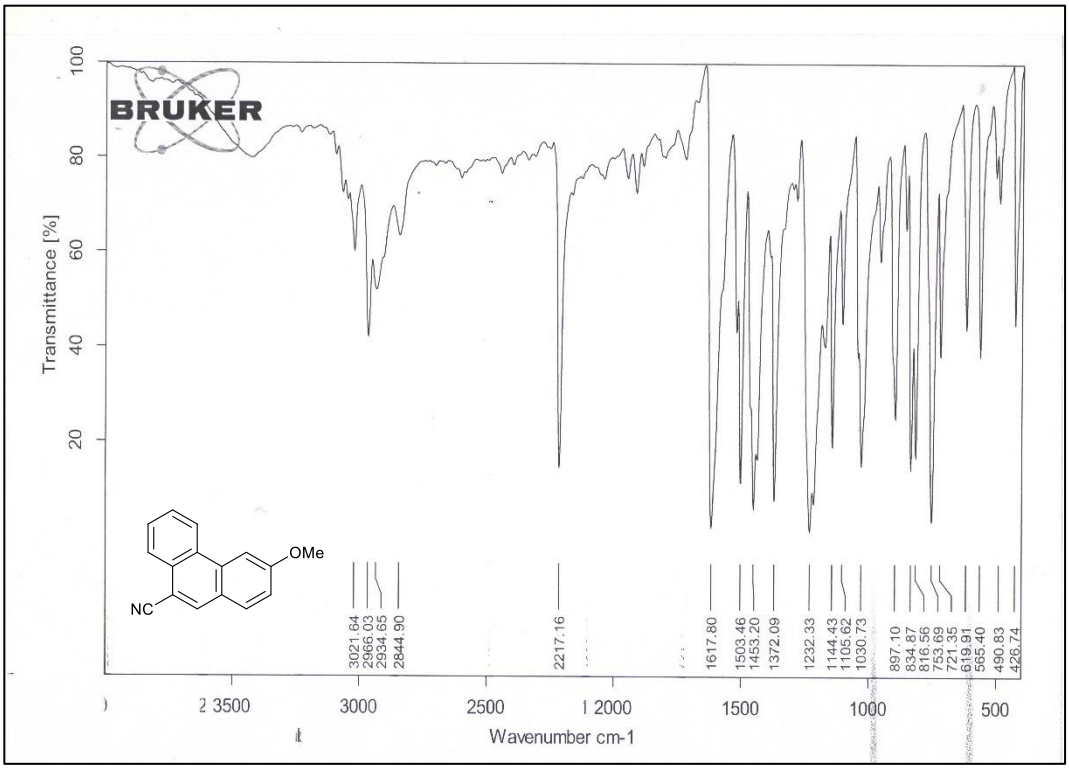

**$^{1}$H NMR Spectra of compound 108 ($CDCl_3$, 400MHz)**



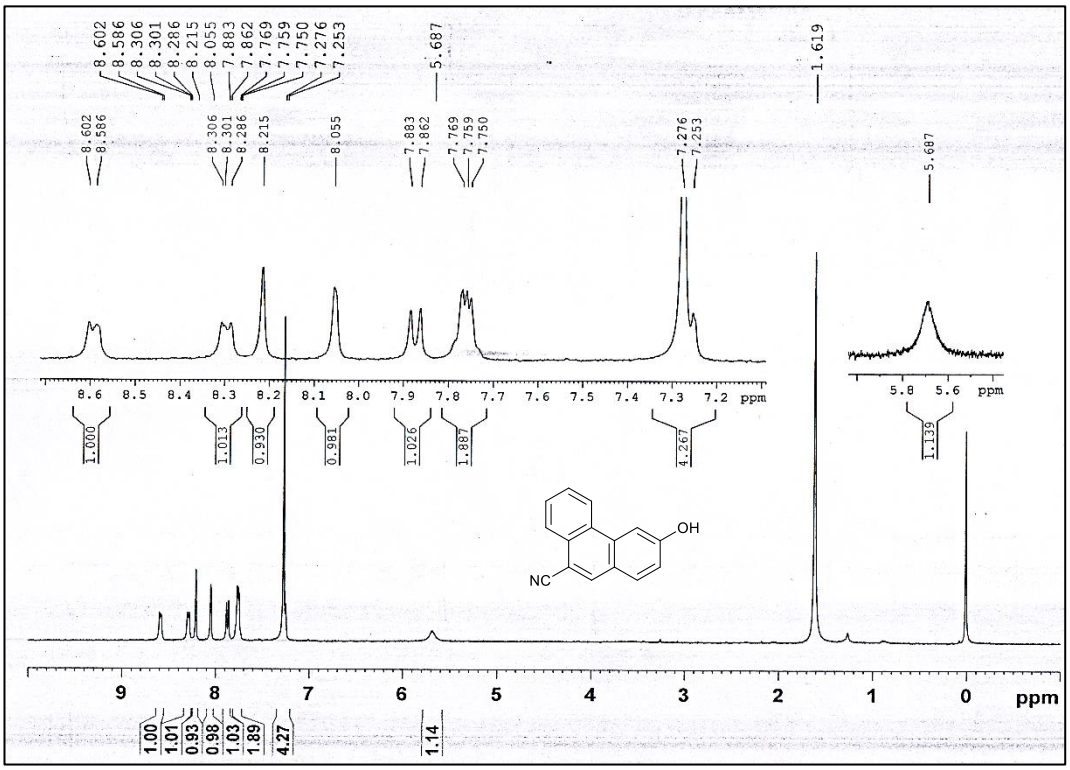

**$^{13}$C NMR Spectra of compound 108 ($CDCl_3$, 100MHz)**



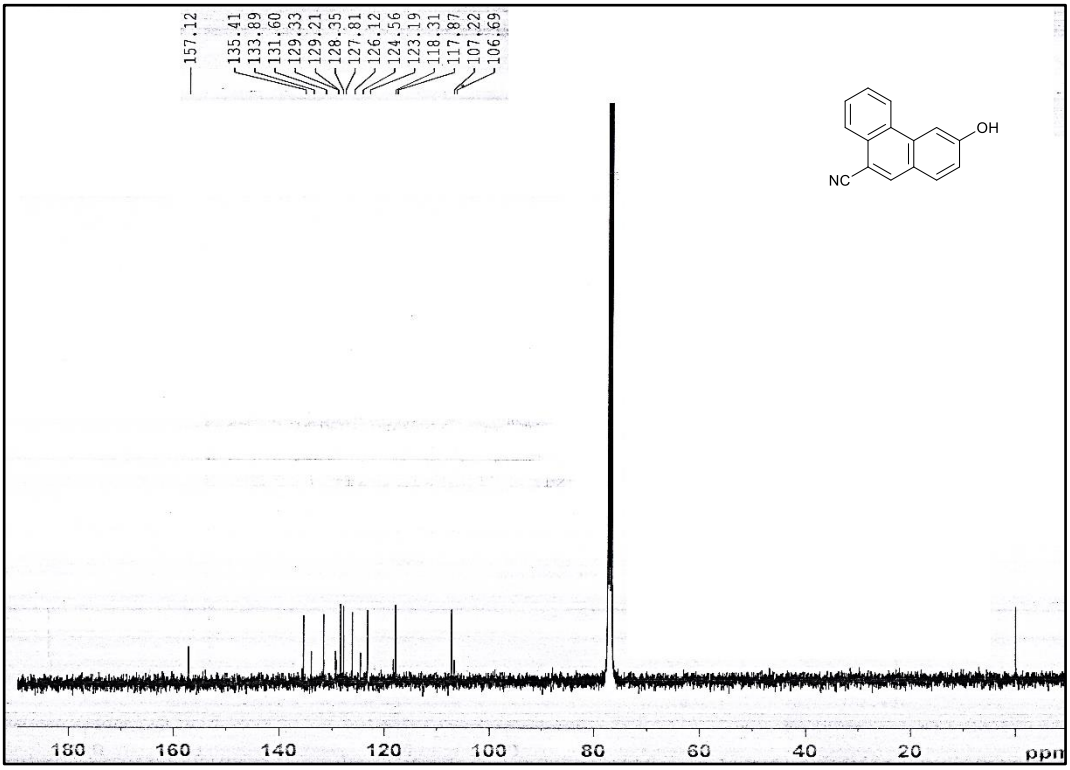

**Mass Spectra of compound 108**



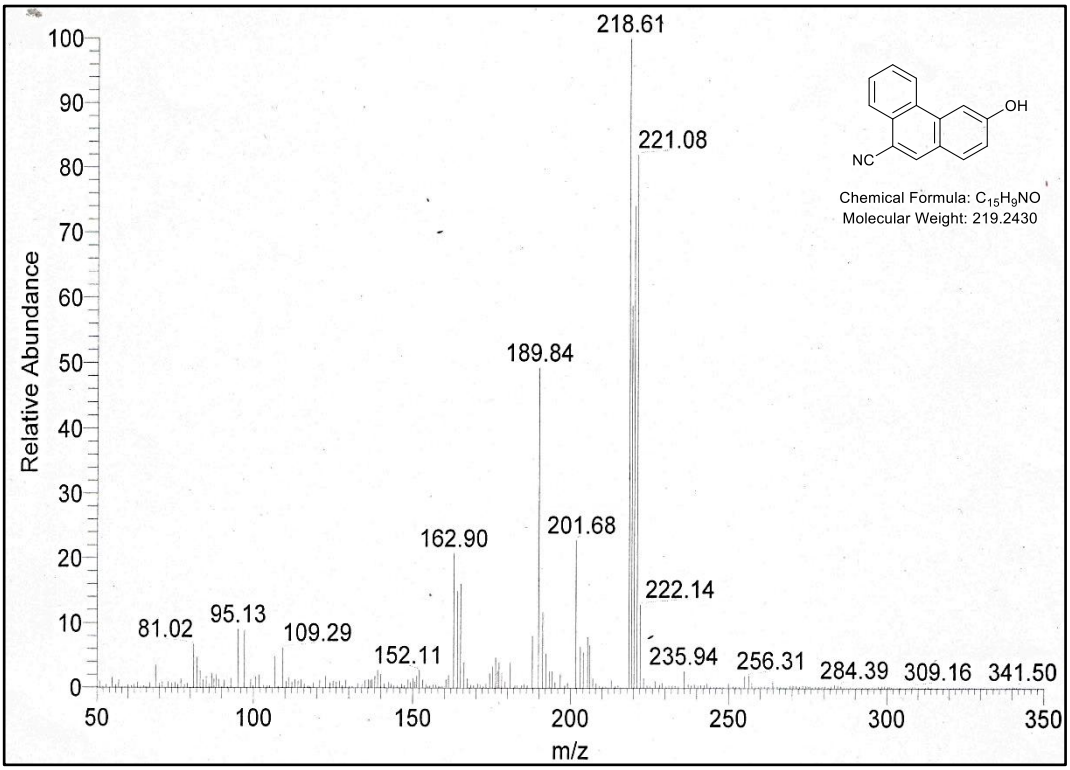

**IR Spectra of compound 108**



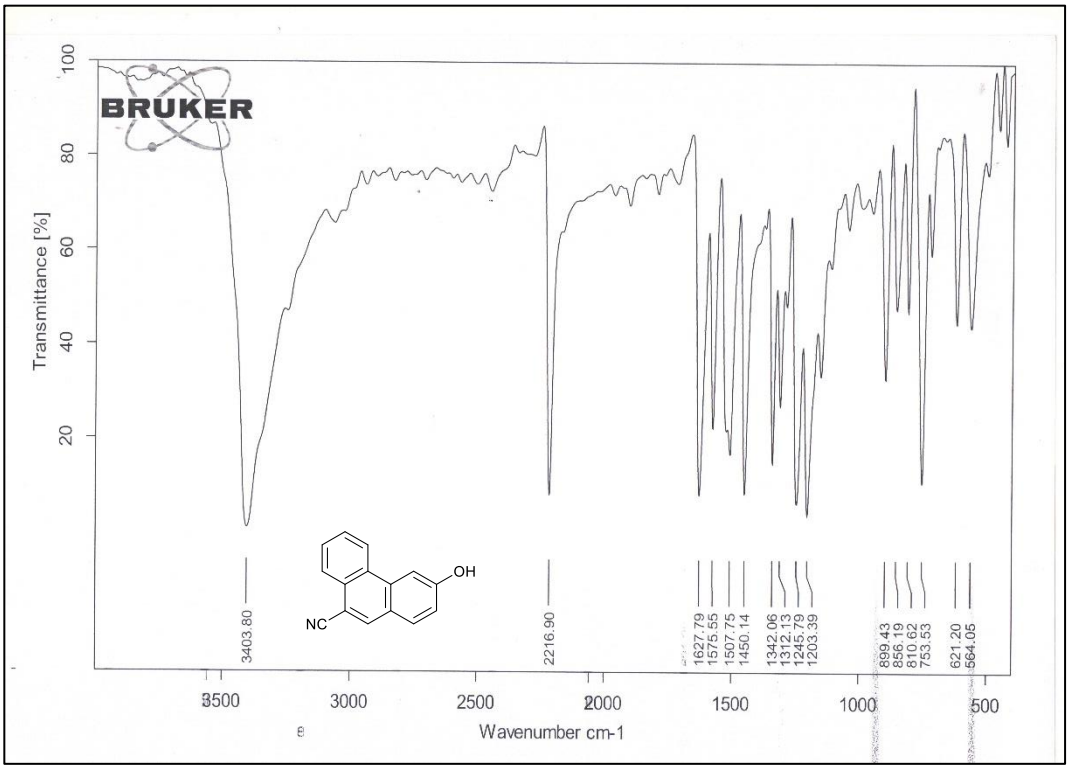

