Synthetic Methods to Access Chiral Bi-2-naphthyl Derivatives

A Thesis

Submitted for the Degree of

DOCTOR OF PHILOSOPHY

By

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To the loving memory of my father

Late Sri M. Venkateswararao

Contents

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Statement

I hereby declare that the matter embodied in this thesis is the result of investigations carried out by me in the School of Chemistry, University of Hyderabad, Hyderabad, under the supervision of **Professor M. Periasamy**.

In keeping with the general practice of reporting scientific observations, due acknowledgement has been made wherever the work described is based on the findings of other investigators.

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Certificate

Certified that the work embodied in this thesis entitled **"Synthetic Methods to Access Chiral Bi-2-naphthyl Derivatives"** has been carried out by **Mr. M. NAGARAJU** under my supervision and the same has not been submitted elsewhere for a Degree.

PROFESSOR M. PERIASAMY
(THESIS SUPERVISOR)

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Miriyala Nagaraju

Abbreviations

[α]	specific rotation [expressed without units; the actual units, deg.mL/g. dm, are understood]
aq.	aqueous
Ac	acetyl
BINOL	1,1′-bi-2-naphthol
Bn	benzyl
Bz	benzoyl
bp	boiling point
br s	broad singlet (spectral)
Bu	butyl
^{t}Bu	*ter*-butyl
^{o}C	degree Celsius
conc.	concentrated
CSC	camphorsulphonic chloride
Cat.	catalytic
cm^{-1}	wavenumber
δ	chemical shift in parts per million downfield from tetramethyl silane
DCM	dichloromethane
DBU	1,8-diazabicyclo(5,4,0)undec-7-ene
DIEA	diisopropylethylamine
DIPEDA	diphenylethylenediamine
DME	dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DPP	diphenylpyrrolidinemethanol
dr	diastereomeric ratio
ee	enantiomeric excess
Et	ethyl
Et_2O	diethyl ether
EtOH	ethyl alcohol
equiv.	equivalent

eqn.	equation
$Fe(acac)_2$	ferrous acetylacetonate
g	gram (s)
h	hour (s)
HMPA	hexamethylphosphoramide
HPLC	high-performance liquid chromatography
Hz	hertz
^{i}Pr	isopropyl
IR	infrared
J	coupling constant (in NMR Spectrometry)
KHMDS	potassium bis(trimethylsilyl)amide
lit.	literature
$LiAlH_4$	lithium aluminium hydride
LDA	lithium diisopropyl amide
m	multiplet (spectral)
Me	methyl
MeOH	methanol
MW	molecular weight
MHz	megahertz
min.	minute(s)
mmol	millimolar
MOMCl	methoxymethyl chloride
mp	melting point
MS	molecular sieves
MsCl	methanesulfonyl chloride
MTPA	α-methoxy-α-(trifluoromethyl)phenylacetic acid
$NaBH_4$	Sodium borohydride
NaH	Sodium hydride
NMP	N-methyl pyrrolidone
NMR	nuclear magnetic resonance
n-	primary

Nu	nucleophile
$Pd(dba)_2$	bis(dibenzylideneacetone)palladium(0)
$Pd(PPh_3)_4$	tetrakis(triphenylphosphine)palladium(0)
Ph	phenyl
q	quartet (in spectroscopy)
α,β,α,α-TAPP	5α,10β,15α,20β -tetra(o-aminophenyl)porphyrin
THF	tetrahydrofuran
TMEDA	tetramethylenediamine
TMSCl	trimethylsilyl chloride
TMSI	trimethylsilyl iodide
TFA	trifluoroacetic acid
TsOH	*p*-toluenesulfonic acid

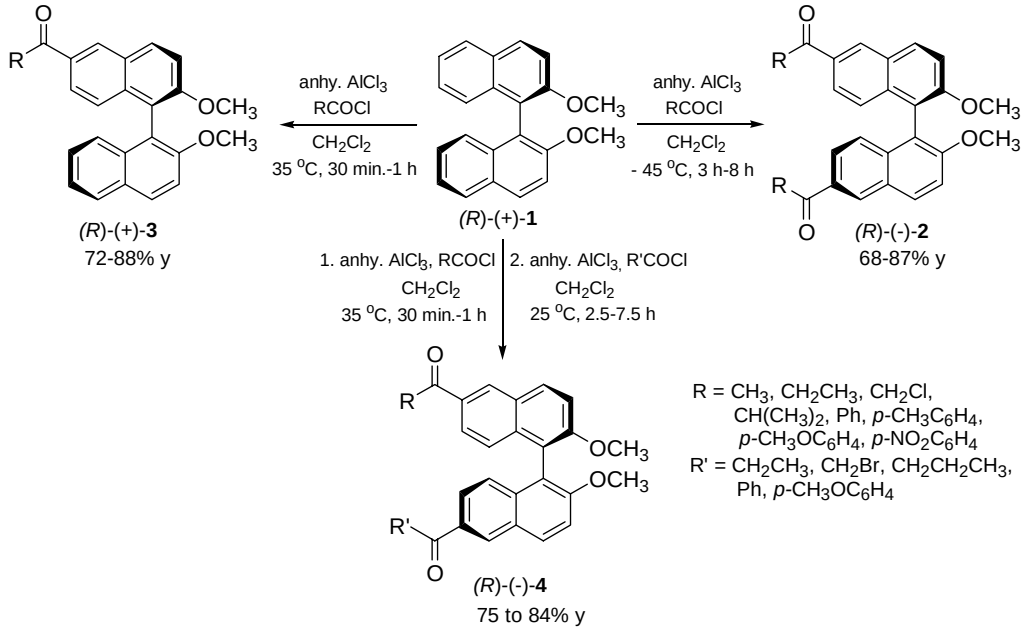
Abstract

This thesis entitled "**Synthetic Methods to Access Chiral Bi-2-naphthyl Derivatives**" comprises of three chapters namely **(i). Introduction**, **(ii). Results and Discussion** and **(iii). Experimental Section** along with **References**. The work described in this thesis is exploratory in nature.

The first chapter describes a brief review on the synthesis of various 3,3′, 4,4′ and 6,6′-substituted-1,1′-bi-2-naphthyl derivatives. Reported applications of these derivatives for organic synthesis are also presented.

In the second chapter, the results and discussion on the synthesis of various 6-monosubstituted and 6,6′-disubstituted-1,1′-bi-2-naphthyl derivatives are described in six sections.

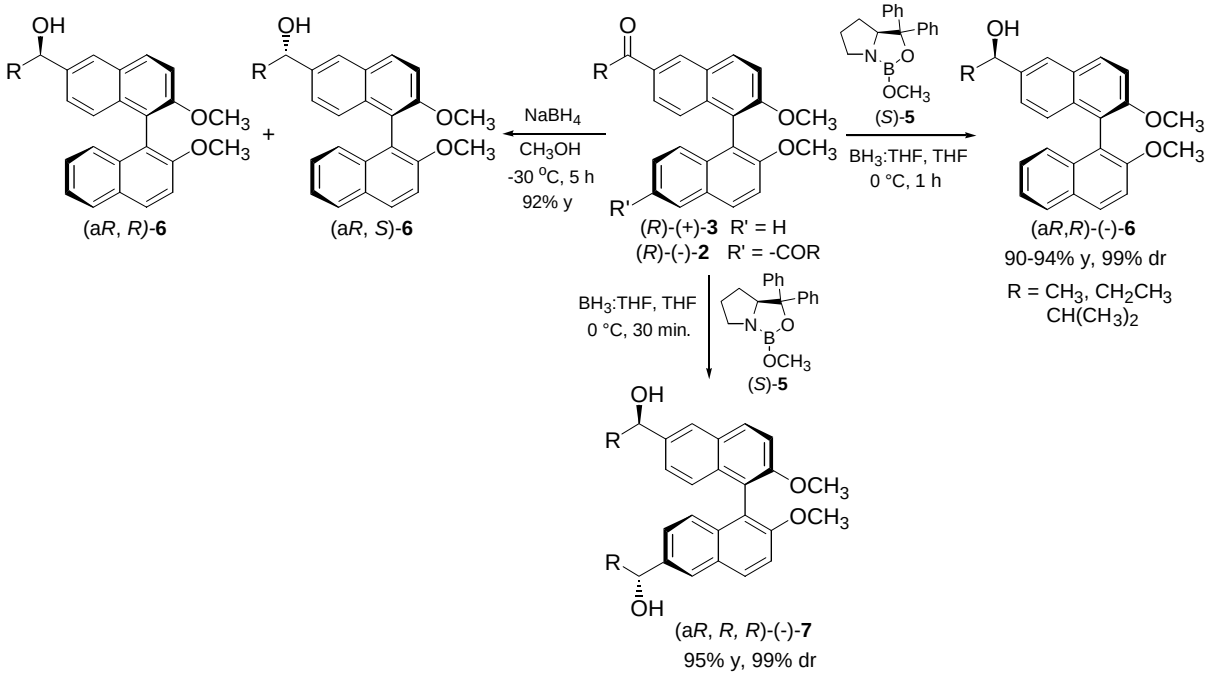
Chart 1



In section 1, studies carried out on the development of methods for the synthesis of monoacyl **3**, symmetrical diacyl **2**, and unsymmetrical diacyl **4** derivatives of (*R*)-(+)-1,1′-bi-2-naphthyl methyl ether **1** are described (Chart 1).

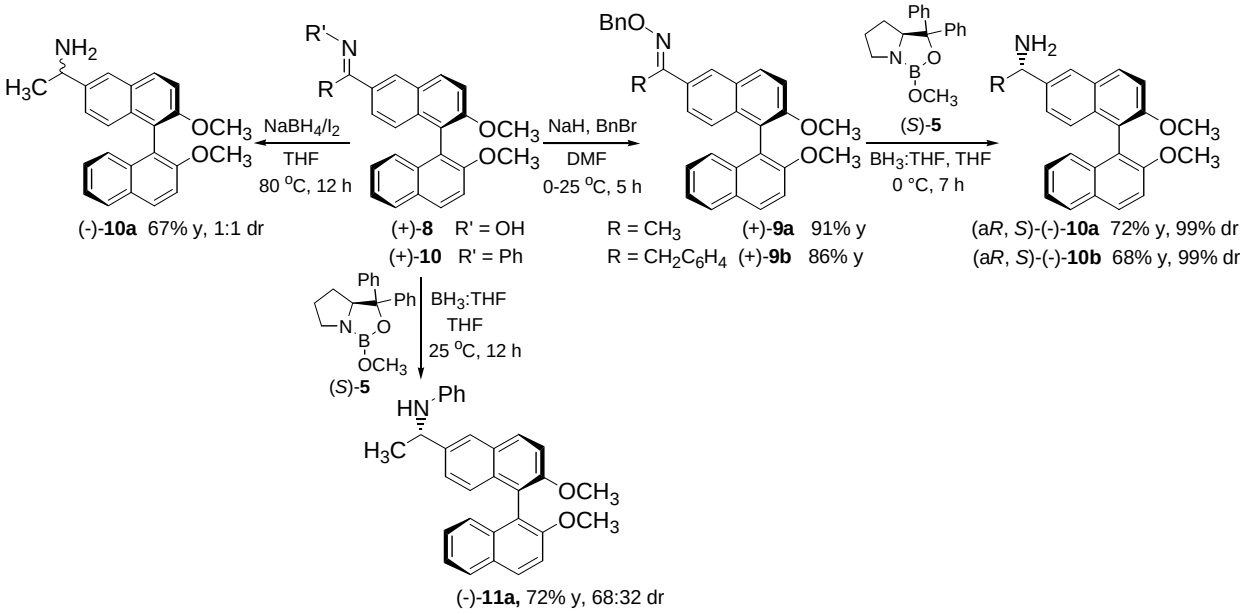
Studies on the reduction of 6-acyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**3** and 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(-)-**2** with the $NaBH_4/CH_3OH$ reagent system are described in section 2. Also, studies on the asymmetric reduction of 6-acyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**3** using chiral oxazaborolidine catalyst (*S*)-**5** are described (Chart 2). The configuration of the newly formed stereogenic centre was assigned as *R* by ^{1}H-NMR analysis of the corresponding Mosher esters.

Chart 2



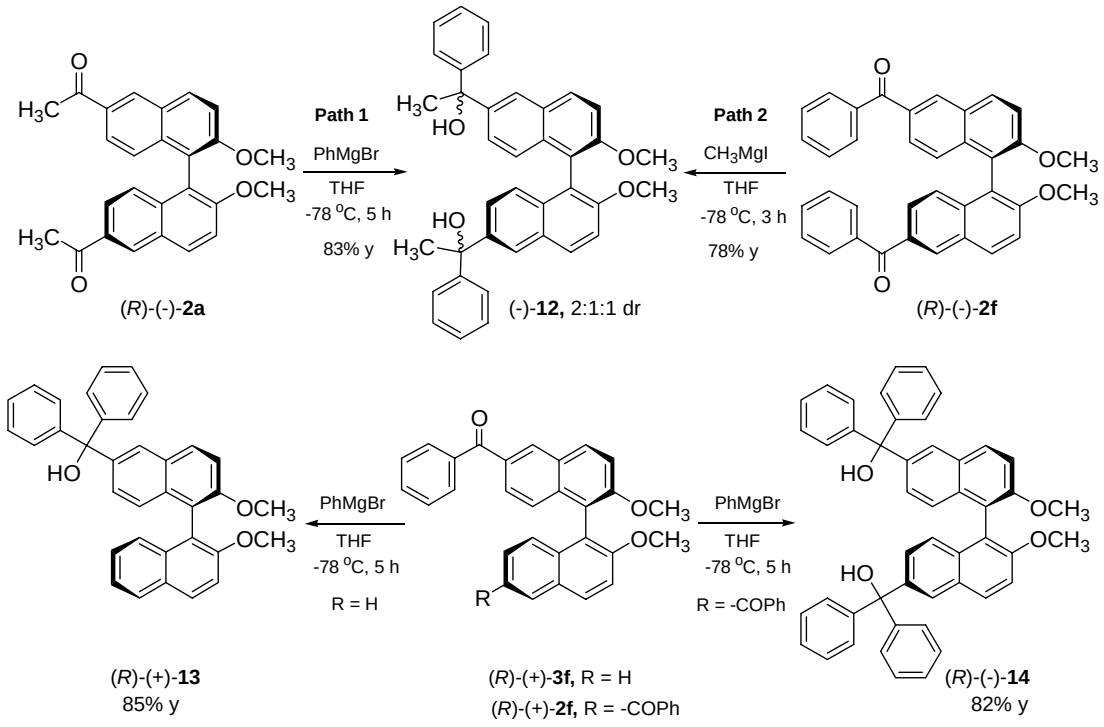
In section 3, studies on the reduction of ketoxime **8** and ketoxime ether **9** using the $NaBH_4/I_2$ reagent system and chiral oxazaborolidine catalyst (*S*)-**5** are described (Chart 3). Asymmetric reduction of ketoxime ether **9** using 30 mol% of oxazaborolidine gave the corresponding amine with high diastereoselectivity (99%).