**$^{1}$H NMR Spectra of compound 109 ($CDCl_3$, 400MHz)**



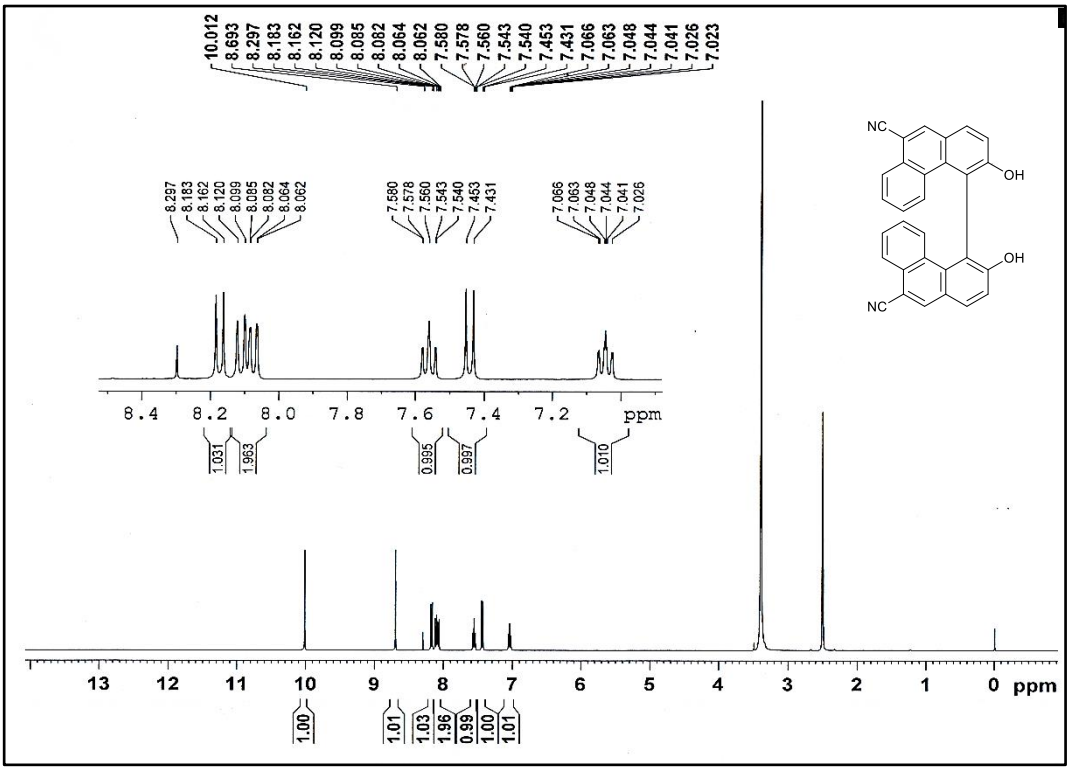

**$^{13}$C NMR Spectra of compound 109 ($CDCl_3$, 100MHz)**



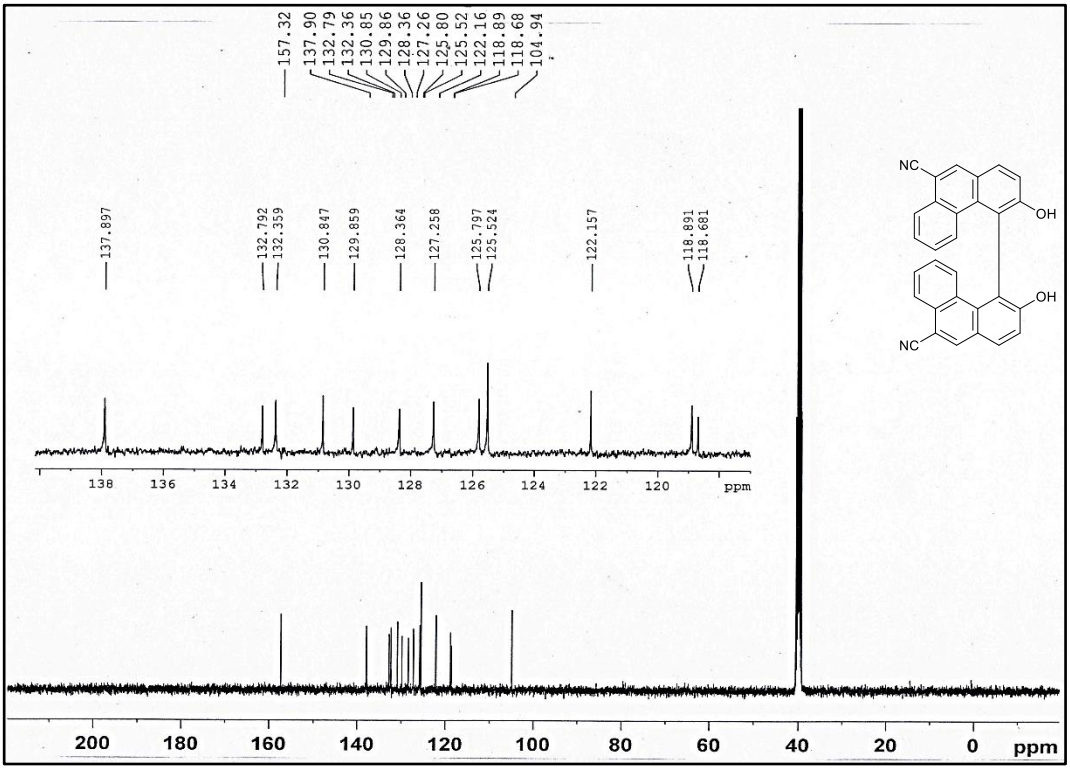

**Mass Spectra of compound 109**



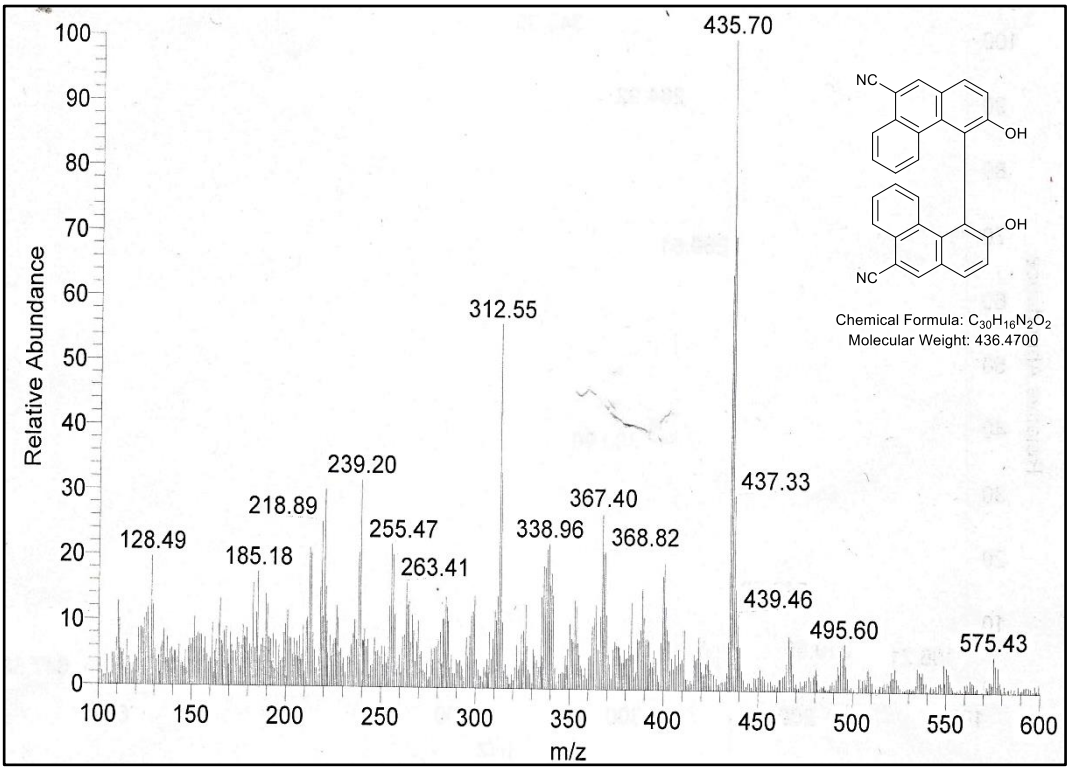

**IR Spectra of compound 109**



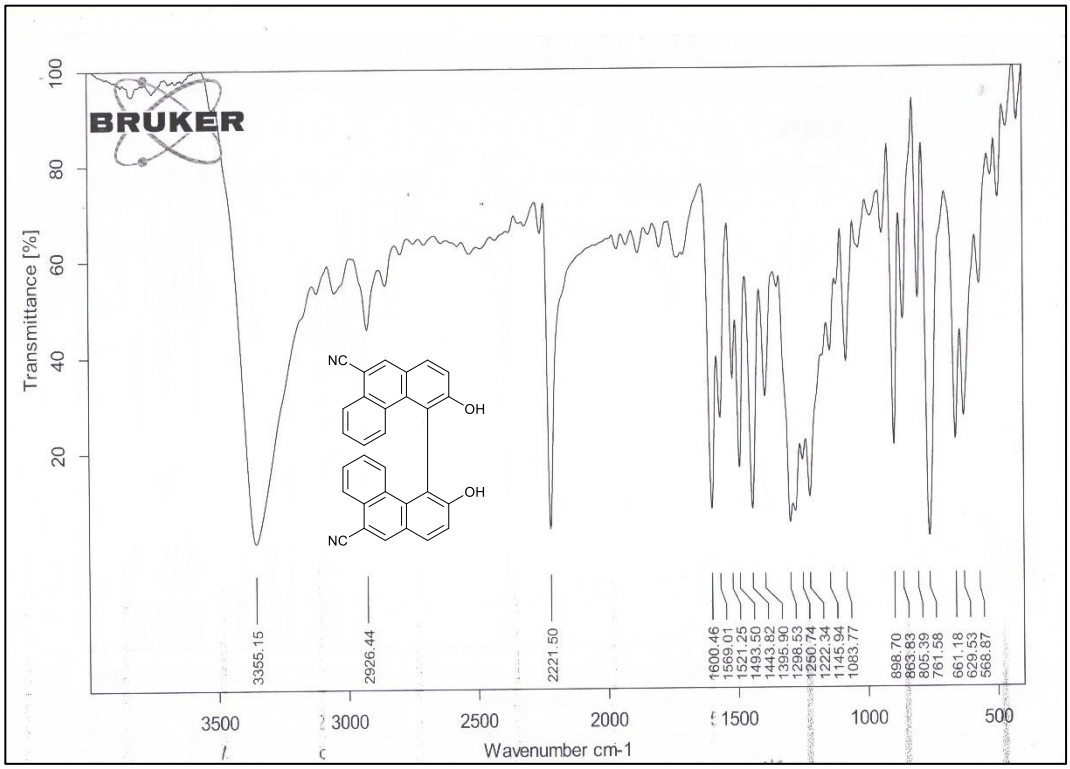

**$^{1}$H NMR Spectra of compound 110 ($d_6$-DMSO, 400MHz)**



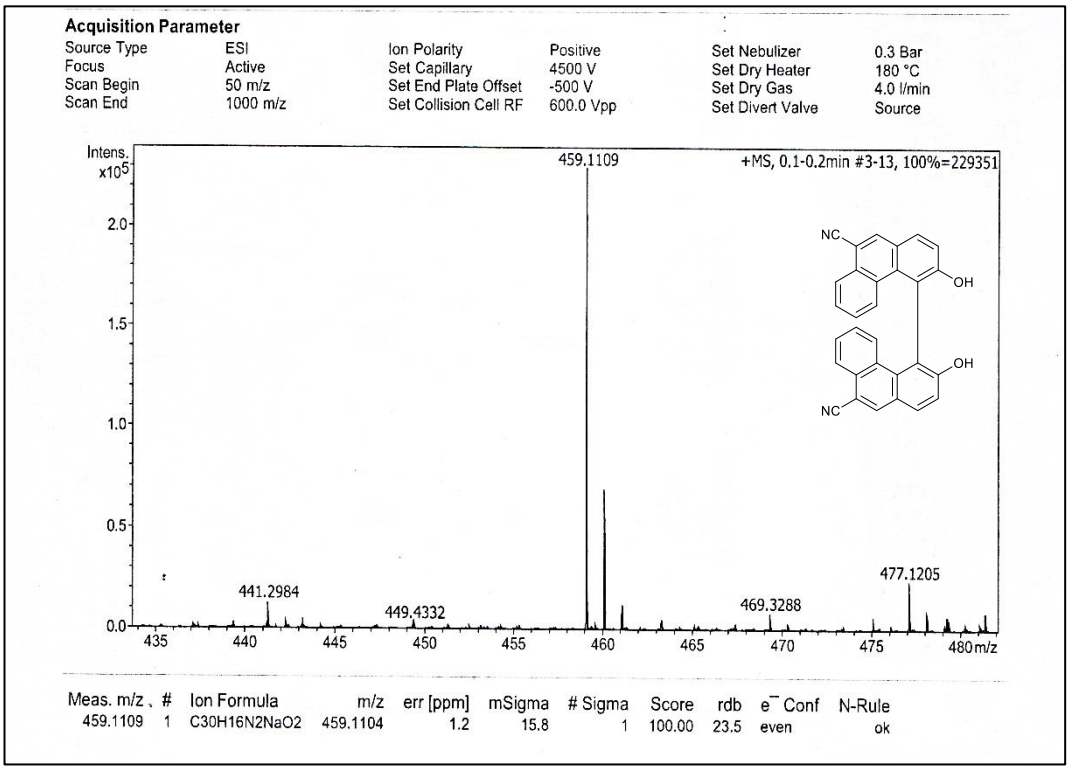

**$^{13}$C NMR Spectra of compound 110 ($d_6$-DMSO, 100MHz)**



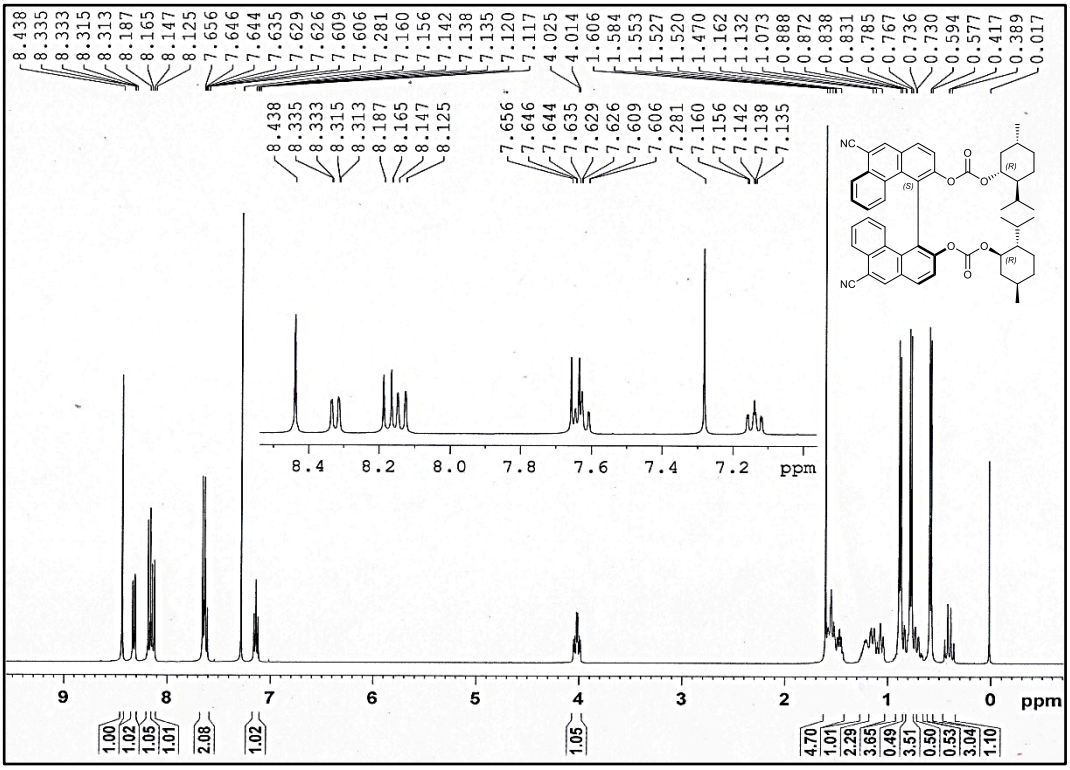

**Mass Spectra of compound 110**



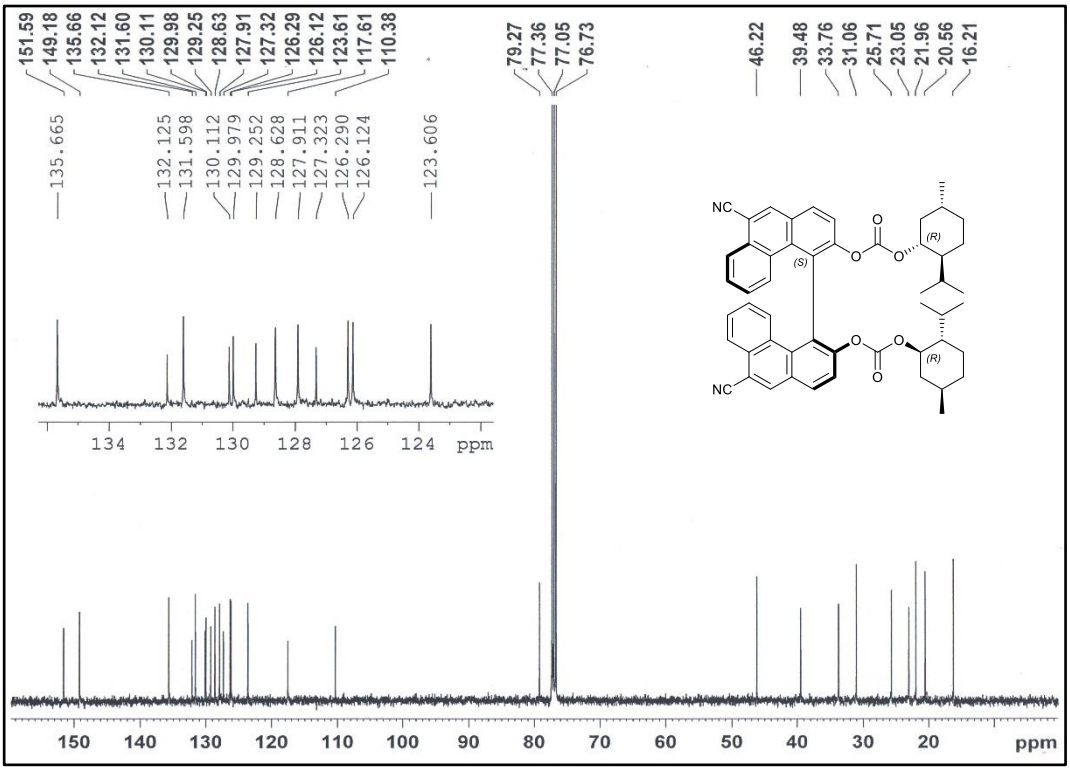

**IR Spectra of compound 110**



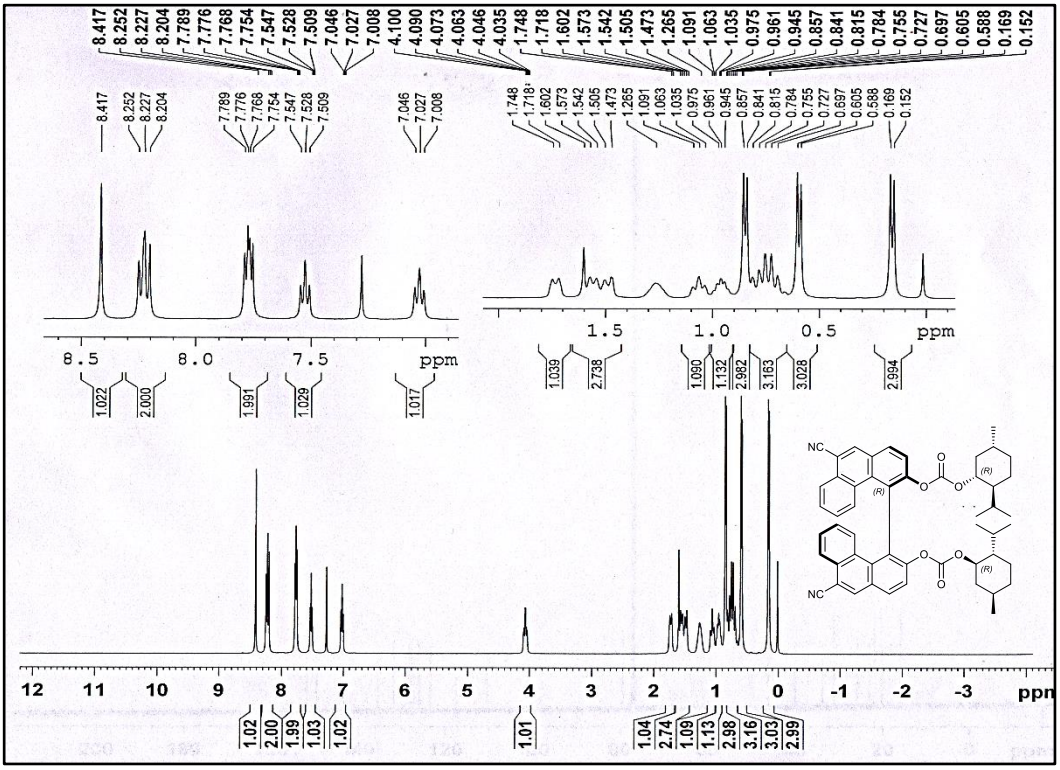