Chart 3



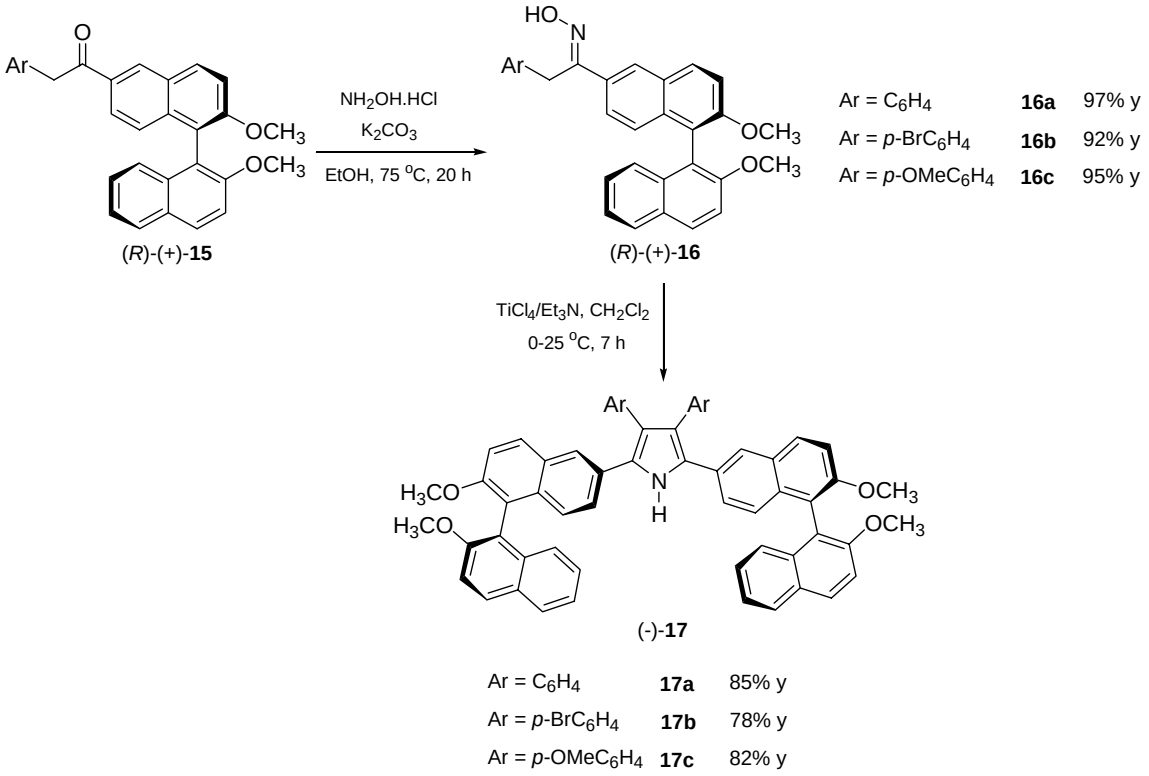
Studies on the addition of Grignard reagents to diketones **2** and **3** are described in section 4 (Chart 4).

Chart 4



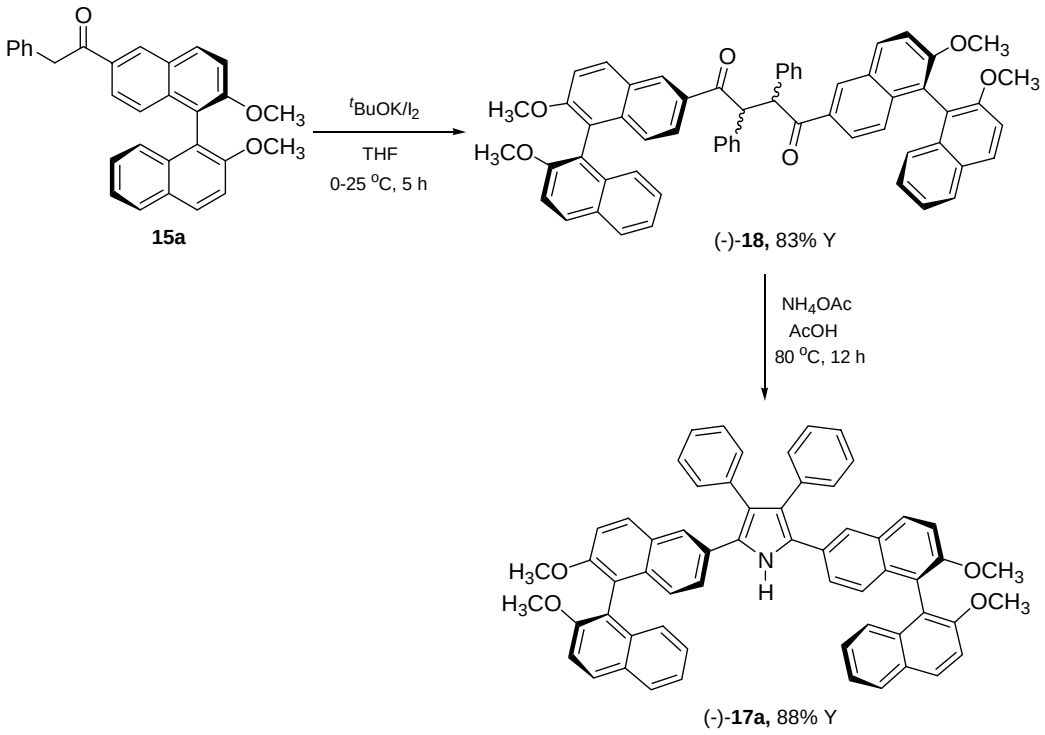
Efforts towards the synthesis of polymeric bi-2-naphthyl derivatives containing pyrrole spacers are described in section 5. Convenient methods developed for the preparation of novel chiral 2,5-bis(bi-2-naphthyl)pyrroles are described in section 6. We have observed that the oxime **16** reacted with the $TiCl_4/Et_3N$ reagent system to give the chiral 2,5-bis(1,1′-bi-2-naphthyl methyl ether)pyrrole **17** in 78-85% yields (Scheme 1).

Scheme 1



Method developed for the synthesis of C_2-symmetric chiral 2,3,4,5-tetrasubstituted pyrrole **17a** from 6-phenacyl-1,1′-bi-2-naphthyl methyl ether **15a** *via* the 1,4-diketone **18** followed by condensation-cyclization using ammonium acetate is also described in section 6 (Scheme 2).

Scheme 2



The results are discussed by considering appropriate mechanisms and stereochemical models. The experimental details are described in chapter 3. The IR, ^{1}H-NMR, ^{13}C-NMR, Mass spectral data, HPLC data and physical constant data are presented.

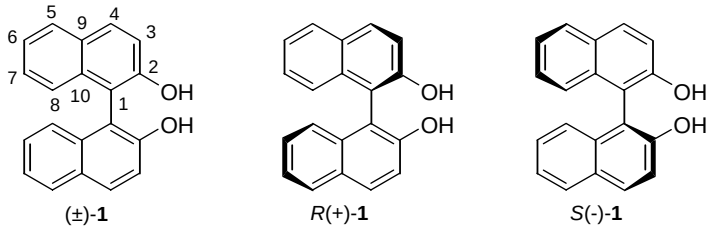
Note: Scheme numbers and compound numbers given in this abstract are different from those given in chapters.

Chapter 1

Introduction

1. Introduction

2,2′-Disubstituted derivatives of 1,1′-binaphthyl have been widely used in organic synthesis.[1] The most important compound of this type is 1,1′-binaphthyl-2,2′-diol or 1,1′-bi-2-naphthol **1** (BINOL). The chiral atropisomers (*R*)-(+)-**1** and (*S*)-(-)-**1** (Figure 1) are stable at temperatures up to 100 ^{o}C and allow numerous asymmetric reactions under various experimental conditions.[2]



(±)-**1** *R*(+)-**1** *S*(-)-**1**

Figure 1

In terms of ligand symmetry, C_2-symmetrical ligands possessing axial chirality have found particularly wide utility in asymmetric catalysis.[3] BINOL **1** is also the best known representative of axial chiral molecule.[4] Chiral 2,2′-bi-2-naphthol (BINOL) and its derivatives have generated particular interest because their versatile backbone can be modified, thereby affecting the reaction environment. Substitution of BINOL may affect not only the steric environment around the molecule but also the electronic properties of the oxygen atoms.

Although BINOL was first synthesized in 1926,[5] its potential use as a ligand for metal-mediated catalysis was first recognized only in 1979 by Noyori in the reduction of aromatic ketones and aldehydes.[6] BINOL itself, however, does not always give satisfactory

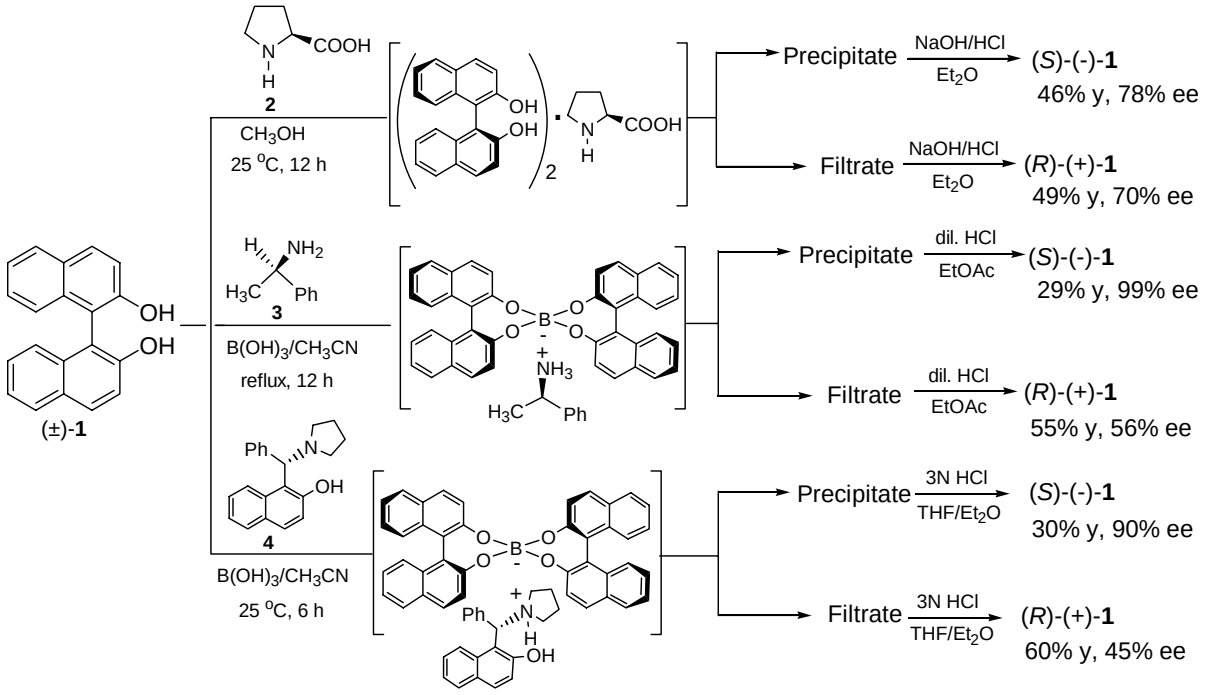
results in asymmetric transformations. Since Noyori's discovery, there has been sustained interest in the synthesis and applications of modified BINOL ligands. The outcome of a given asymmetric transformation depends on both steric and electronic properties of the chiral ligand. Therefore, strategic placement of substituents within the framework of a given BINOL derivative may lead to improved catalysts.

BINOL **1** is a white solid with a melting point of 208-210 °C and a p*K*a(H_2O) value of 10.28.[7] It is soluble in most organic solvents such as THF, MeCN, DMSO, methanol and dichloromethane. Although resistant toward racemization under neutral conditions, BINOL is known to racemize under basic or acidic conditions.[8] The original synthesis of BINOL, reported by Pummerer *et al.* in 1926, involves facile oxidative coupling of the two 2-naphthol units induced by $FeCl_3$.[5] Since then, a wide range of other coupling methods for the preparation of both enantiomerically pure and racemic BINOL ligands have been developed. Generally, there are two methods for the preparation of chiral bi-2-naphthol ligands: (a) through coupling reactions of substituted naphthol units and (b) through regioselective modification of the bi-2-naphthol scaffold. Both methods have received considerable attention.

1.1 Previous reports on 1,1′-bi-2-naphthol from this laboratory

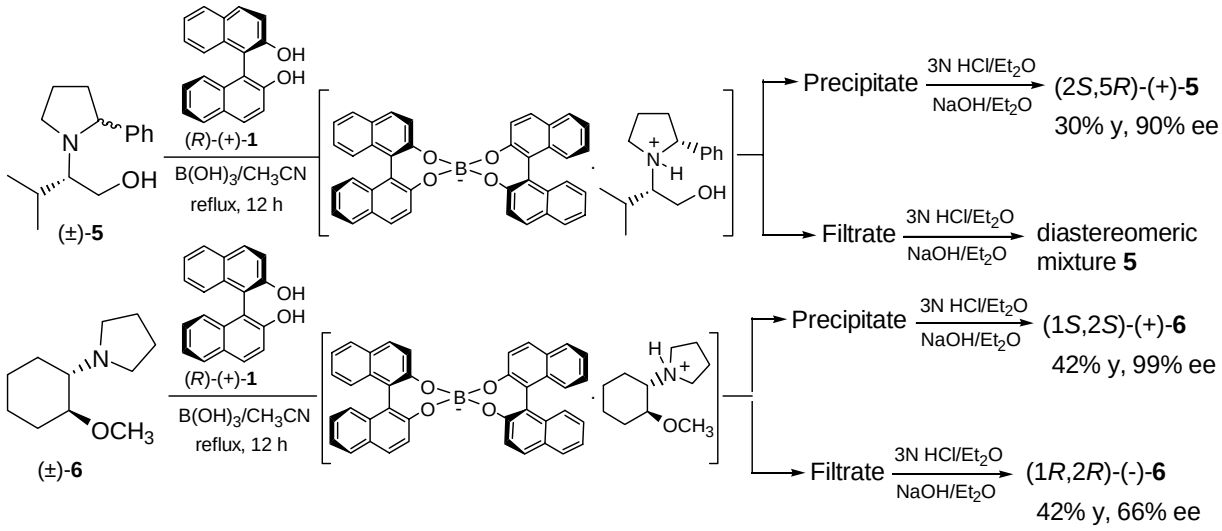
In recent years, methods have been developed in this laboratory to easily access chiral 1,1′-bi-2-naphthol in optically pure form. For example, the racemic 1,1′-bi-2-naphthol **1** was resolved using boric acid and (*S*)-proline **2** as well as chiral α-methylbenzylamine **3** in this laboratory.[9] Recently, racemic BINOL was resolved with (*S*)-amino naphthol **4** and boric acid in CH_3CN solvent (Scheme 1).