**HRMS Spectra of compound 110**



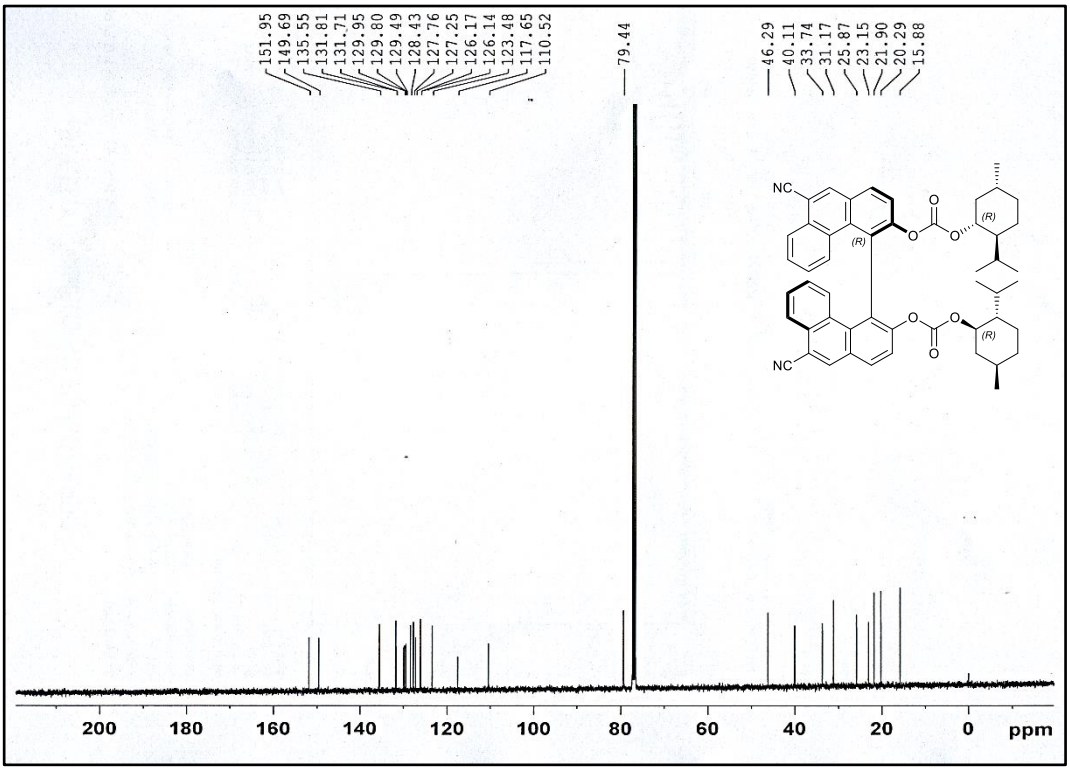

**$^{1}$H NMR Spectra of compound *(S)*-114 ($CDCl_3$, 400MHz)**



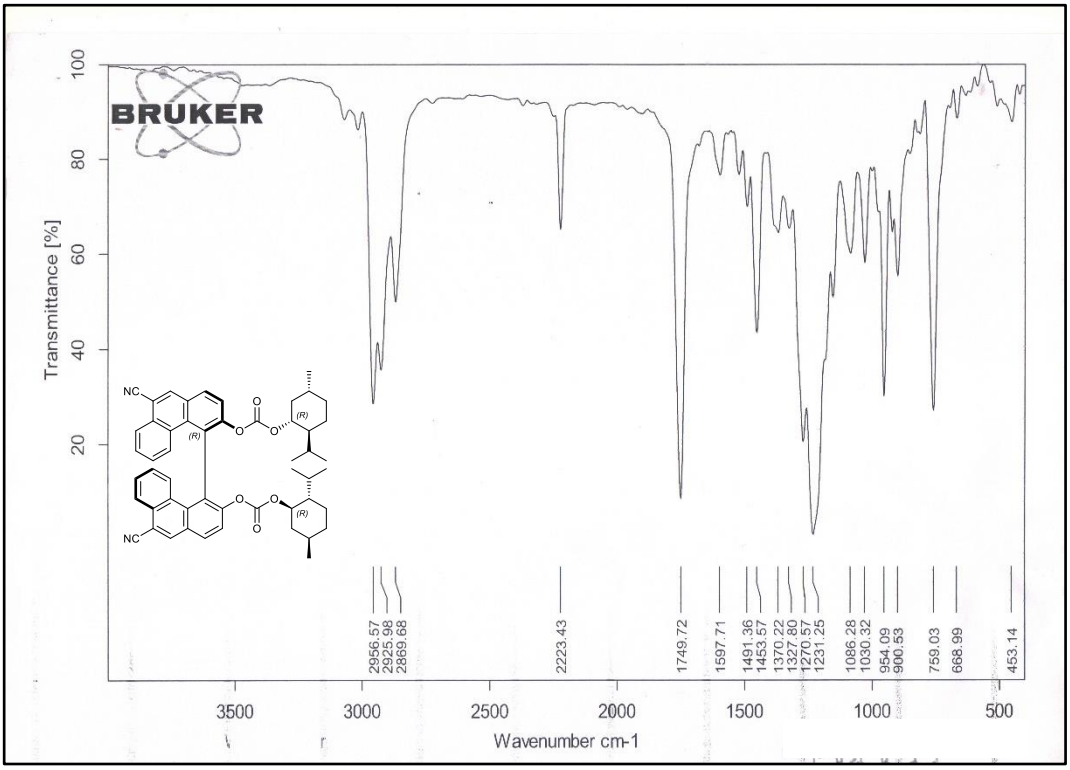
**$^{13}$C NMR Spectra of compound *(S)*-114 ($CDCl_3$, 100MHz)**



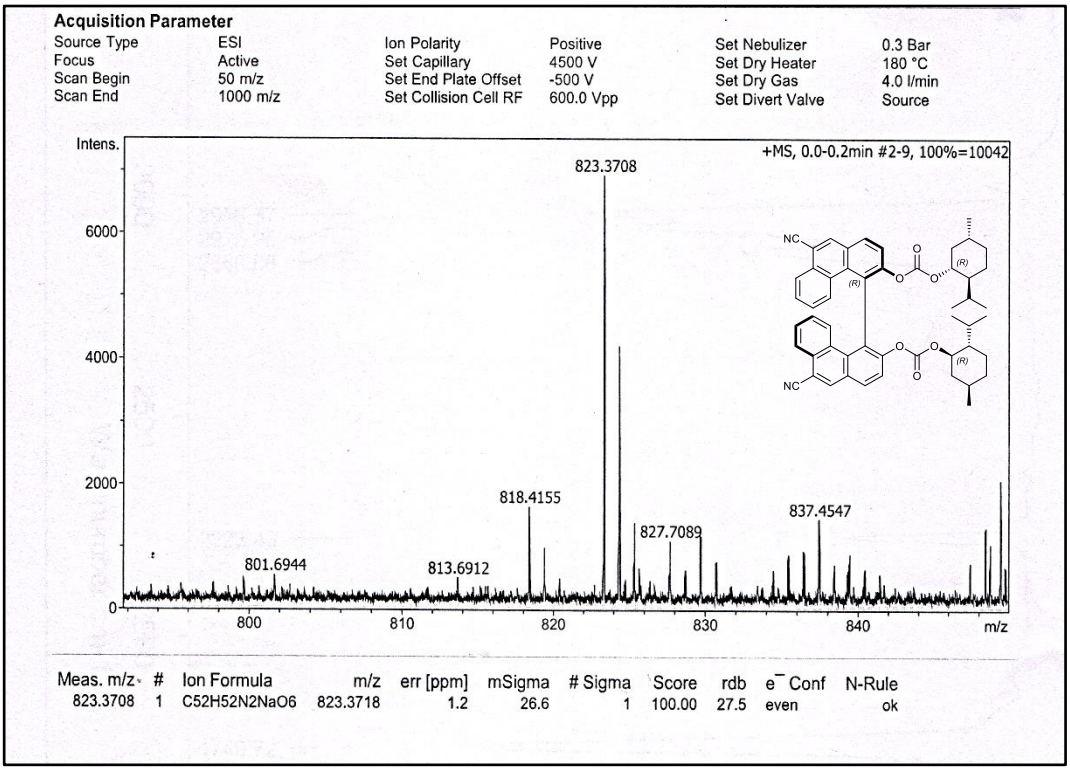
**$^{1}$H NMR Spectra of compound *(R)*-114 ($CDCl_3$, 400MHz)**



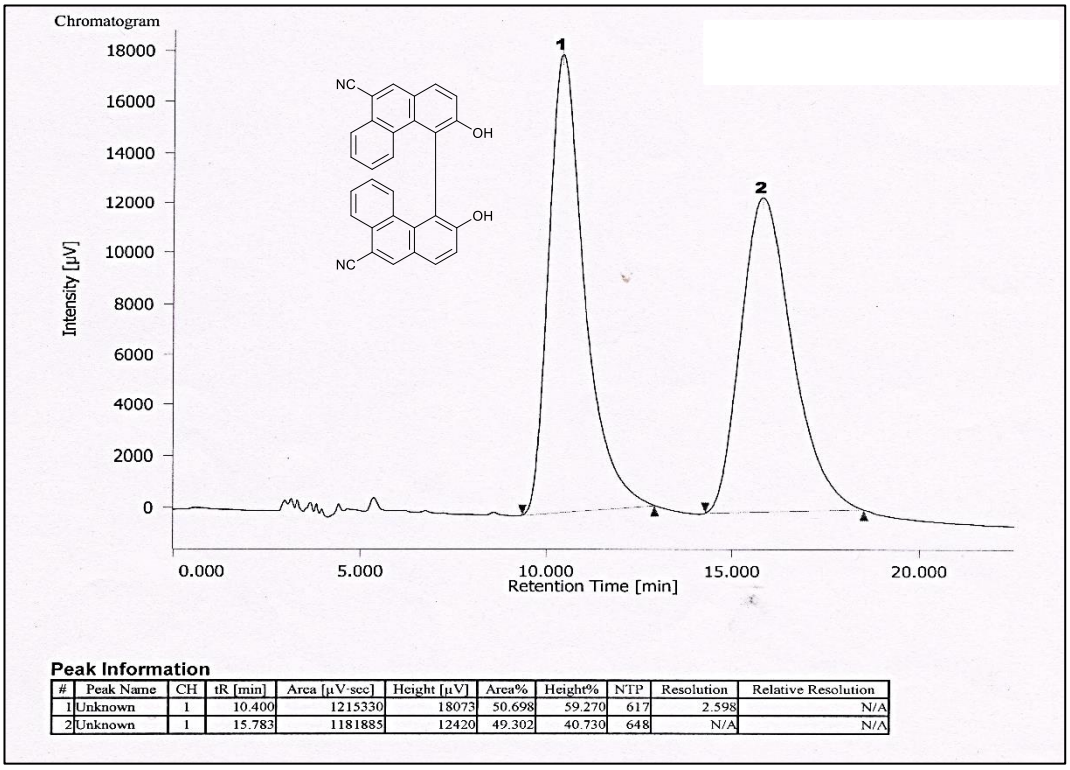

**$^{13}$C NMR Spectra of compound *(R)*-114 ($CDCl_3$, 100MHz)**



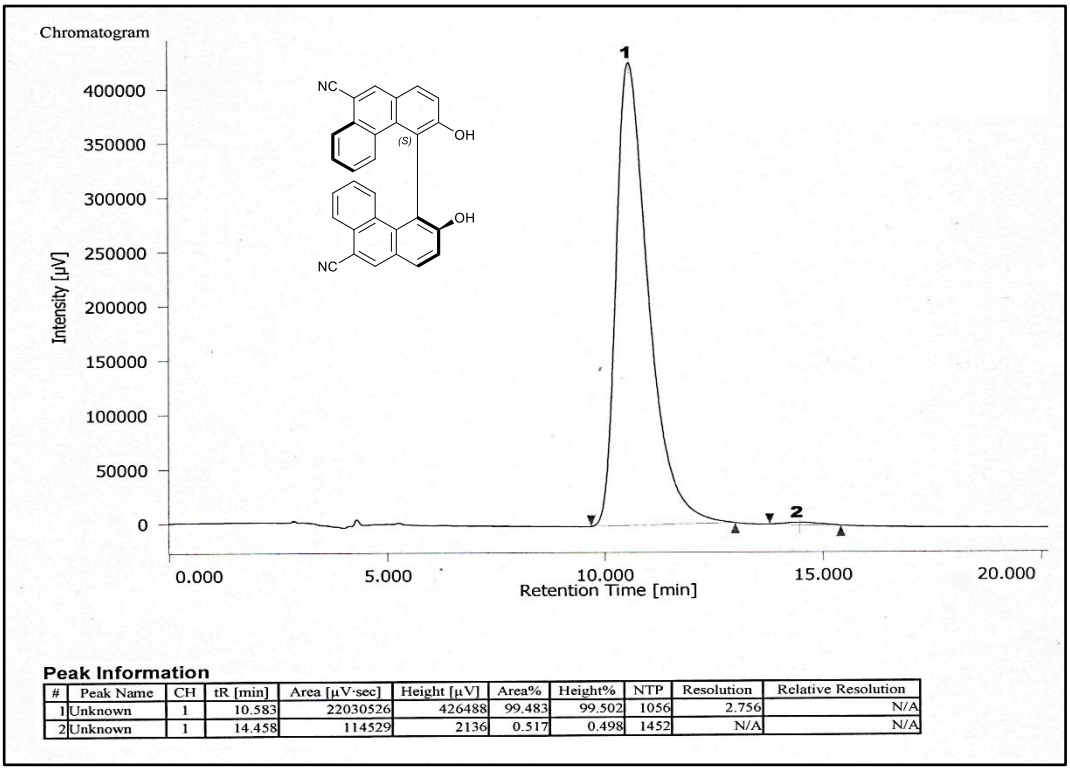

**IR Spectra of compound *(R)*-114**




**HRMS Spectra of compound *(R)*-114**



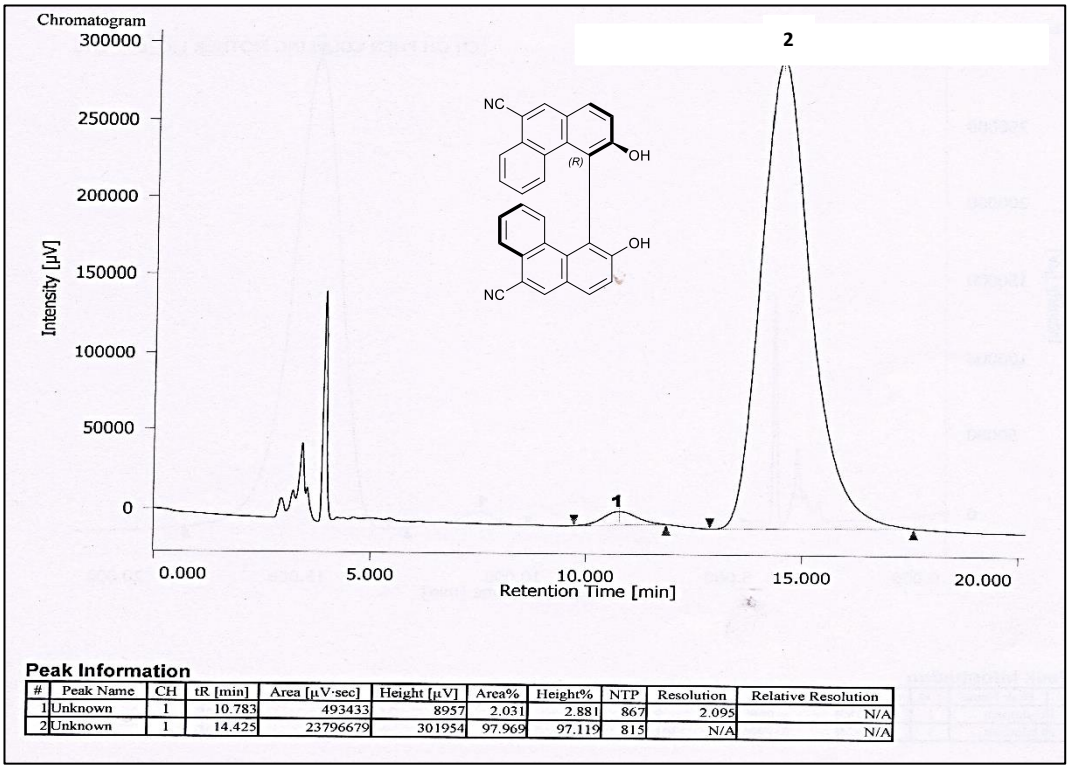

**HPLC Chromatogram of compound (±)-110**




**Peak Information**

| # | Peak Name | CH | tR [min] | Area [µV·sec] | Height [µV] | Area% | Height% | NTP | Resolution | Relative Resolution |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 10.583 | 22030526 | 426488 | 99.483 | 99.502 | 1056 | 2.756 | N/A |
| 2 | Unknown | 1 | 14.458 | 114529 | 2136 | 0.517 | 0.498 | 1452 | N/A | N/A |

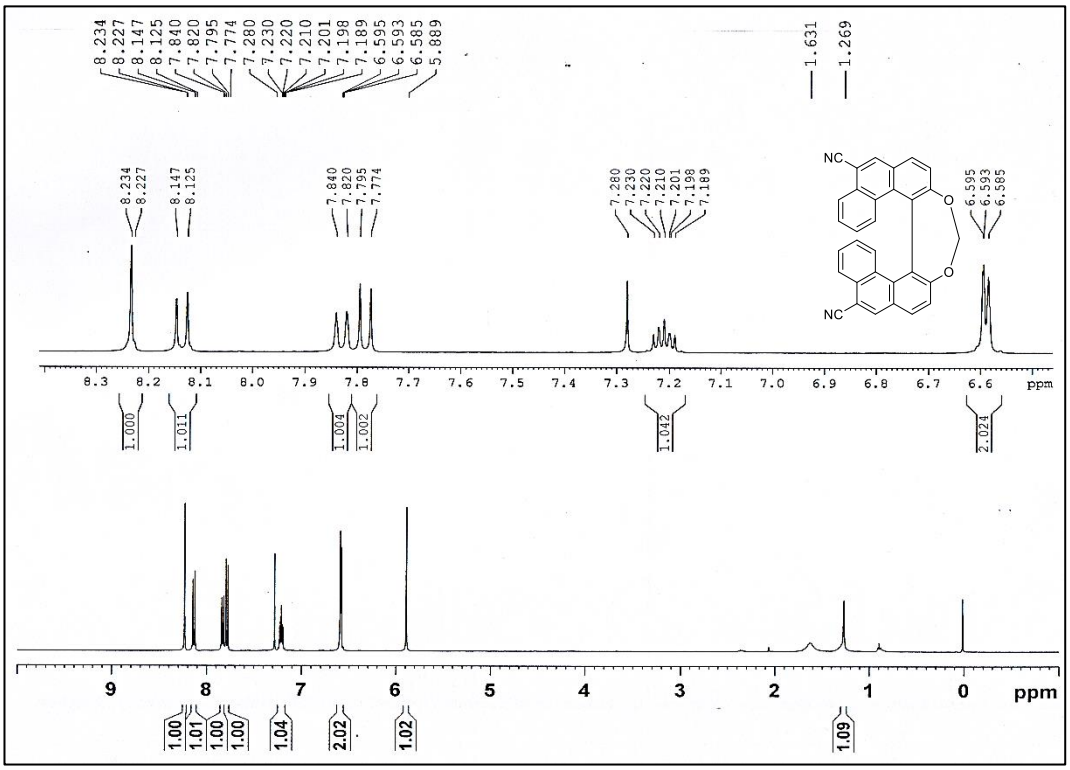
**HPLC Chromatogram of compound *(S)*-110**



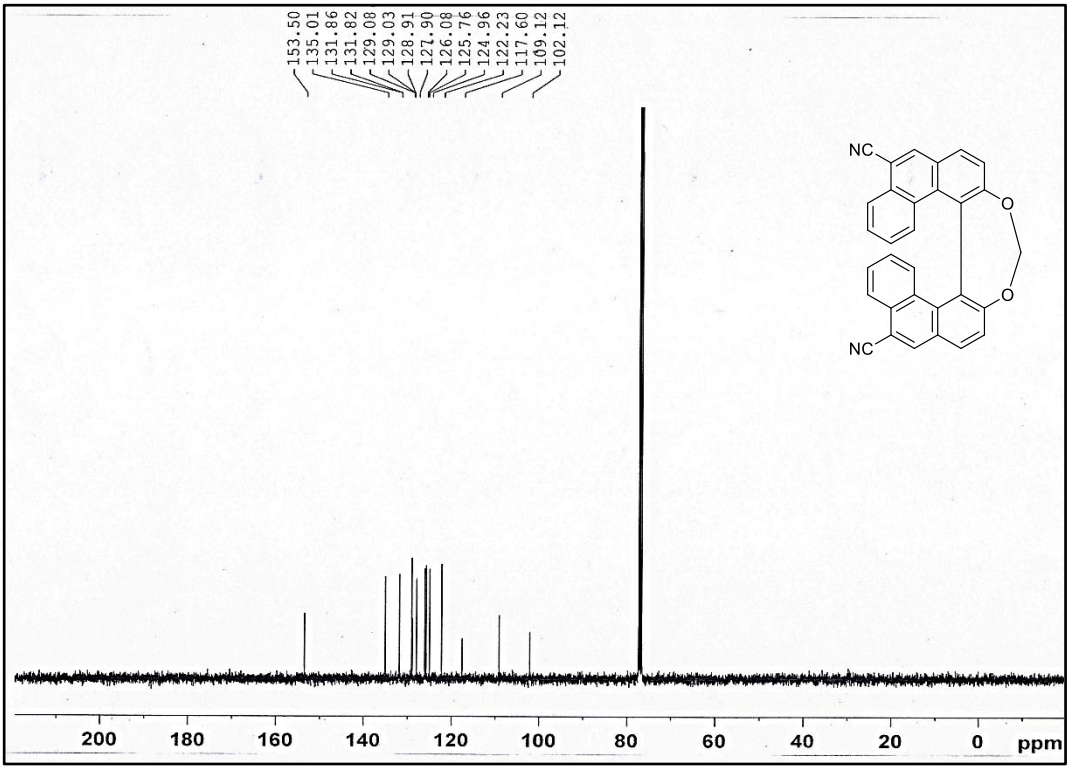

**Peak Information**

| # | Peak Name | CH | tR [min] | Area [µV·sec] | Height [µV] | Area% | Height% | NTP | Resolution | Relative Resolution |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Unknown | 1 | 10.783 | 493433 | 8957 | 2.031 | 2.881 | 867 | 2.095 | N/A |
| 2 | Unknown | 1 | 14.425 | 23796679 | 301954 | 97.969 | 97.119 | 815 | N/A | N/A |

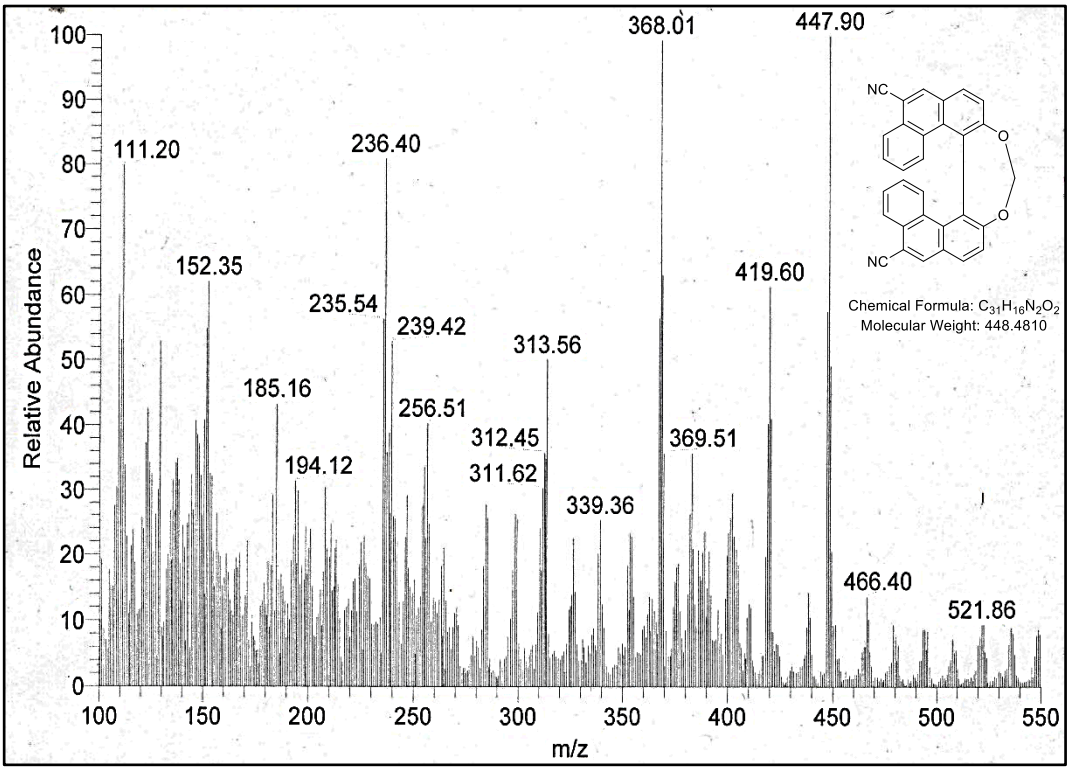
**HPLC Chromatogram of compound *(R)*-110**