Scheme 1



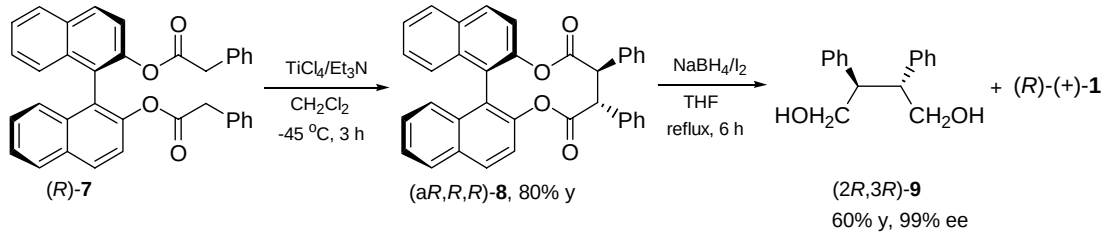
Chiral 1,1′-bi-2-naphthol **1** in alliance with boric acid was utilized for the purification of diastereomeric mixture **5** as well as for the resolution of trans-(±)-2-(pyrrolidinyl)cyclohexanol and its methyl ether derivative **6** (Scheme 2).[10]

Scheme 2



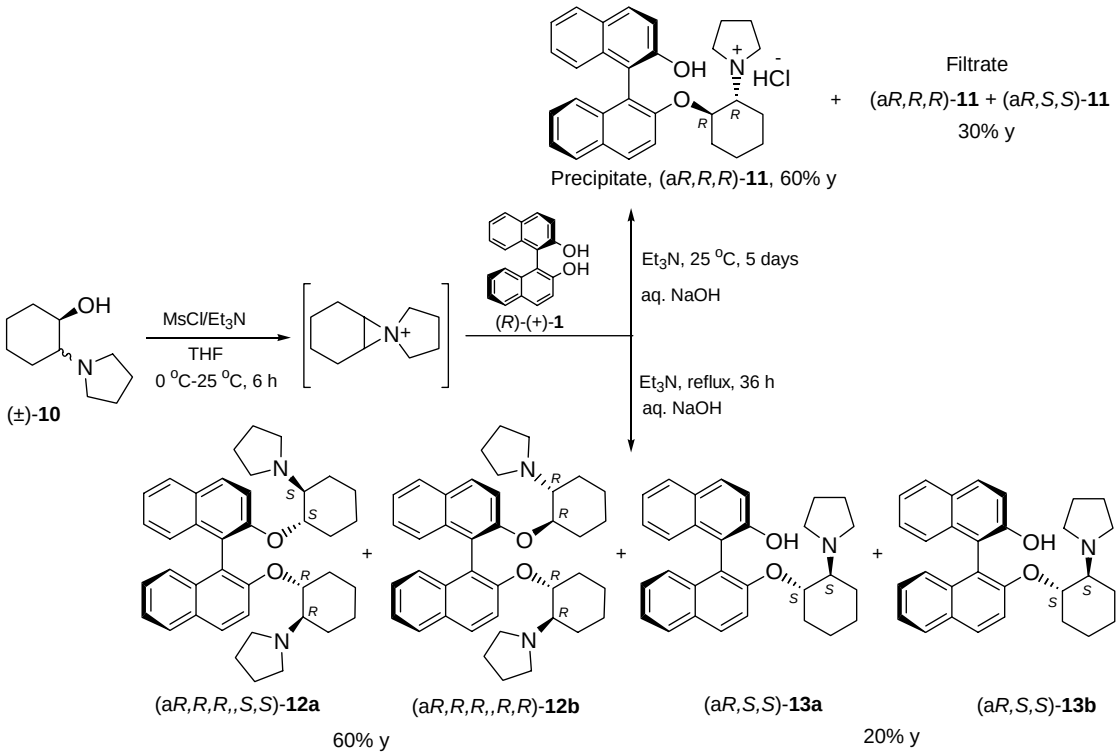
Enantiomerically pure 2,3-diphenyl-1,4-butanediol **9** was synthesized in good yields through intramolecular oxidative coupling of the titanium enolates of phenylacetic acid esters **7** of enantiomerically pure 1,1′-bi-2-naphthol followed by the reduction with the $NaBH_4/I_2$ reagent system (Scheme 3).[11]

Scheme 3



Convenient methods were also developed for the preparation of chiral 1,1′-bi-2-naphthol derived amino ether derivatives **11**, **12** and **13** through opening of aziridinium ion intermediate, prepared from *trans*-(±)-2-(1-pyrrolidinyl)cyclohexanol **10** (Scheme 4).[12]

Scheme 4



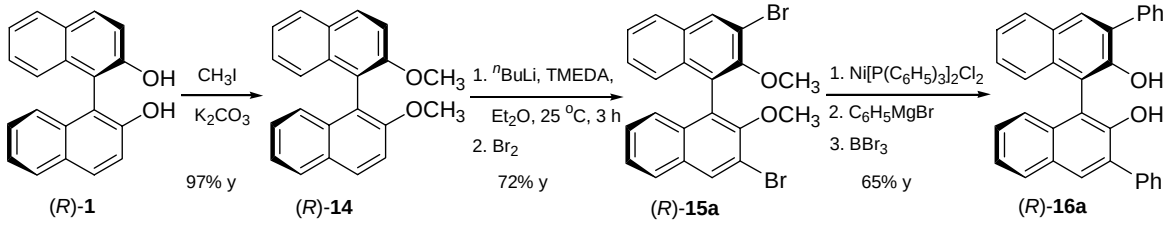
In continuation of these research efforts on the synthesis and applications of chiral bi-2-naphthol derivatives, we became interested in developing methods for the synthesis of 6- and 6,6′-substituted 1,1′-bi-2-naphthol derivatives for use in asymmetric transformations, synthesis of chiral pyrroles, chiral pyrrole polymers and chiral inclusion complexes. Accordingly, it is of interest to briefly review the literature reports on these topics.

1.2 Substitution on Bi-2-naphthol

1.2.1 *3,3′-Substituted BINOL derivatives*

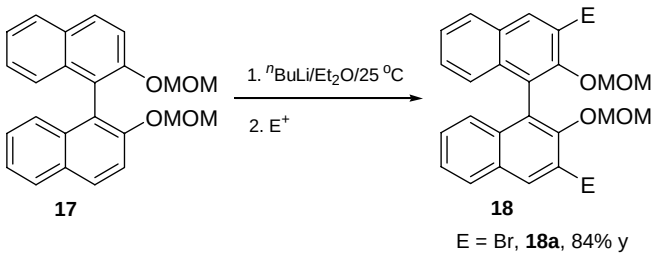
Cram and co-workers[13] prepared a series of 3,3′-disubstituted BINOLs through Mannich intermediates by Grignard cross-coupling reaction of 3,3′-dibromo-bi-2-naphthyl methyl ether and arylmagnesium bromides using dichlorobis(triphenylphosphine)nickel(II) as catalyst (Scheme 5).[14]

Scheme 5



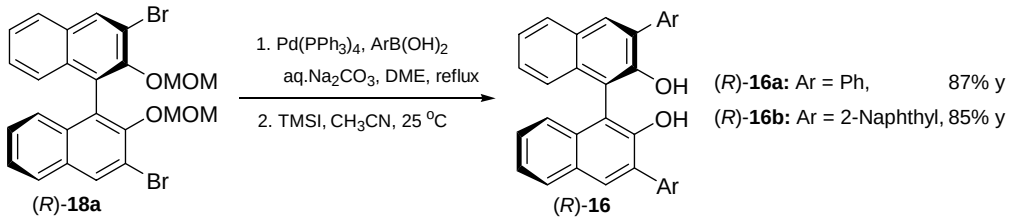
Snieckus and co-workers[15] reported a convenient method to synthesize 3- or 3,3′-substituted 1,1′-bi-2-naphthols **18** by direct ortho metalation followed by quenching with electrophile (Scheme 6).

Scheme 6



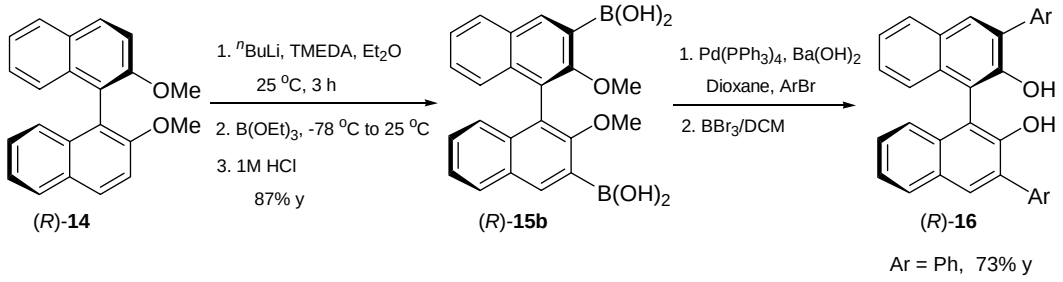
Reaction of the BINOL derivative **18a** with phenyl or 2-naphthylboronic acids under modified Suzuki cross-coupling conditions, followed by MOM deprotection gave the compounds **16a** and **16b** in 87% and 85% yields, respectively (Scheme 7).

Scheme 7



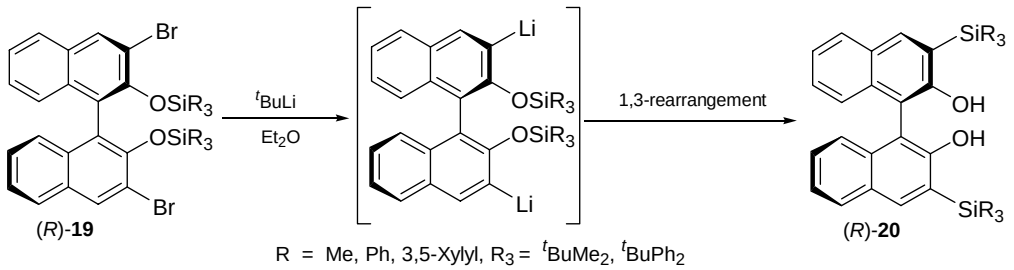
Jorgensen *et al.*[16] reported another method for the synthesis of 3,3′-diaryl-BINOLs **16a** by the reaction of the 3,3′-diboronic acid of bis(methoxy)-BINOL with commercially available aromatic bromides by Suzuki cross-coupling reaction (Scheme 8).

Scheme 8



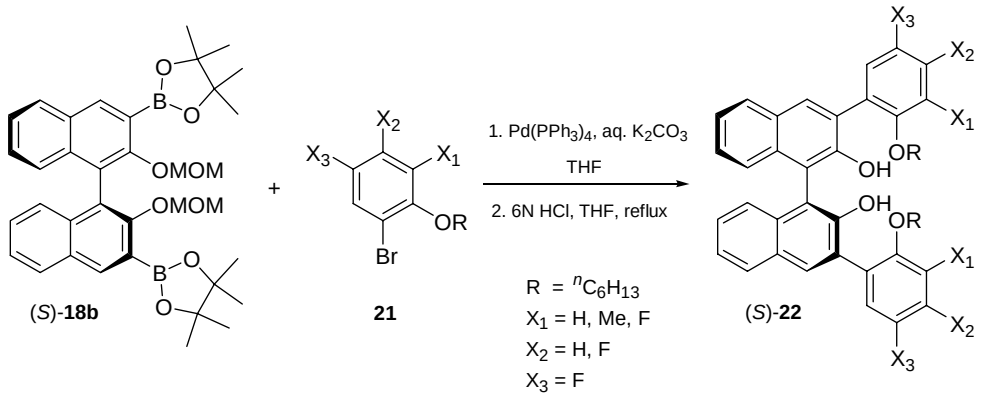
Yamamoto and co-workers[17] reported a method for the synthesis of sterically hindered chiral 3,3′-bis-(trialkylsilyl)-1,1′-bi-2-naphthol (*R*)-**20** by facile 1,3-rearrangement of the corresponding bis(trialkylsilyl ether) derivative **19** with ^{t}BuLi (Scheme 9).

Scheme 9



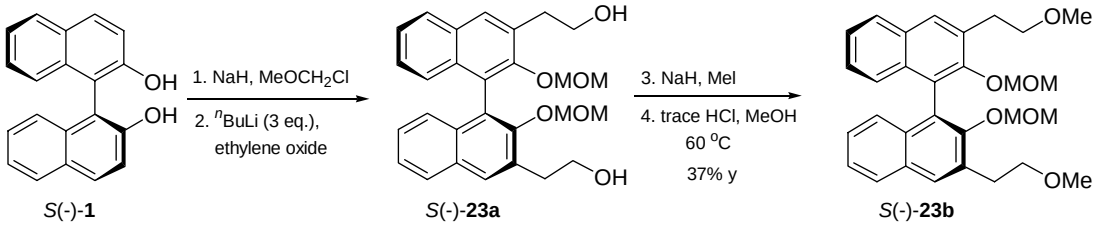
Pu and co-workers[18] reported a method of synthesis of the chiral bi-naphthyl derivative (*S*)-**22** containing multiple electron-withdrawing fluorine atoms in the 3,3′-aryl groups, by the Suzuki coupling reaction of **18b** with aryl bromides **21**, followed by acid hydrolysis (Scheme 10).

Scheme 10



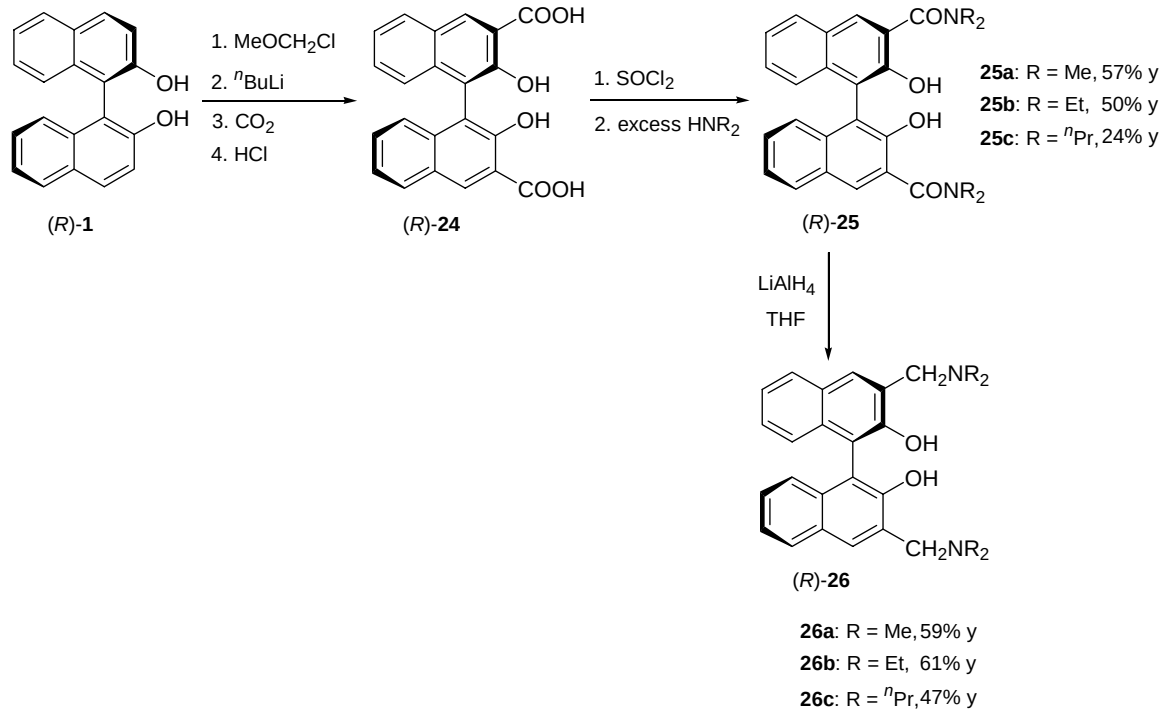
Qian *et al.*[19] reported a method of synthesis of (*S*)-3,3′-bis(methoxyethyl)-BINOL **23b** in an overall yield of 37% from (*S*)-BINOL in four steps (Scheme 11).