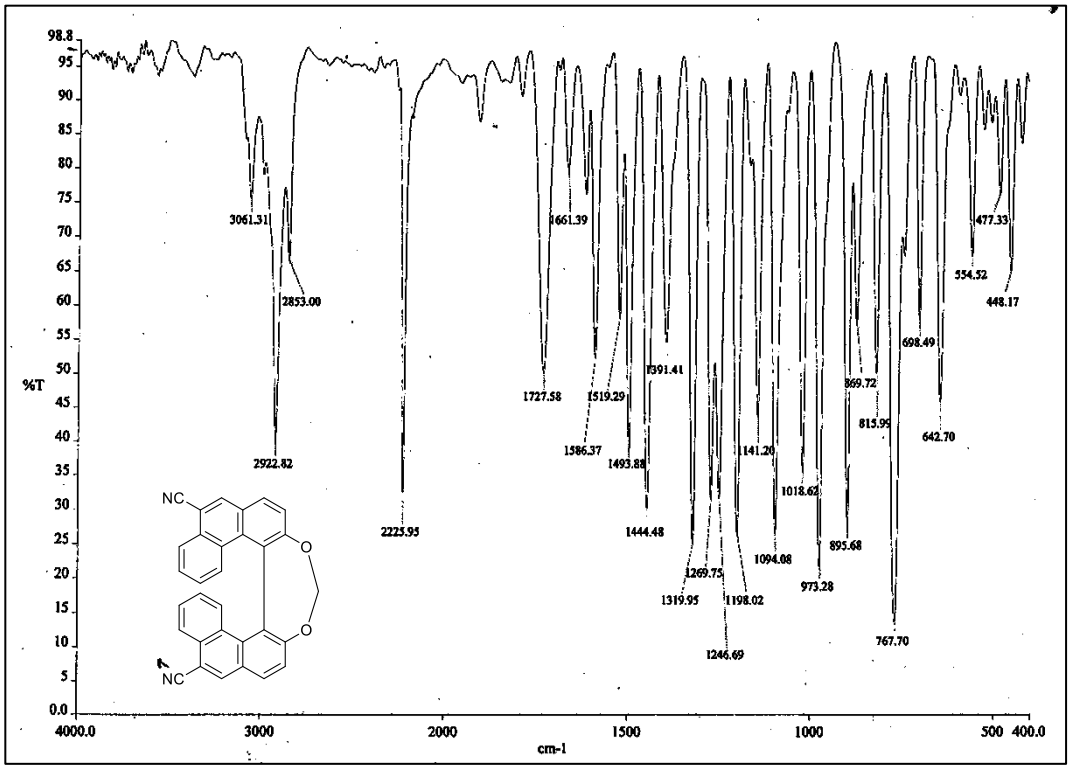

**$^{1}$H NMR Spectra of compound 113 ($CDCl_3$, 400MHz)**



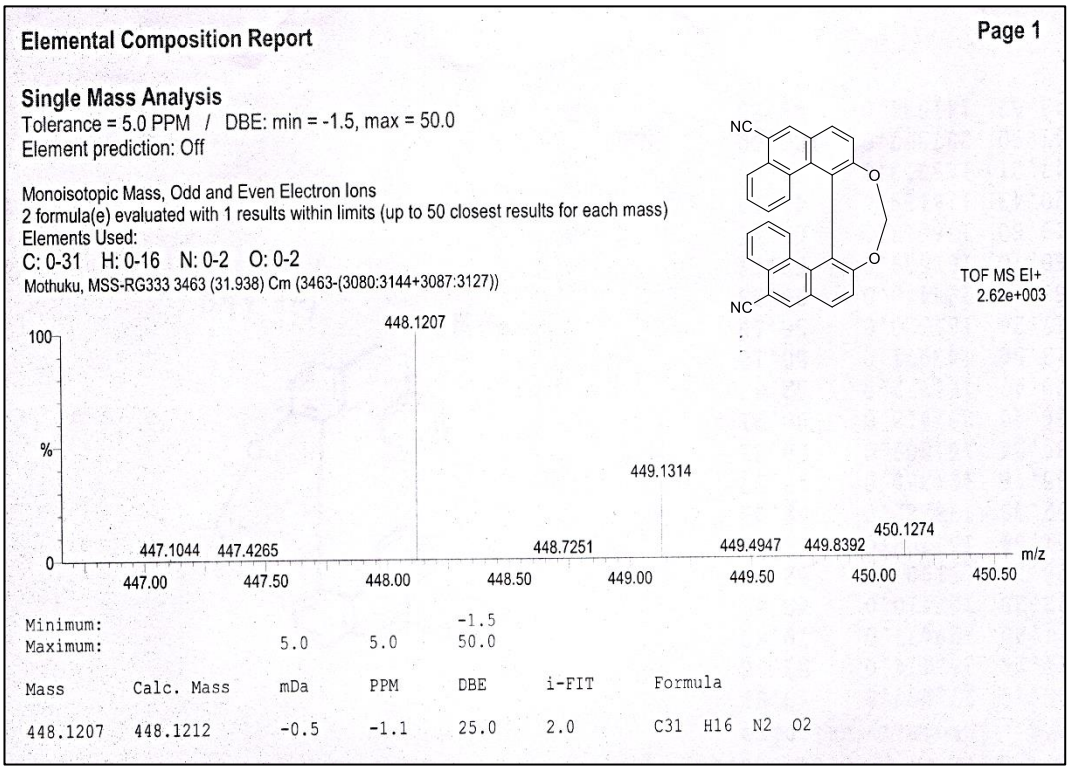

**$^{13}$C NMR Spectra of compound 113 ($CDCl_3$, 100MHz)**



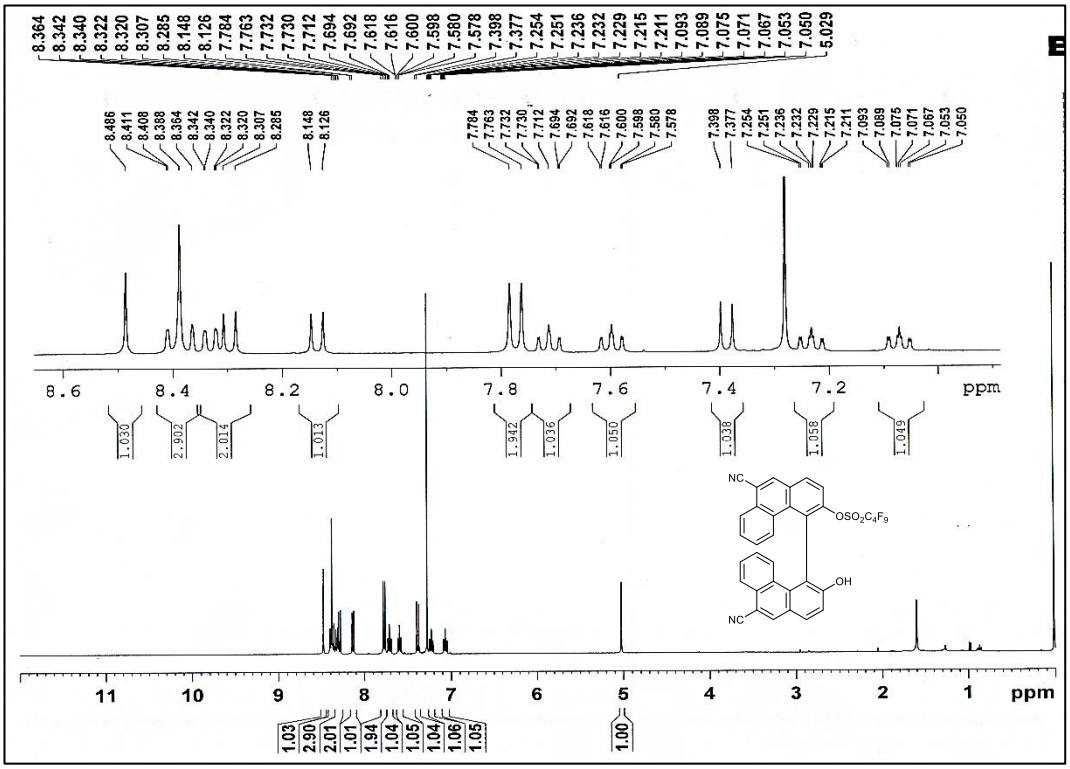

**Mass Spectra of compound 113**



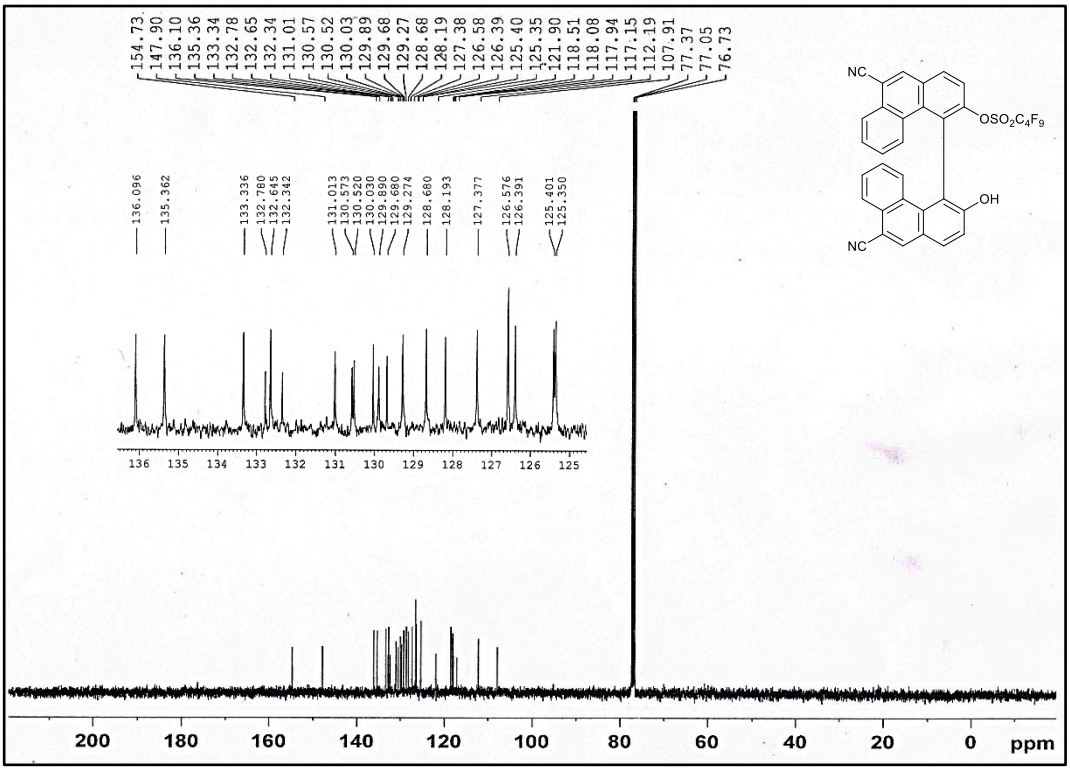

**IR Spectra of compound 113**



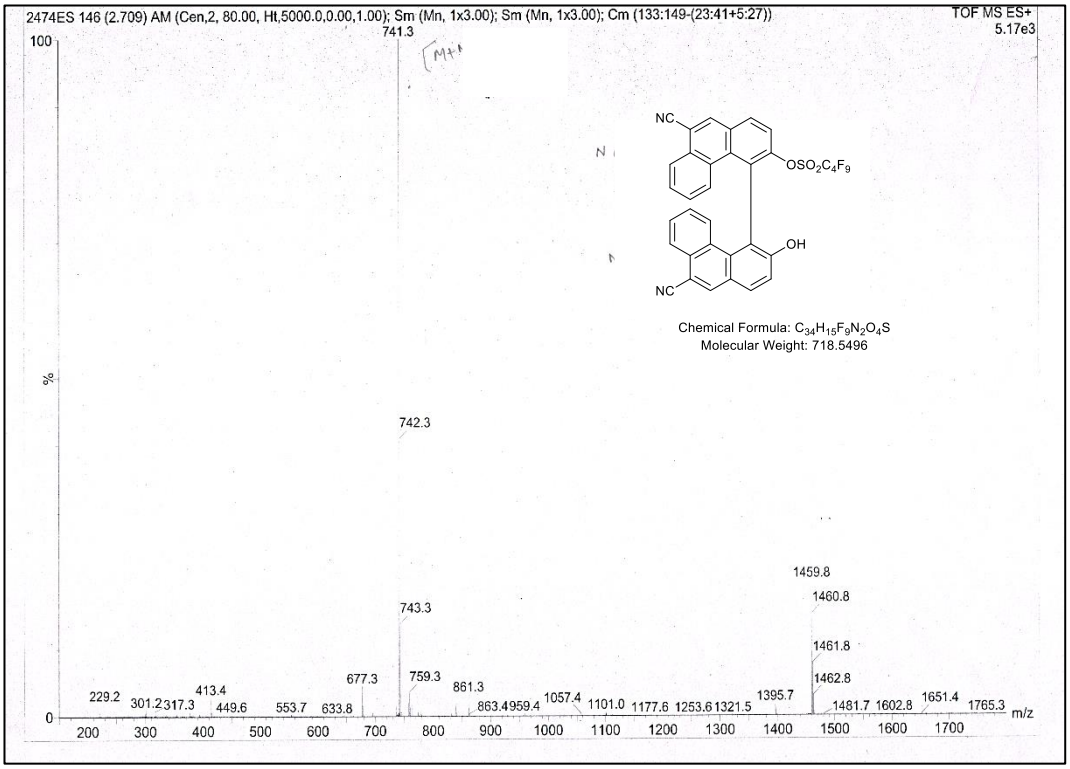

**HRMS Spectra of compound 113**



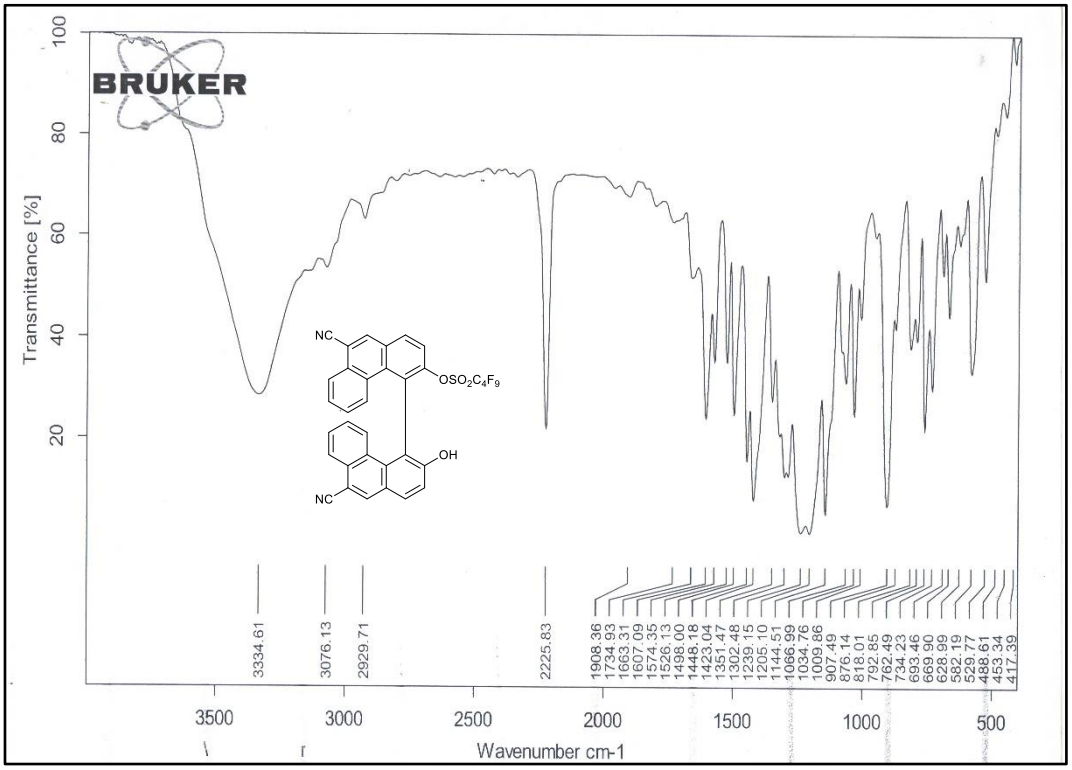

**$^{1}$H NMR Spectra of compound 111 ($CDCl_3$, 400MHz)**



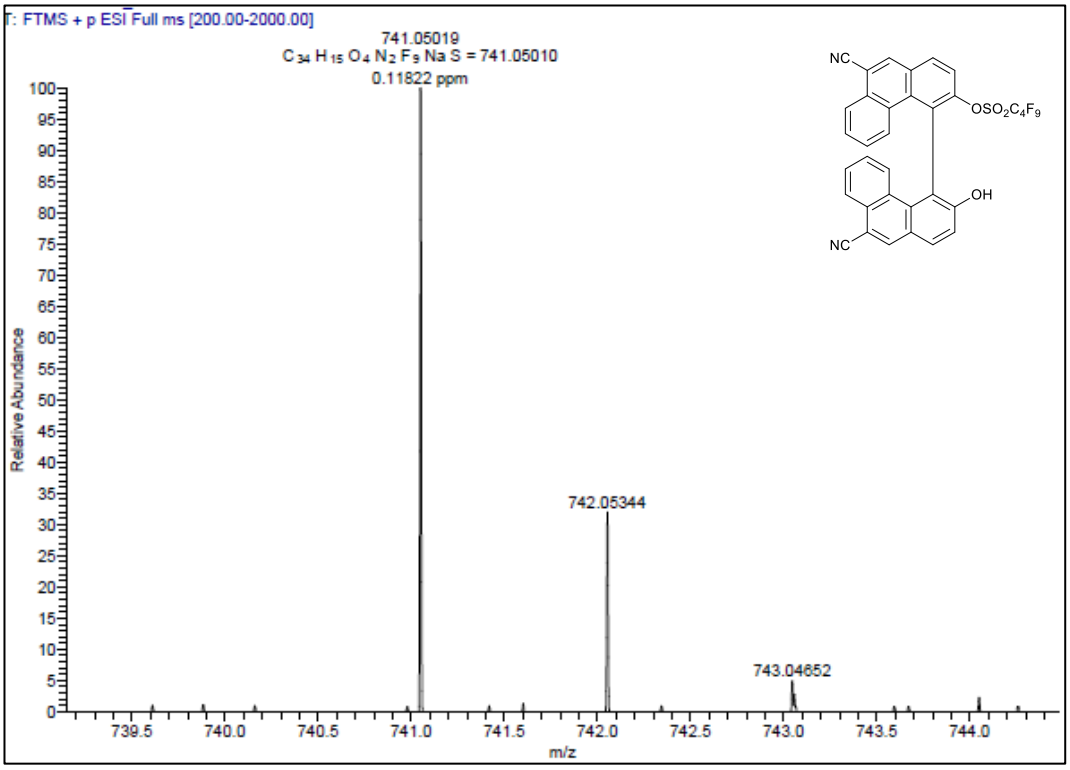

**$^{13}$C NMR Spectra of compound 111 ($CDCl_3$, 100MHz)**



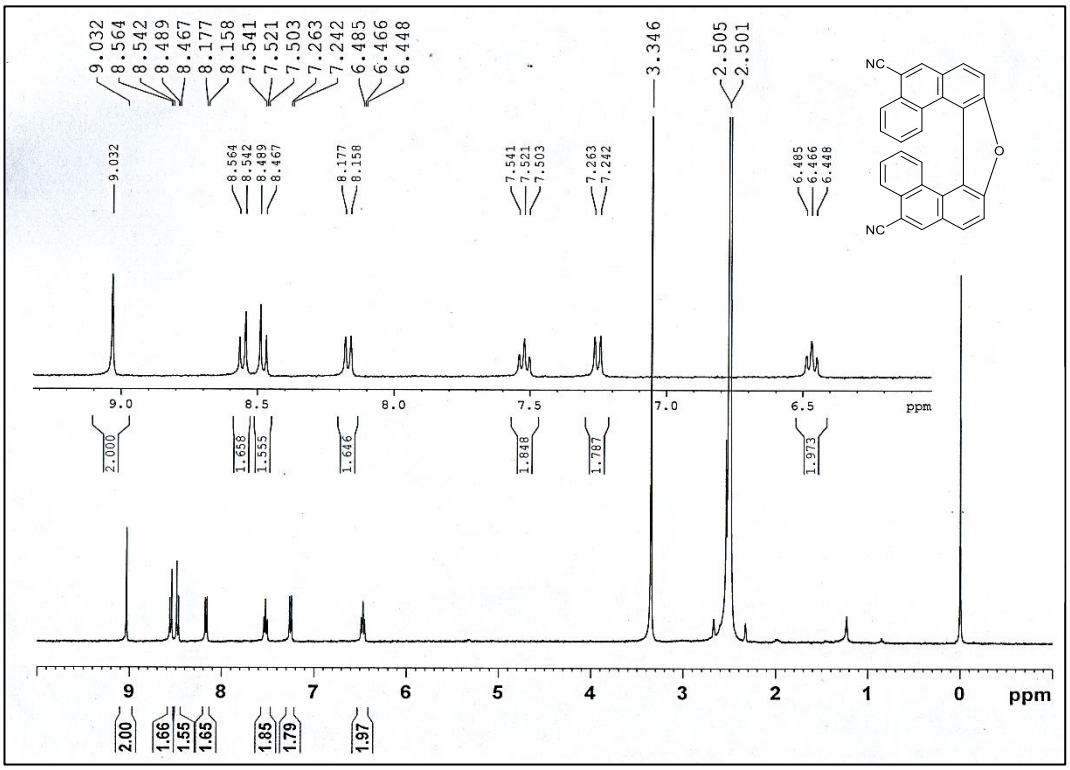

**Mass Spectra of compound 111**



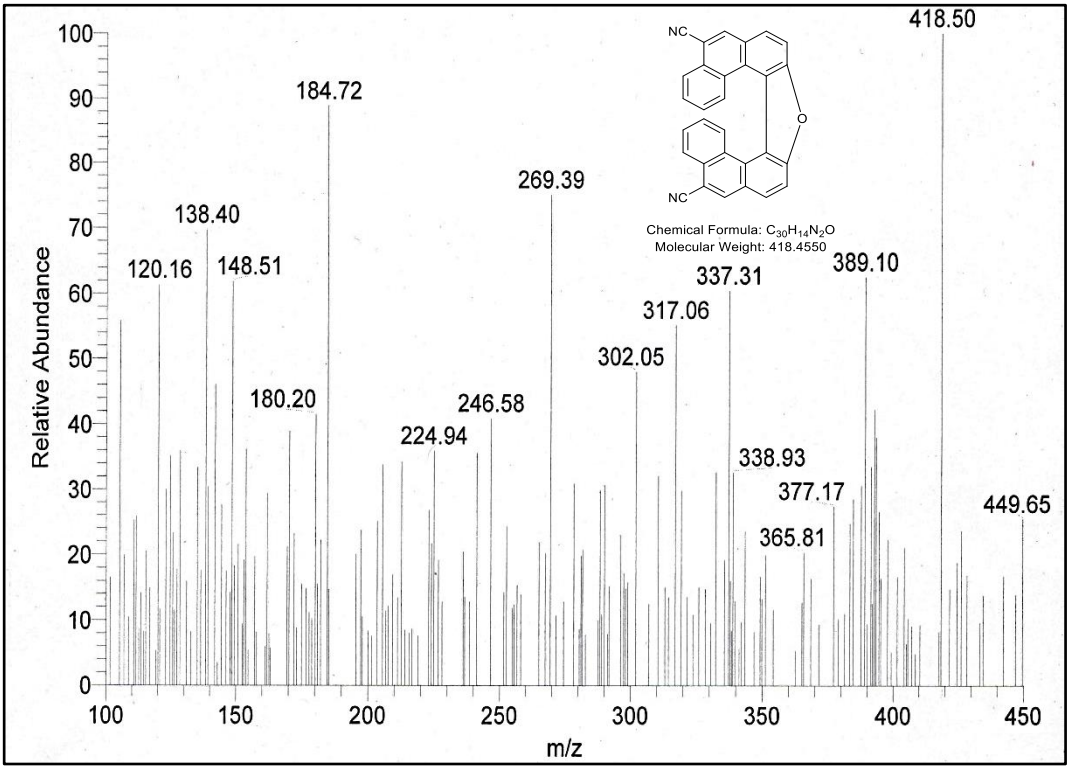

**IR Spectra of compound 111**



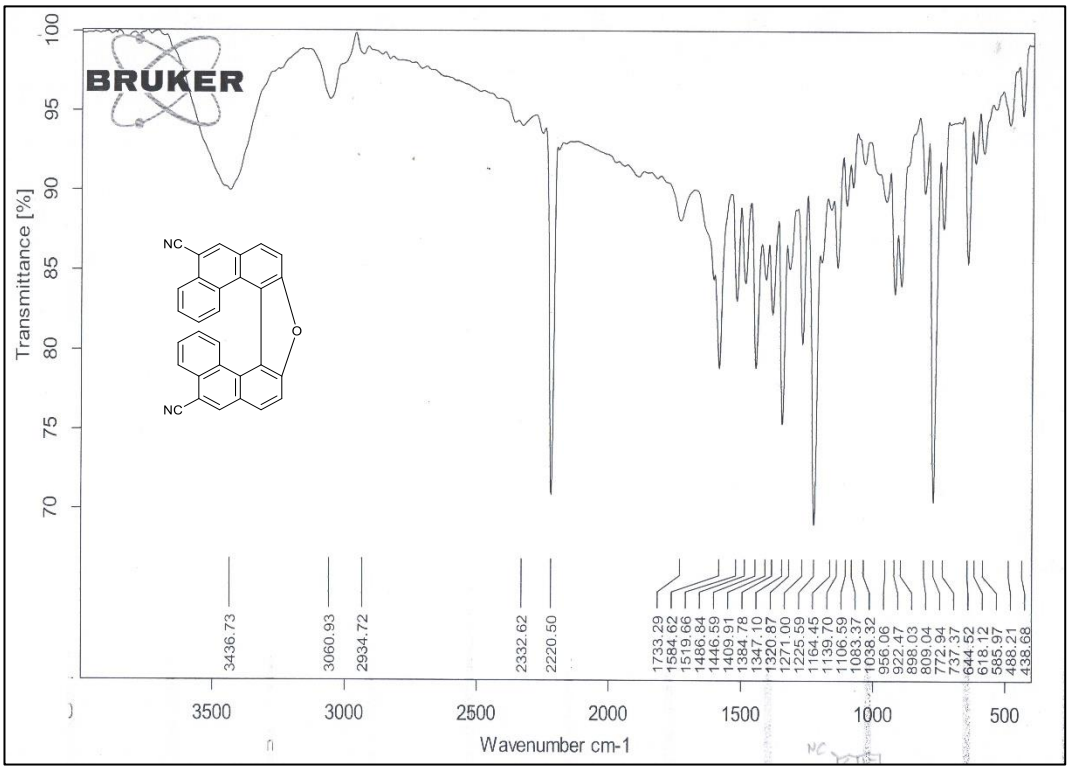

**HRMS Spectra of compound 111**



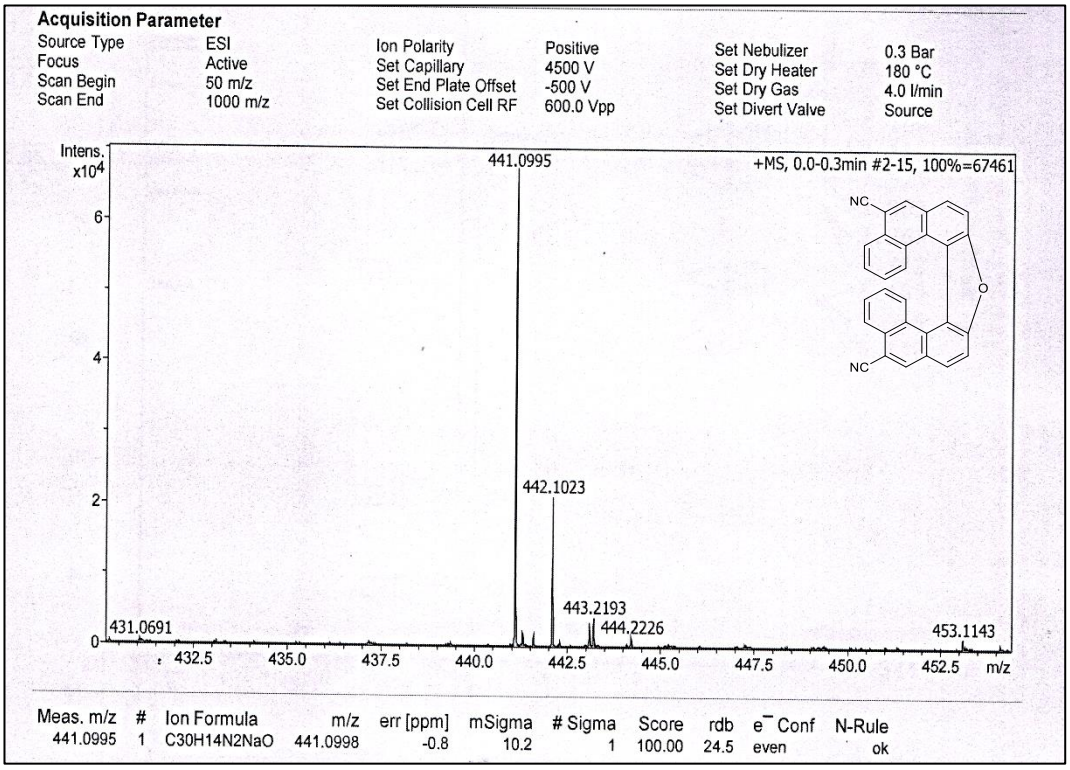

**$^{1}$H NMR Spectra of compound 112 ($d_6$-DMSO, 400MHz)**




**Mass Spectra of compound 112**




**IR Spectra of compound 112**




**HRMS Spectra of compound 112**

## 3.6 Crystallographic Data:

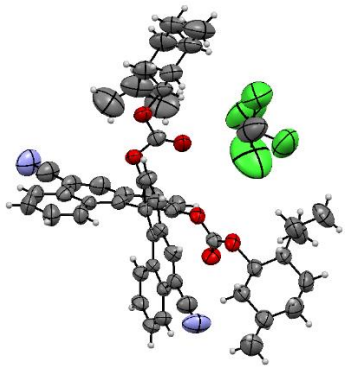