Scheme 11



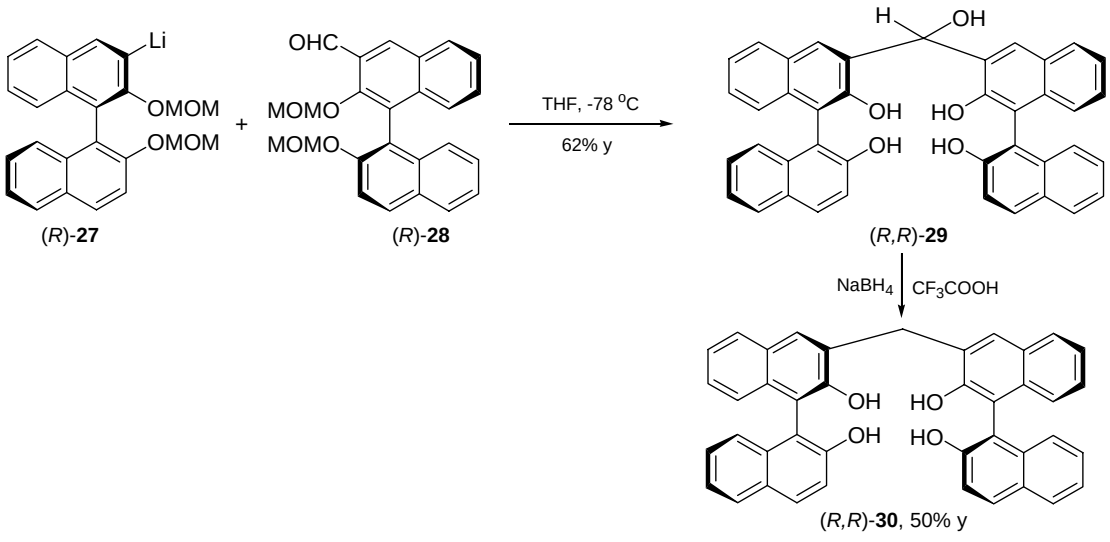
Katsuki and co-workers[20] reported the synthesis of 1,1′-bi-2-naphthol-3,3′-dicarboxamides **25**, and their application as chiral ligands in the asymmetric Simmons-Smith cyclopropanation of (*E*)-allylic alcohols. The ligands **25** were prepared from (*R*)-BINOL in six steps (Scheme 12). Reduction of **25** by $LiAlH_4$ gave the product **26** bearing tertiary amino methyl groups at the 3,3′-positions.

Scheme 12

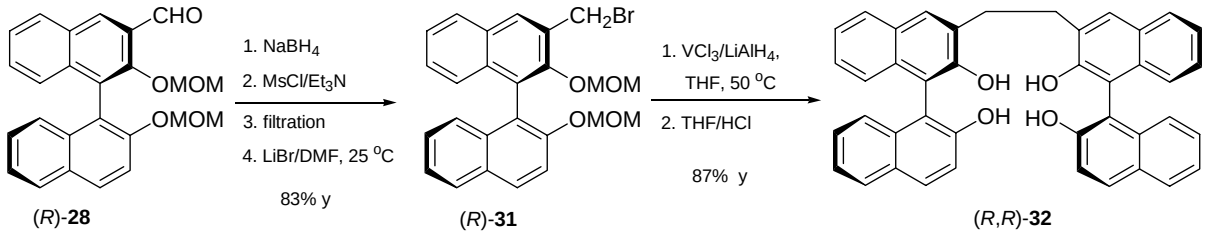


Shibasaki and co-workers[21] reported a novel class of linked BINOL ligands **30** and **32**, which introduced new possibilities for multifunctional asymmetric catalysis applications. The carbon-linked BINOL derivatives **30** and **32** have been synthesized as outlined in Scheme 13 and Scheme 14.

Scheme 13



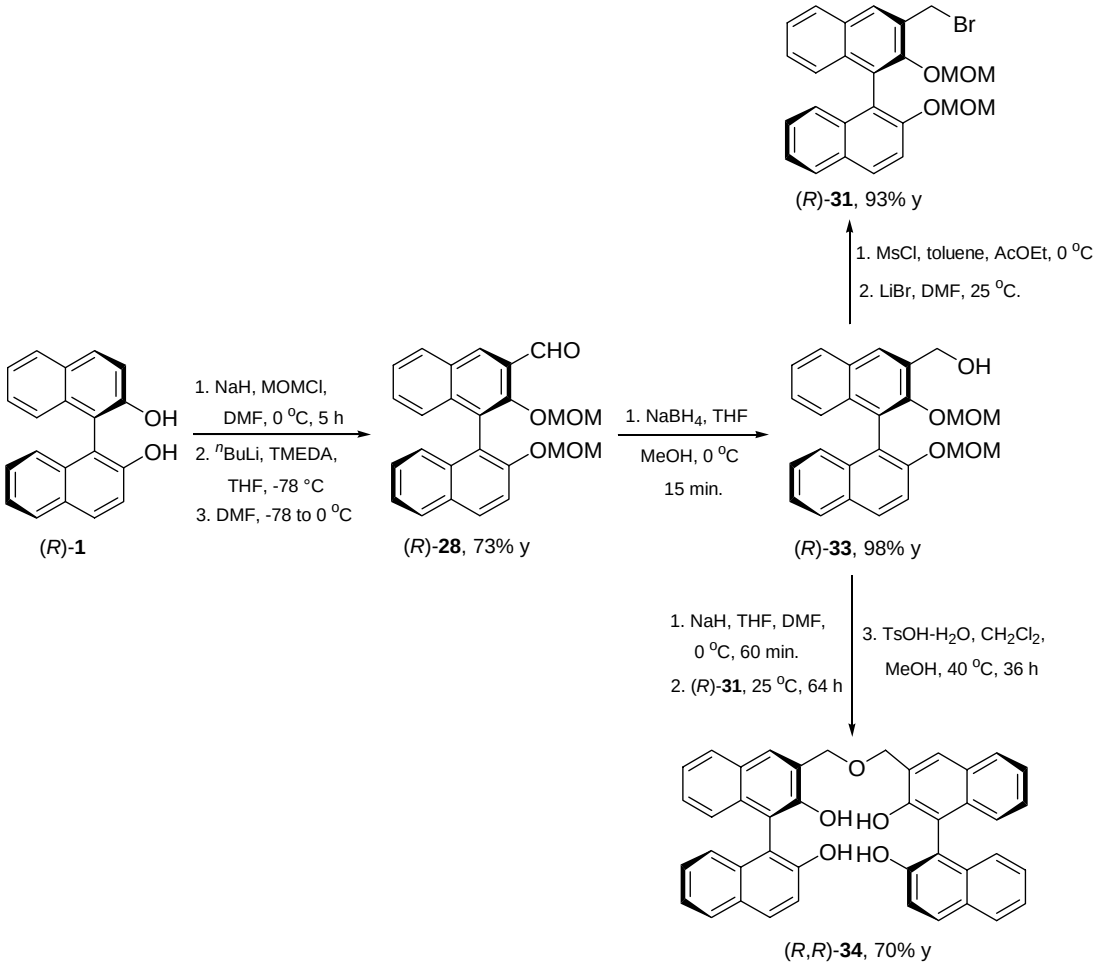
Scheme 14



(*R*)-**28** (*R*)-**31** (*R*,*R*)-**32**

Shibasaki *et al.*[22] also reported the preparation of oxygen-linked chiral ligand **34** based on earlier reports by Cram and coworkers (Scheme 15).[13]

Scheme 15

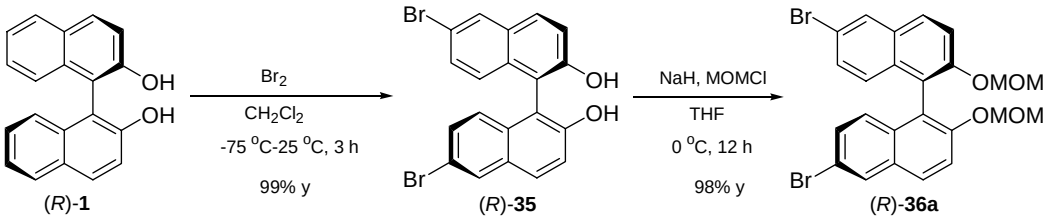


(*R*)-**1** (*R*)-**28**, 73% y (*R*)-**33**, 98% y (*R*,*R*)-**34**, 70% y

1.2.2 *6,6′-Substituted BINOL derivatives*

The most common precursor to the 6,6′-disubstituted BINOL ligands described in the literature is the 6,6′-dibromo-1,1′-bi-2-naphthol **35.** This BINOL derivative is prepared *via* electrophilic aromatic bromination of BINOL (Scheme 16).[23]

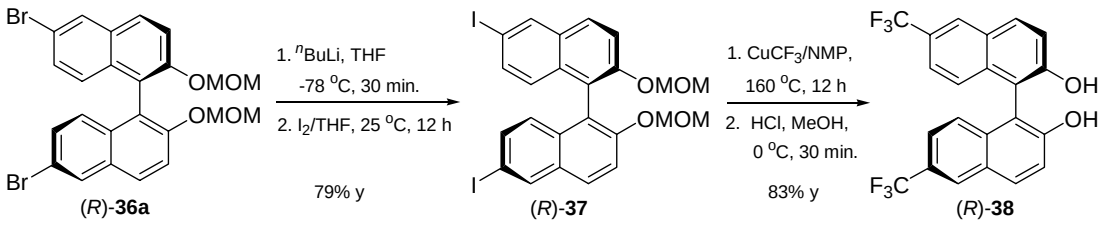
Scheme 16



This readily available derivative **35** has been used as an entry into a wide range of other derivatives. The protection of the hydroxyl groups as the formation of the corresponding MOM ether allows for lithiation of the aryl bromide with ^{n}BuLi, followed by reaction with various electrophiles, resulting in a variety of different 6,6′-disubstituted BINOL ligands.

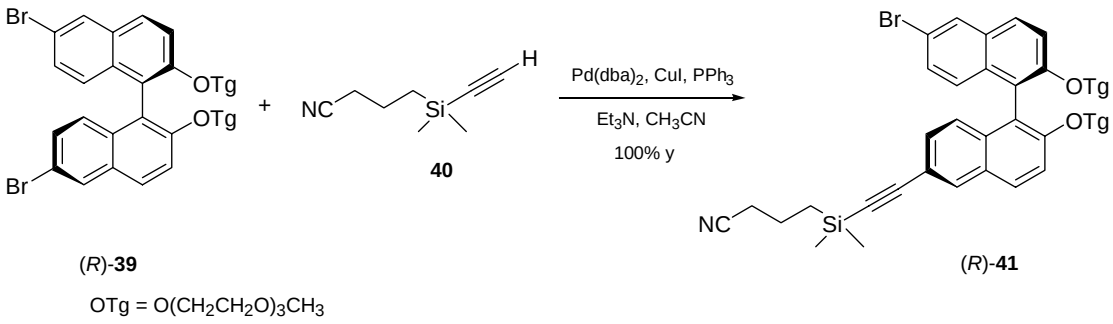
Kobayashi and co-workers[24] reported the synthesis of (*R*)-6,6′-bis-(trifluoromethyl)-1,1′-bi-2-naphthol, [6,6′-$(CF_3)_2$-BINOL] **38** by converting the bromo substituents at the 6,6′-positions into the iodo groups using the *n*-BuLi/I_2 reagent system, and then to trifluoromethyl groups using $CuCF_3$ in *N*-methylpyrrolidin-2-one (NMP). After deprotection of the MOM groups, the 6,6′-$(CF_3)_2$-BINOL **38** was isolated (Scheme 17).

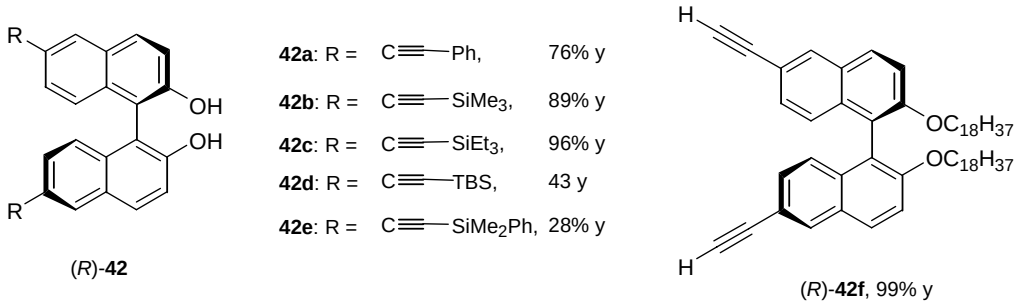
Scheme 17



Other 6,6′-disubstituted ligands **41** and **42a-g** have been prepared through Sonogashira coupling of Br_2-BINOL derivative **39** with different alkynes (Scheme 18 and Figure 2). These substituents are especially useful as hetero-bimetallic catalysts.[25]

Scheme 18





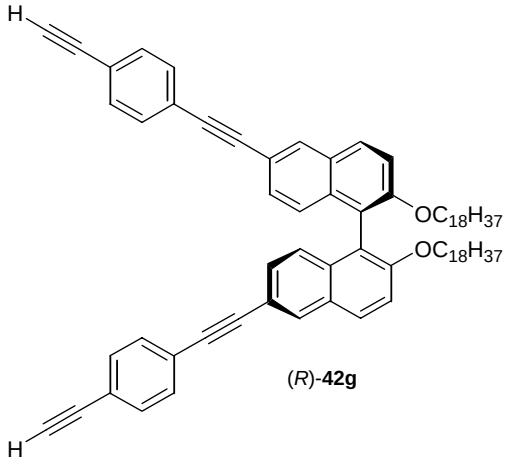
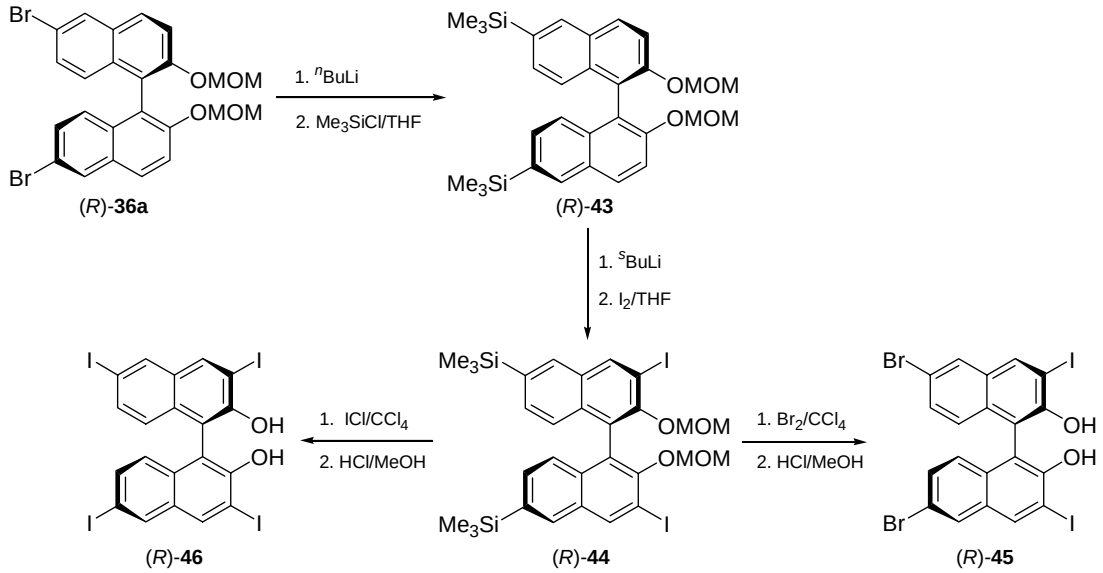