**Figure 17:** ORTEP diagram of **(*S*)-114** with ellipsoids shown at Probability level of 50%

**Table 4:** Crystal data and Structural Refinement of compound ***(S)*-114** (CCDC No. 1816361)

| | |
|---|---|
| Empirical formula | $C_{53}H_{52}Cl_{2.41}N_2O_6$ |
| Formula weight | 898.48 |
| Temperature/K | 295.0 |
| Crystal system | orthorhombic |
| Space group | $P2_12_12_1$ |
| a/Å | 10.9043(9) |
| b/Å | 13.3879(11) |
| c/Å | 33.757(3) |
| α/° | 90 |
| β/° | 90 |
| γ/° | 90 |
| Volume/Å$^3$ | 4928.0(7) |
| Z | 4 |
| $\rho_{calc}$g/cm$^3$ | 1.2109 |
| μ/mm-$^1$ | 0.204 |
| F(000) | 1894.2 |
| Crystal size/mm$^3$ | 0.46 × 0.34 × 0.12 |
| Radiation | Mo Kα (λ = 0.71073) |
| 2Θ range for data collection/° | 6.54 to 58.24 |
| Index ranges | $-14 \leq h \leq 11$, $-17 \leq k \leq 17$, $-45 \leq l \leq 45$ |
| Reflections collected | 18204 |
| Independent reflections | 10822 [$R_{int}$ = 0.0457, $R_{sigma}$ = 0.1191] |
| Goodness-of-fit on $F^2$ | 0.965 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0787, $wR_2$ = 0.1800 |
| Final R indexes [all data] | $R_1$ = 0.1744, $wR_2$ = 0.2421 |
| Flack parameter | 0.1(3) |

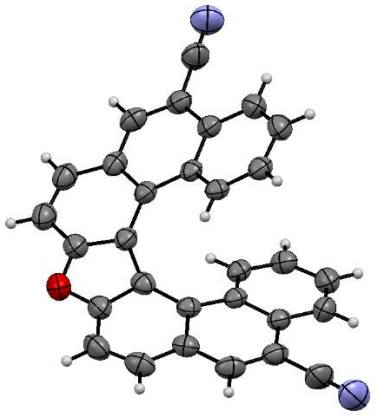