Figure 2

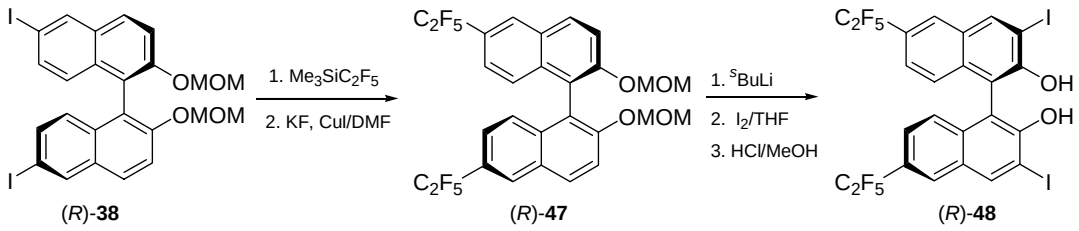
Reported methods for the syntheses of selected examples of 3,3′,6,6′-substituted bi-2-naphthol derivatives **43** and **46** are outlined in Scheme 19.[1]

Schemes 19



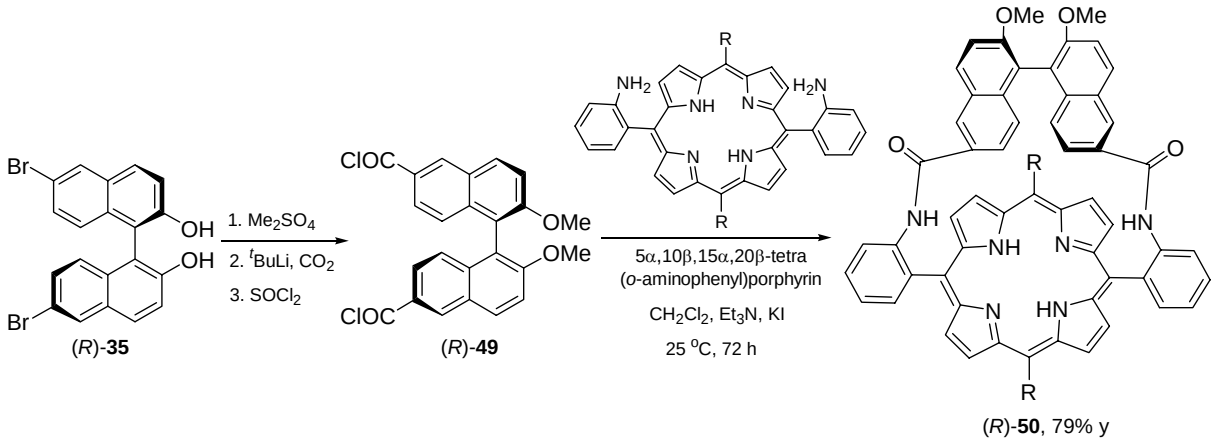
The BINOL derivative **48** has been synthesized by a coupling reaction of the 6,6′-diiodo-bi-2-naphthol derivative **38** with the $Me_3SiC_2F_5$ followed by iodination at 3,3′-positions using ^{s}BuLi and I_2 (Scheme 20).[1]

Scheme 20



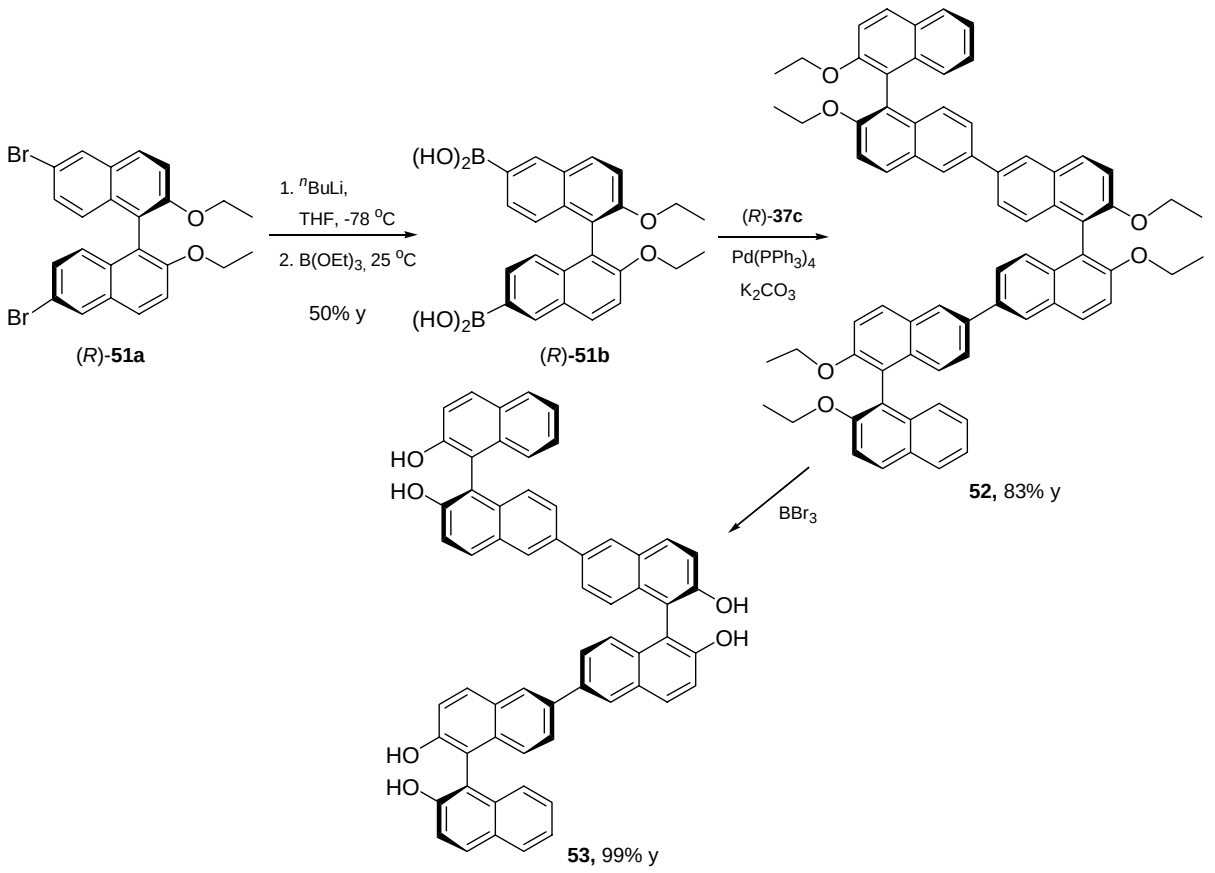
Methods for synthesis of bi-2-naphthyl-containing metalloporphyrin derivatives **50** from the 6,6′-substituted bi-2-naphthol **35** were reported. The porphyrin **50** is useful for asymmetric hydroxylation, epoxidation and sulfoxidation reactions (Scheme 21).[26]

Scheme 21



Lin and co-workers[27] reported the synthesis of the 6,6′-di(bi-2-naphthyl)-1,1′-bi-2-naphthol **53** (Scheme 22).

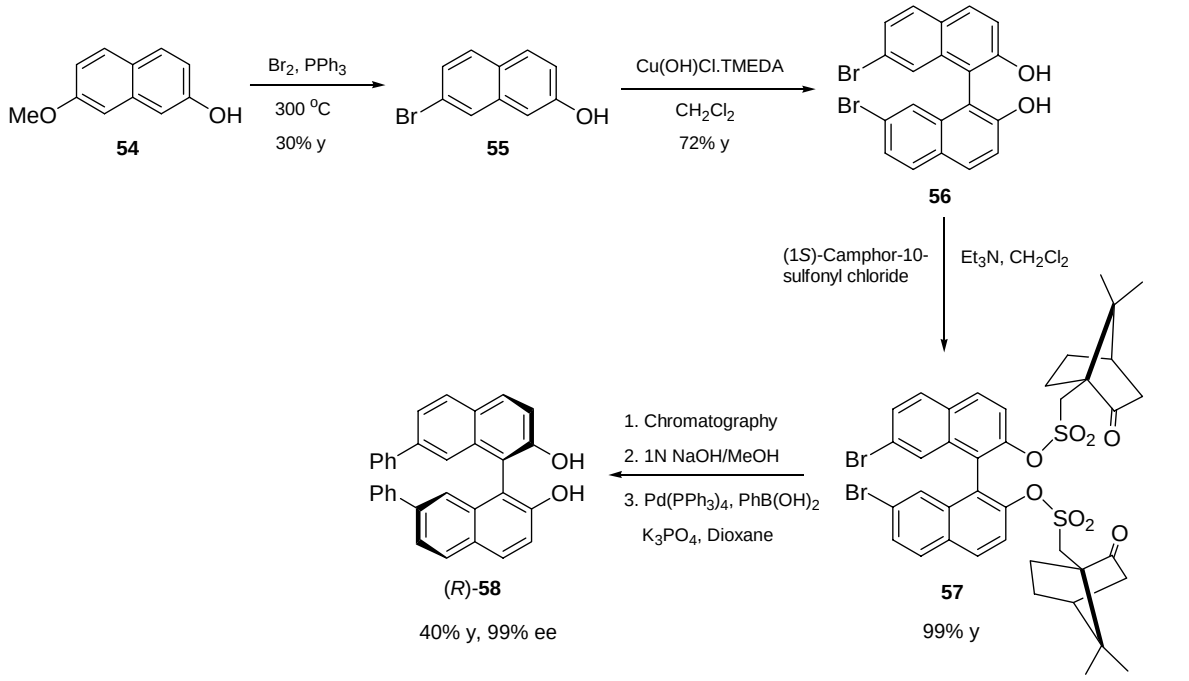
Scheme 22



1.2.3 *7,7'-Substituted BINOL derivatives*

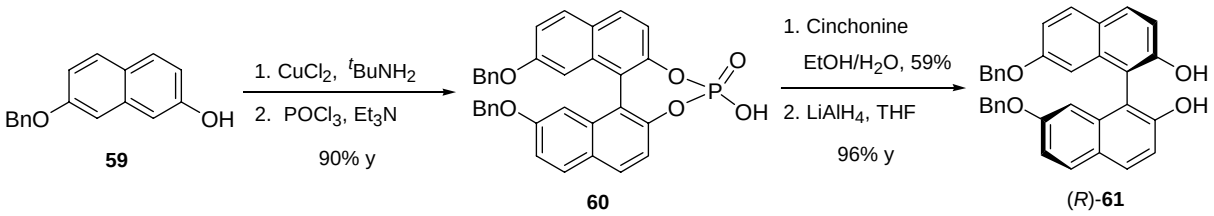
Methods for synthesis of the bi-2-naphthol **58** derivatives were reported by Mikami and co-workers (Scheme 23)[28].

Scheme 23



Diederich and co-workers[29,30] reported the synthesis of the 7,7′-substituted bi-2-naphthol derivative **61** through coupling of 2-benzyloxy-7-hydroxynaphthalene **59** with $CuCl_2$ and $^tBuNH_2$ (Scheme 24). The optically pure ligand **61** was obtained by resolution of the racemic acid using chiral cinchonine followed by $LiAlH_4$ reduction.

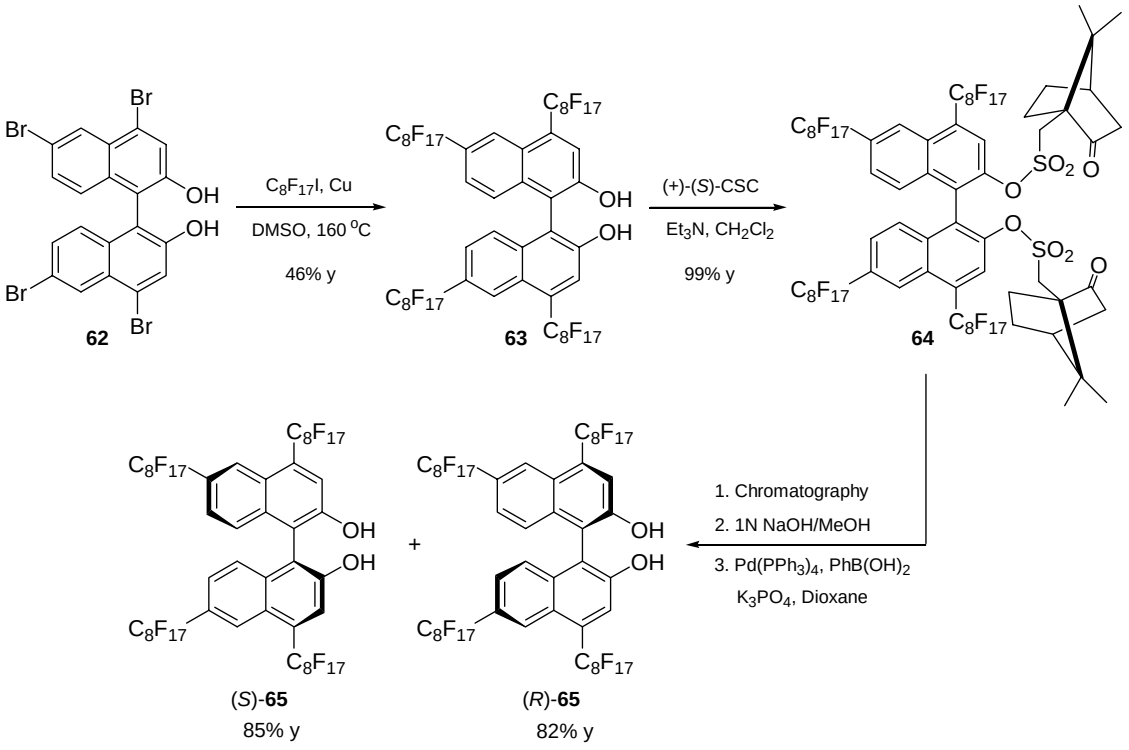
Scheme 24



1.2.4 *4,4',6,6'-Substituted BINOL derivatives*

A method for the synthesis of 4,4′,6,6′-substituted fluorous bi-2-naphthol derivative **65** involving perfluoroalkylation of the corresponding bromo-BINOL **62** with Cu/$C_8H_{17}I$ in DMSO was reported (Scheme 25).[31]

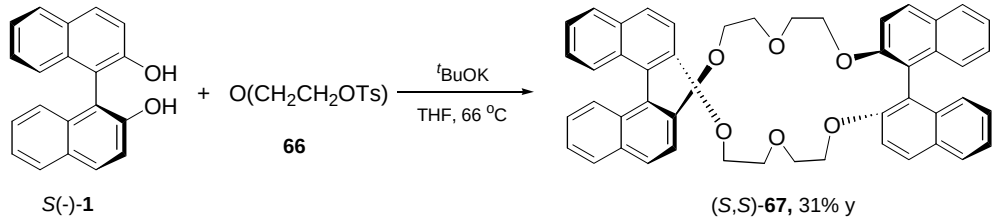
Scheme 25



1.2.5 *Chiral bi-2-naphthyl macrocycles*

The first chiral bis(bi-2-naphthyl) crown ether (*S*,*S*)-**67** was reported in 1973 by Cram and coworkers (Scheme 26).[32]

Scheme 26



Syntheses of several 6,6′-substituted chiral macrocycles **68**-**71** were also reported (Figure 3).[32]

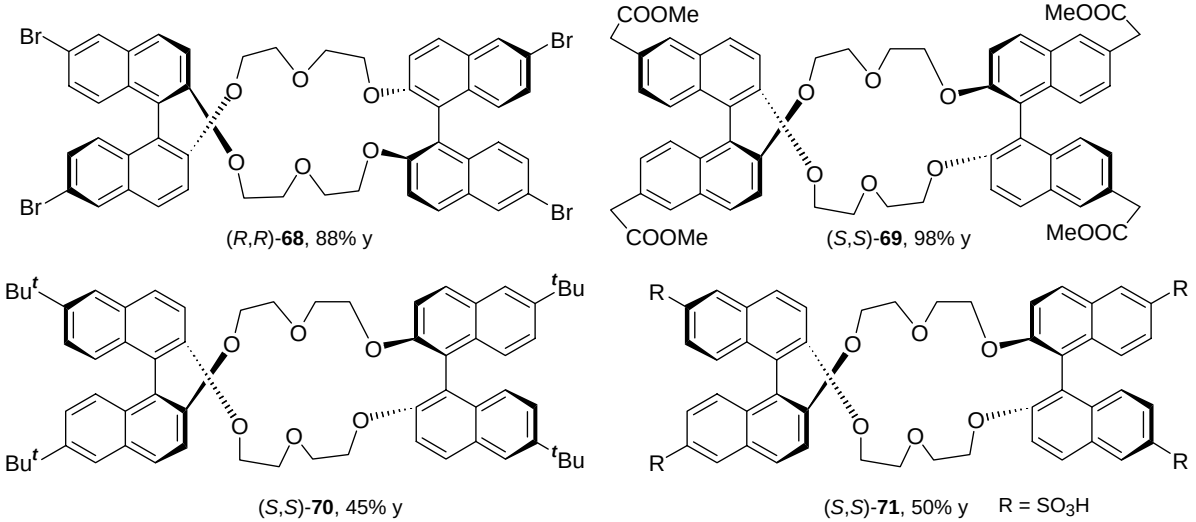
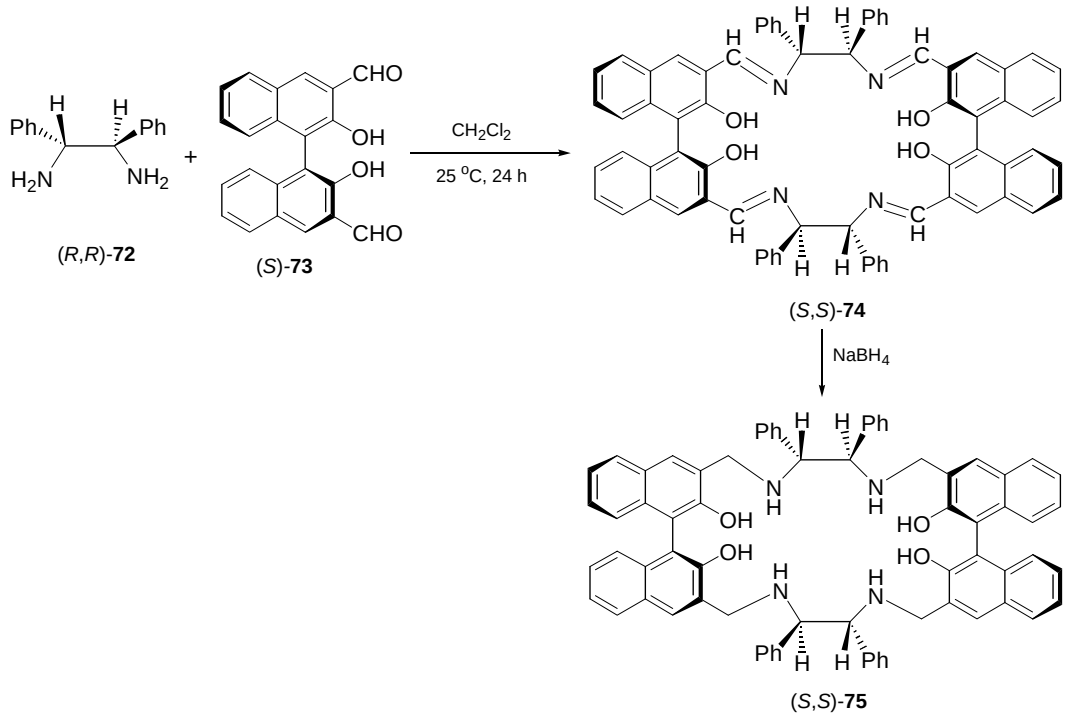


Figure 3

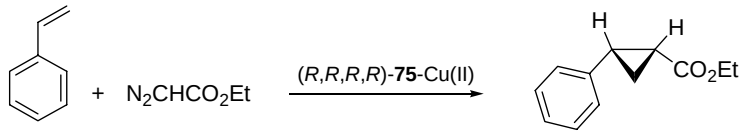
Brunner *et al.*[33] reported that the reaction of (*R*,*R*)-**72** with (*S*)-**73** gave a bis(bi-2-naphthyl) macrocycle (*S*,*S*)-**75** (Scheme 27).

Scheme 27



The chiral compound (*S*,*S*)-**75** was used as ligand in the Cu-(II)-catalyzed cyclopropanation of styrene with ethyl diazoacetate (Scheme 28).[34]

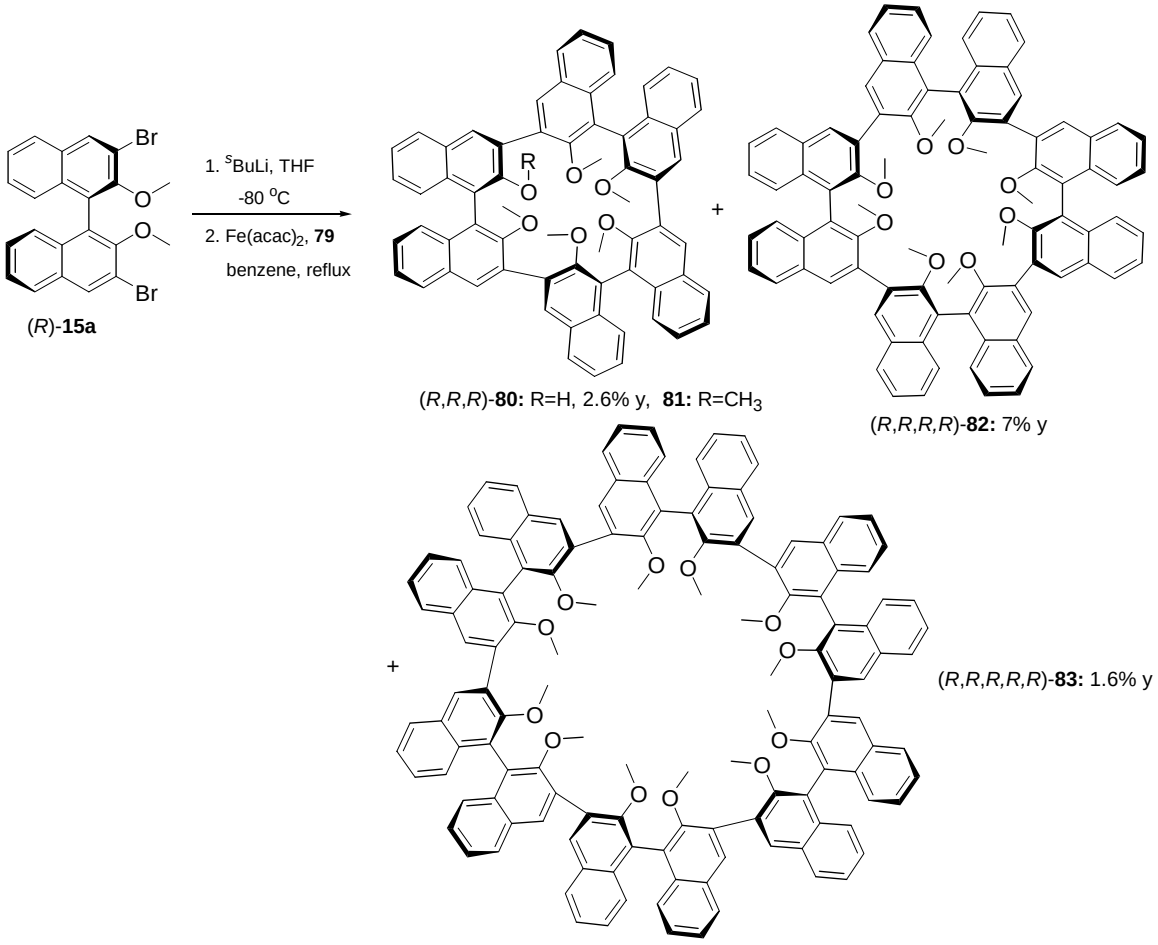
Scheme 28



76 **77** **78**, 36.6% ee

Cram and co-workers[35] reported the self coupling of (*R*)-3,3′-dibromo-2,2′-dimethoxy-1,1′-bi-2-naphthyl (*R*)-**79** using $Fe(acac)_2$ to obtain a mixture of chiral macrocycles (Scheme 29).

Scheme 29



(*R*)-**15a**

(*R*,*R*,*R*)-**80:** R=H, 2.6% y, **81:** R=CH_3

(*R*,*R*,*R*,*R*)-**82:** 7% y

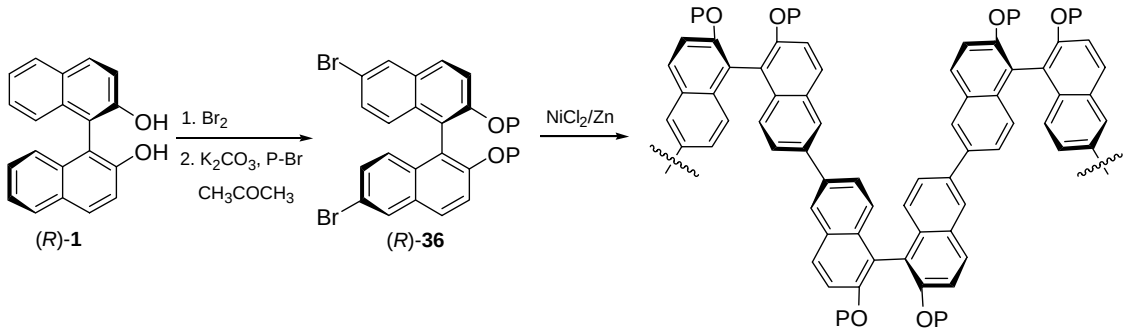
(*R*,*R*,*R*,*R*,*R*)-**83:** 1.6% y

1.2.6 *Bi-2-naphthyl polymers*

Several polymeric materials containing 3,3′, 4,4′, 6,6′ and 7,7′-bi-2-naphthol moiety have been synthesized. We have also undertaken research efforts on the synthesis of 6- and 6,6′-substituted bi-2-naphthol derivatives. Accordingly, only the reports on the synthesis of 6,6′-polymers containing bi-2-naphthol moiety are briefly outlined here.

Pu and co-workers[36-38] used chiral bi-2-naphthol derivatives to make novel rigid and stereo regular polymers **84** for use in asymmetric catalysis. For example, the 6,6′-dibromo-bi-2-naphthyl monomer is polymerized in the presence of Ni(0) or Ni(II)/Zn catalysts (Scheme 30).

Scheme 30

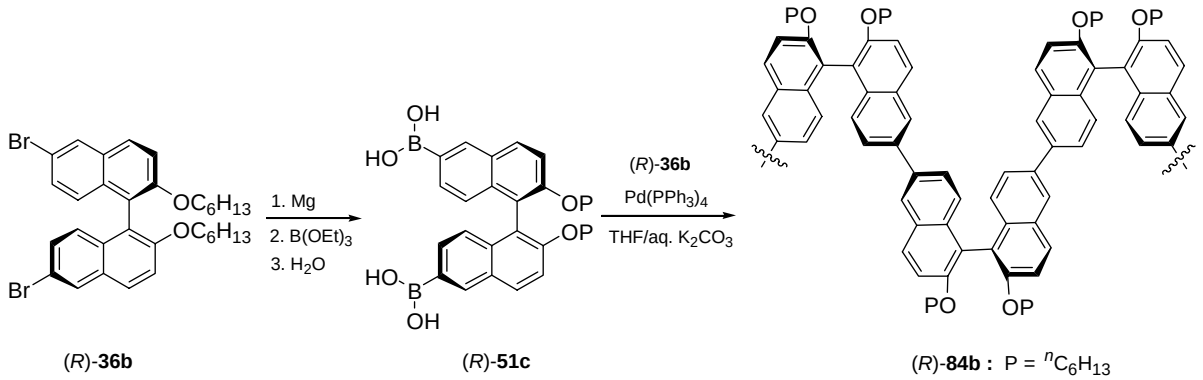


(*R*)-**1** (*R*)-**36**

(*R*)-**84a** : P = CH_2OCH_3
(*R*)-**84b** : P = $^nC_6H_{13}$
(*R*)-**84c** : P = Ac

The 6,6′-dibromo-bi-2-naphthyl dihexyl ether (*R*)-**36b** was also converted to its corresponding 6,6′-diboronic acid- bi-2-naphthyl (*R*)-**51c** by reaction with magnesium and triethylborate (Scheme 31). The subsequent Suzuki coupling of 6,6′-dibromo-bi-2-naphthyl dihexyl ether (*R*)-**36b** with 6,6′-diboronic acid- bi-2-naphthyl (*R*)-**51c** in the presence of $Pd(PPh_3)_4$ catalyst gave the poly(BINOL) derivative product (*R*)-**84b**.

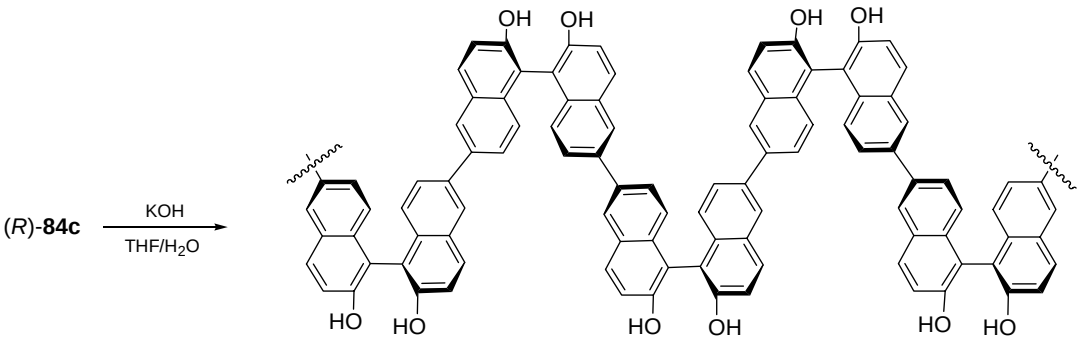
Scheme 31



(*R*)-**36b** (*R*)-**51c** (*R*)-**84b :** P = $^{n}C_6H_{13}$

Hydrolysis of poly(BINOL) derivative (*R*)-**84c** in the presence of potassium hydroxide generated the first optically active and stereo regular bi-2-naphthyl polymer **86** (Scheme 32).