**Figure 18:** ORTEP diagram of **112** with ellipsoids shown at Probability level of 30%

**Table 5:** Crystal data and Structural Refinement of compound **112** (CCDC No. 1527971)

| | |
|---|---|
| Empirical formula | $C_{30}H_{14}N_2O$ |
| Formula weight | 418.43 |
| Temperature/K | 293(2) |
| Crystal system | triclinic |
| Space group | P-1 |
| a/Å | 9.5343(14) |
| b/Å | 9.8029(13) |
| c/Å | 13.042(2) |
| α/° | 78.428(12) |
| β/° | 72.104(13) |
| γ/° | 61.234(14) |
| Volume/Å$^3$ | 1014.8(3) |
| Z | 2 |
| $\rho_{calc}$g/cm3 | 1.369 |
| μ/mm-$^1$ | 0.084 |
| F(000) | 432.0 |
| Radiation | MoKα (λ = 0.71073) |
| 2Θ range for data collection/° | 6.66 to 57.82 |
| Index ranges | $-12 \leq h \leq 12$, $-13 \leq k \leq 13$, $-17 \leq l \leq 17$ |
| Reflections collected | 8215 |
| Independent reflections | 4567 [$R_{int}$ = 0.0377, Rsigma = 0.0785] |
| Data/restraints/parameters | 4567/0/298 |
| Goodness-of-fit on $F^2$ | 1.047 |
| Final R indexes [I>=2σ (I)] | $R_1$ = 0.0710, $wR_2$ = 0.1650 |
| Final R indexes [all data] | $R_1$ = 0.1308, $wR_2$ = 0.1927 |
| Largest diff. peak/hole | e Å$^{-3}$0.16/-0.16 |

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