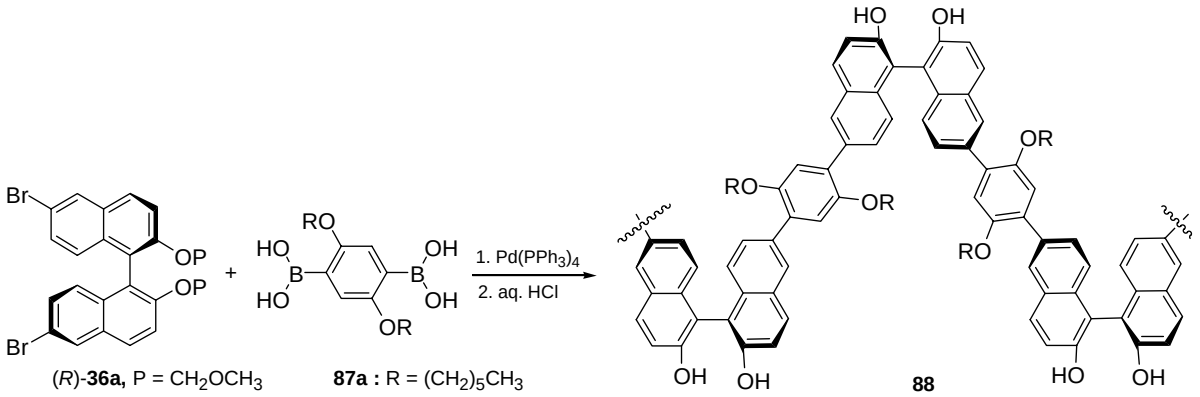
Scheme 32



86

The poly(BINOL) derivative (*R*)-**88** was prepared via the Suzuki coupling of 6,6′-dibromo-bi-2-naphthyl dimethoxy methyl ether (*R*)-**36a** with *p*-phenylenediboronic acid **87a** followed by hydrolysis (Scheme 33).[39,40] Unlike the polymeric (*R*)-**86**, the poly(BINOL) derivative (*R*)-**88** was soluble in common organic solvents such as toluene, methylene chloride, chloroform, and THF.

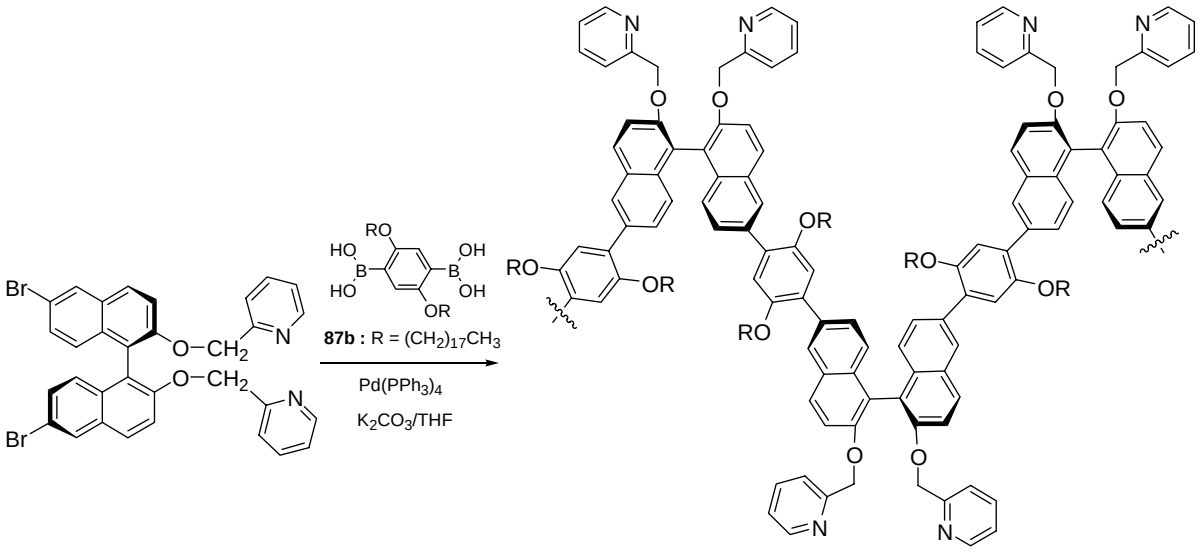
Scheme 33



(*R*)-**36a,** P = CH_2OCH_3 **87a :** R = $(CH_2)_5CH_3$ **88**

The organic solvents soluble optically active bi-2-naphthyl polymer (*R*)-**90** containing pyridine functional groups was synthesized by the Suzuki coupling reaction of the 6,6′-dibromo-bi-2-naphthyl ether (*R*)-**89** with the boronic acid derivative **87b** (Scheme 34).[40]

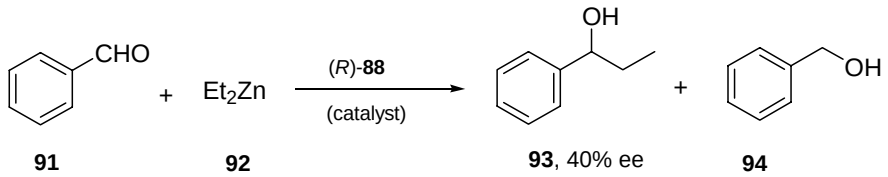
Scheme 34



(*R*)-**89** (*R*)-**90,** R = $C_{18}H_{37}$

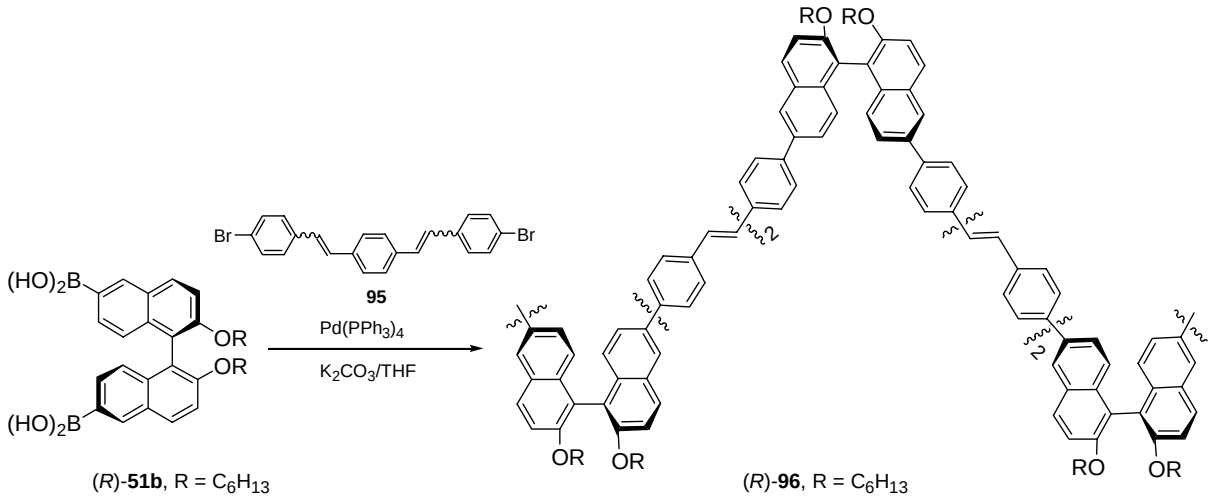
Applications of the polymeric derivatives (*R*)-**86**, (*R*)-**88**, and (*R*)-**90** in the reaction of benzaldehyde and diethylzinc were also reported.[39,40] A mixture of 1-phenyl-propan-1-ol **93** and benzyl alcohol was generated in a 71:29 ratio with 40% ee when polymer (*R*)-**88** used (Scheme 35). The polymer derivative (*R*)-**90** showed no catalytic activity for this reaction.

Scheme 35



Pu and co-workers[36-40,41-57,10] have also reported a series of bi-2-naphthyl based main chain chiral conjugated polymers (*R*)-**96,** (*R*)-**98**, (*R*)-**99** and (*R*)-**100** by polymerization at the 6,6′-positions of optically active bi-2-naphthyl monomers (Chart 1).

Chart 1



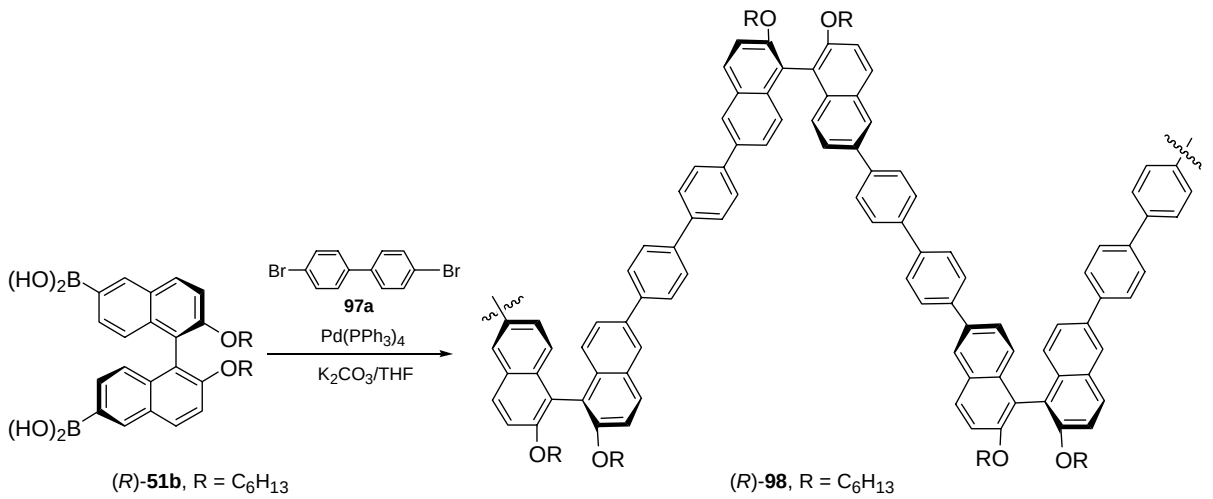
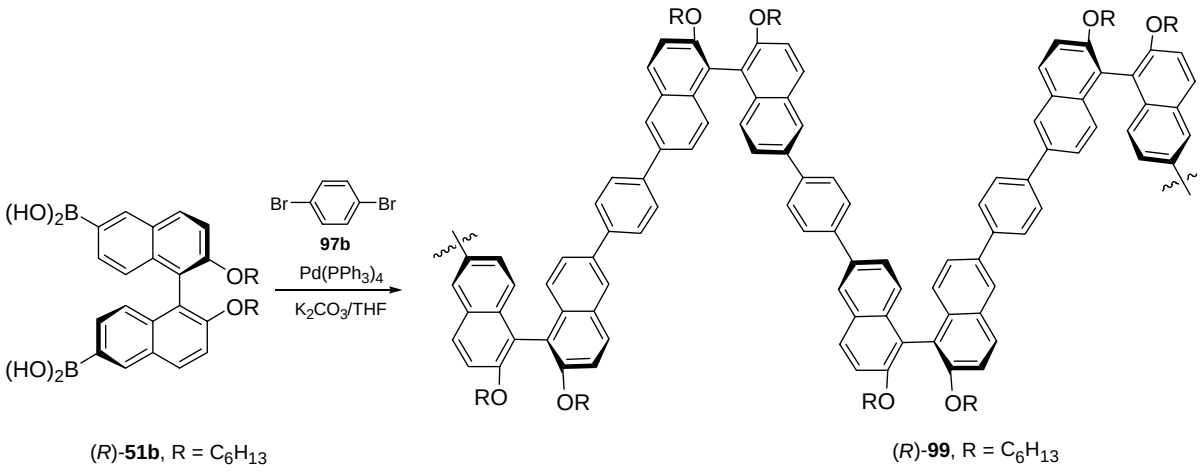
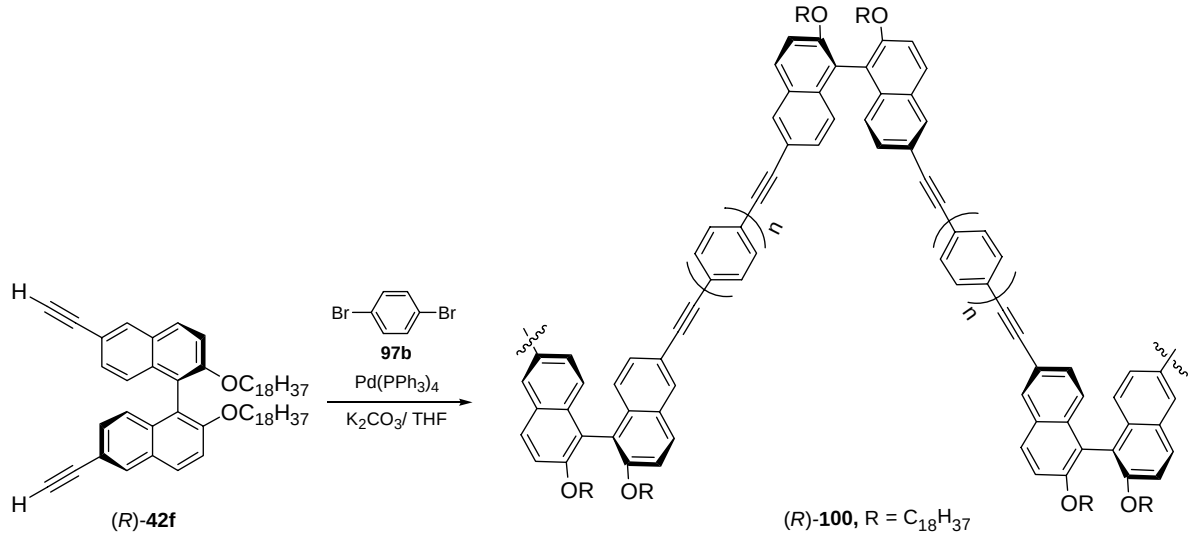


Chart 1 continued…



(*R*)-**51b**, R = C_6H_{13} (*R*)-**99**, R = C_6H_{13}



(*R*)-**42f** (*R*)-**100,** R = $C_{18}H_{37}$

We have undertaken research efforts on the development of simple and convenient methods for the synthesis of 6- and 6,6′-substituted bi-2-naphthyl derivatives. The results are discussed in the next section.

Chapter 2

Results and Discussion

2. Results and Discussion

Optically active bi-2-naphthol (BINOL) **1** derivatives have been widely used in both catalytic and stoichiometric asymmetric transformations.[49] There has been immense interest in modified BINOL ligands as the outcome of a given asymmetric transformation depends on both steric and electronic properties of the chiral ligand. Several 6,6′-bi-2-naphthol derivatives were found to be useful in asymmetric transformations.[25,50] For example, the La-Li complex of 6,6′-dimethyl-bi-2-naphthol is useful as asymmetric catalyst for the nitro aldol reaction[25] and the chiral 6,6′-dibromo-bi-2-naphthol zirconium catalyst is useful for enantioselective Mannich-type reaction.[50]

As outlined in the introductory section, methods have been reported from this laboratory for the synthesis and resolution of chiral bi-2-naphthol **1** (Scheme 1). Also, methods have been reported for the intramolecular oxidative coupling (Scheme 3) and opening of aziridinium ion intermediate to access new bi-2-naphthol derivatives (Figure 2). We have undertaken studies on the development of methods to access new chiral 6,6′-diacyl-bi-2-naphthol derivatives. The results are described in the next six sections. Detailed studies on the development of methods for acylation of bi-2-naphthol and for reduction of 6-acyl and 6,6′-diacyl-bi-2-naphthyl derivatives are described under section 1 and 2, respectively. Whereas studies on reductive amination of oxime and imine derivatives of 6-acyl-bi-2-naphthyl methyl ether are described in section 3. Studies on Grignard addition on 6-acyl-bi-2-naphthyl methyl ether are described in section 4. Finally, studies on synthesis of chiral bi-

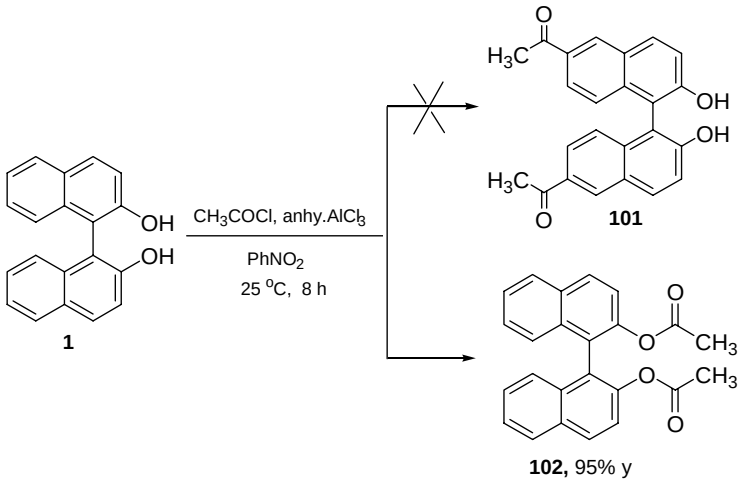
2-naphthol polymers with pyrrole spacers and chiral bi-2-naphthol pyrroles are described in section 5 and 6, respectively.

2.1.1 Synthesis of chiral 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ethers

As outlined in chapter 1, the most common precursor for the synthesis of the 6,6′-disubstituted BINOL ligands is the 6,6′-dibromo-bi-2-naphthol **36**. This derivative is prepared *via* electrophilic aromatic bromination of BINOL (Scheme 16).[23] A variety of 6,6′-disubstituted BINOL derivatives were prepared using 6,6′-dibromo-bi-2-naphthol **36** (Scheme 17).[24] However, there is no direct method available to obtain 6,6′-diacyl-bi-2-naphthyl ether derivatives.[51]

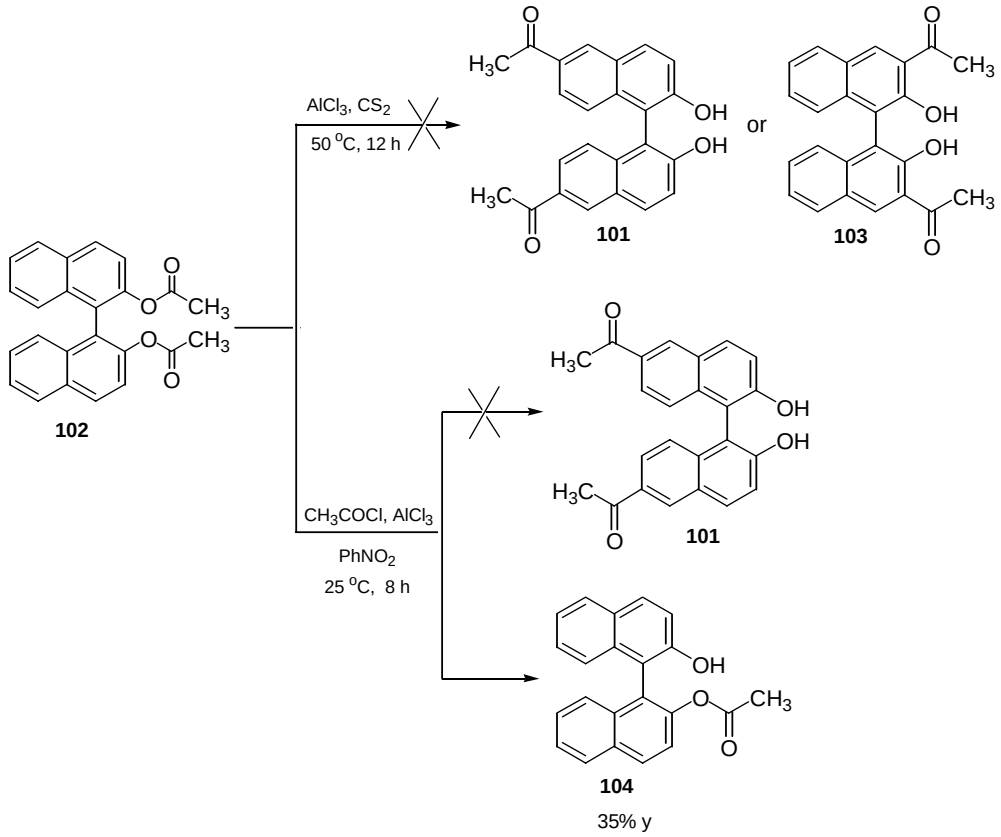
Initially, we have examined the acylation of bi-2-naphthol **1** using various Lewis acids like anhydrous $AlCl_3$, $TiCl_4$ and $ZrCl_4$. We have observed that the reaction of bi-2-naphthol **1** with acetyl chloride in the presence of $AlCl_3$ in nitrobenzene gave the diester derivative **102** in 95% yield instead of the desired diketone **101** (Scheme 36).

Scheme 36



We have made efforts to carry out the Fries rearrangement of the diester **102** in a separate step using the Lewis acid $AlCl_3$ to obtain the product **101** or **103** (Scheme 37). These attempts were not successful. Also, acylation of diester **102** did not proceed further in the presense of $AlCl_3$ in nitrobenzene at 25 °C. In this run, only the monoester **104** was obtained in 35% yield and the starting material was recovered in 58% yield (Scheme 37).

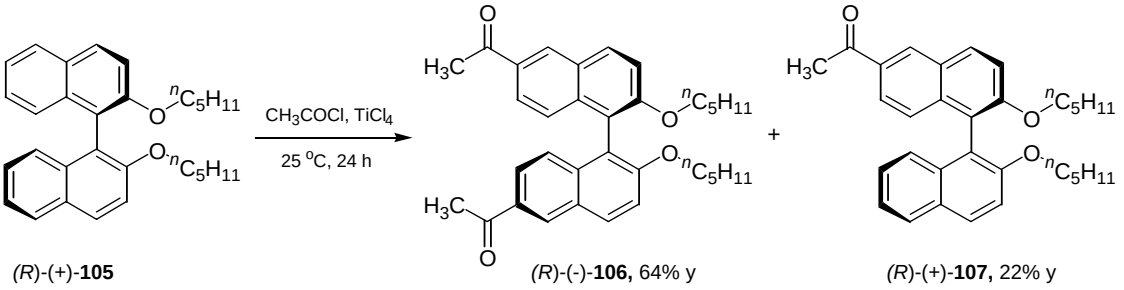
Scheme 37



However, protection of bi-2-naphthol using *n*-alkyl halides facilitates acylation to take place at 6,6′-positions. When the reaction was carried out using the *n*-pentyl protected bi-2-naphthol **105,** the mono and diacylated derivatives were obtained. The acylation reaction using 4 equiv. of acetyl chloride and (*R*)-(+)-bi-2-naphthyl *n*-pentyl ether derivative

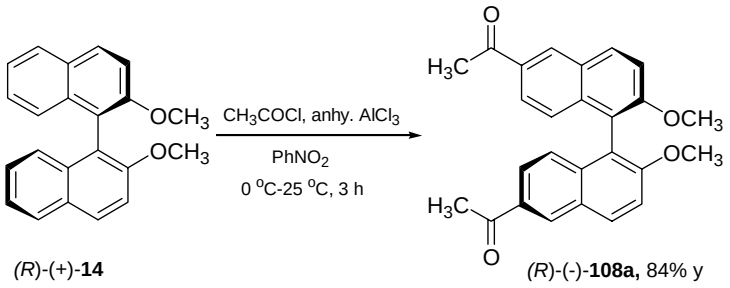
105 in the presence of $TiCl_4$ gave the 6,6′-diacetyl derivative **106** in 64% yield along with the 6-acetyl derivative **107** in 22% yield (Scheme 38).

Scheme 38



The acylation of methyl protected bi-2-naphthol **14** failed when the $TiCl_4$ was used as Lewis acid. However, the 2,2′-dimethoxy-bi-2-naphthyl **14** was successfully acylated in the presence of anhydrous $AlCl_3$ in nitrobenzene to obtain the diketone **108a** in 84% yield (Scheme 39).

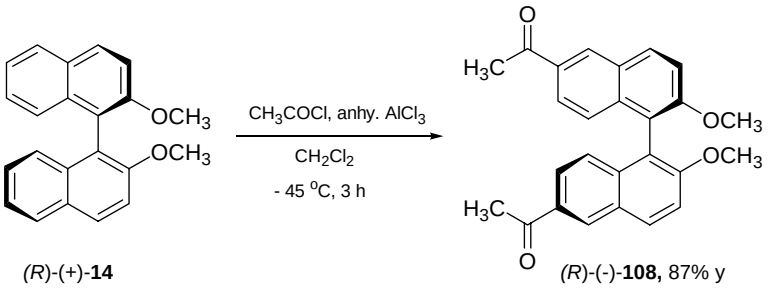
Scheme 39



To avoid the difficulty in removing nitrobenzene from the reaction mixture, we have examined the acylation reaction in CH_2Cl_2 solvent. In this run, using 4 equiv. of acetyl chloride, 4 equiv. of $AlCl_3$ and 1 equiv. of 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14** in CH_2Cl_2 at 0 °C, the desired diketone **108a** was obtained in 82% yield. Also, we have

observed that the expected diketone 6,6′-diacetyl-1,1′-bi-2-naphthyl methyl ether **108a** was obtained in 87% yield at -45 ^{o}C (Scheme 40).

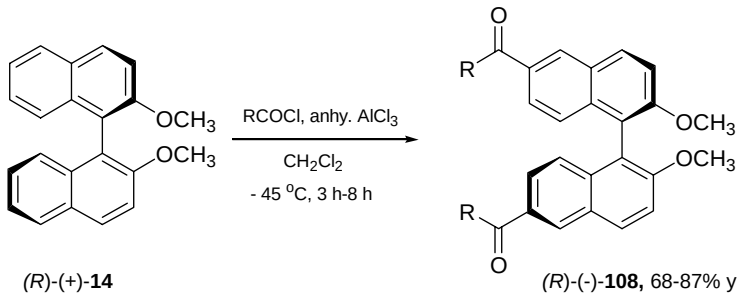
Scheme 40



(R)-(+)-**14** *(R)*-(-)-**108,** 87% y

The reaction was also carried out using various other acid chlorides and the corresponding diketones **108a-k** were obtained in good yields (Scheme 41). The results are summarized in Table 1. The reaction using propionyl chloride gave the dipropionyl product **108b** in 85% yield. In runs using butyroyl chloride, isobutyroyl chloride and chloroacetyl chloride, the products **108c, 108d** and **108e** were obtained in 78%, 75% and 72% yields, respectively. When the reaction was carried out using benzoyl chloride and 1-naphthoyl chloride, the corresponding diacyl products **108g** and **108j** were obtained in 75% and 71% yields, respectively. With substrates containing electron donating substituents like 4-methylbenzoyl chloride and 4-methoxybenzoyl chloride, the corresponding diacyl products **108h** and **108i** were obtained in 72% and 70% yields, respectively. Substrates with electron withdrawing substituents like 4-nitrobenzoyl chloride and 4-bromobenzoyl chloride gave the corresponding diacyl products **108f** and **108k** in 68% and 73% yields, respectively. Overall, there is not much difference in the reactivity when the benzoyl chloride was substituted with either electron donating groups or electron withdrawing groups.

Scheme 41



(R)-(+)-**14** *(R)*-(-)-**108,** 68-87% y

Table 1: Synthesis of **108** using various acid chlorides[a]

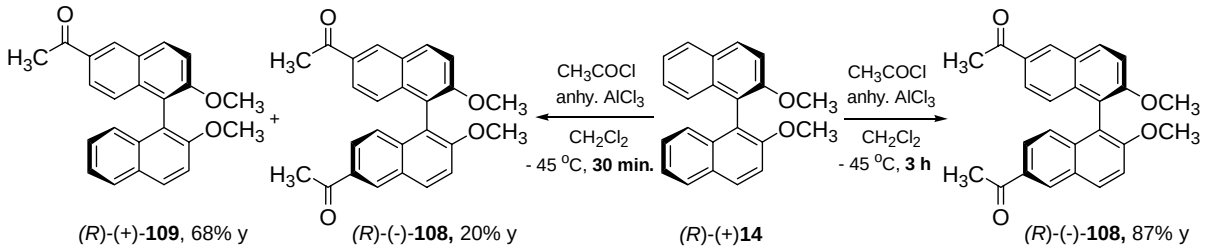
S.No	R	Time	**108**	Yield (%)[b]
1	CH_3	3 h	**108a**	87
2	CH_3CH_2	3 h	**108b**	85
3	$CH_3CH_2CH_2$	5 h	**108c**	78
4	$(CH_3)_2CH$	5 h	**108d**	75
5	$ClCH_2$	5 h	**108e**	72
6	$O_2NC_6H_4$	8 h	**108f**	68
7	C_6H_5	5 h	**108g**	75
8	$H_3CC_6H_4$	5 h	**108h**	72
9	$H_3COC_6H_4$	8 h	**108i**	70
10	Naphthyl	8 h	**108j**	71
11	BrC_6H_4	8h	**108k**	73

[a]All the reactions were carried out using bi-2-naphthyl methyl ether (*R*)-(+)-**14** (5 mmol), anhy. $AlCl_3$ (20 mmol) and acid chloride (20 mmol) in CH_2Cl_2 (40 mL) at -45 °C. [b]The product was identified by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR, MASS) and the yields are of isolated products.

When the reaction was carried out using 1:4:4 equiv. of 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14,** $AlCl_3$ and acetyl chloride in CH_2Cl_2 at -45 °C, the 6-acetyl-1,1′-bi-2-

naphthyl methyl ether **109** was formed within 30 min. time along with about 20% of 6,6′-diacetyl-1,1′-bi-2-naphthyl methyl ether **108** but the product **108** is obtained in 87% yield in 3 h (Scheme 42). This indicates that the conversion of monoacyl product to diacyl product is slow.

Scheme 42



2.1.2 Synthesis of chiral 6-acyl-1,1′-bi-2-naphthyl methyl ethers

There are mainly two active electrophilic positions *viz.* 6 and 6′ positions present in the bi-2-naphthyl moiety of 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14** as the other two electrophilic sites *viz*. 3 and 3′ positions are not sufficiently activated for electrophilic reactions (Figure 4). Reactions under mild conditions would be expected to give mono acylation of 1,1′-bi-2-naphthyl methyl ether since the diacylation seems to be slow.0

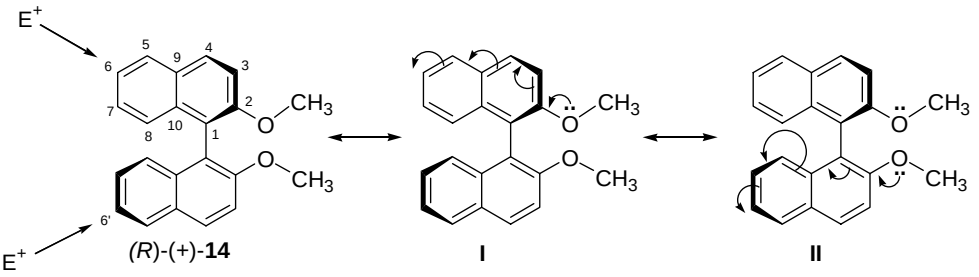
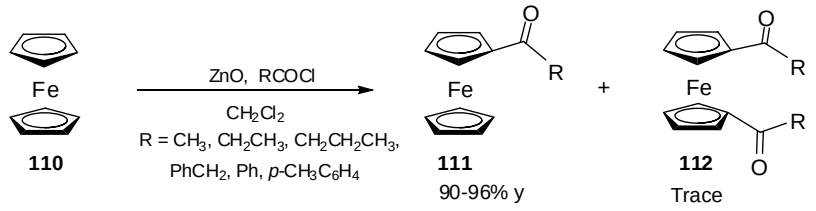


Figure 4

Wang *et al.*[52] reported a convenient method for the synthesis of monoacyl ferrocenes by using ZnO as Lewis acid (Scheme 43).

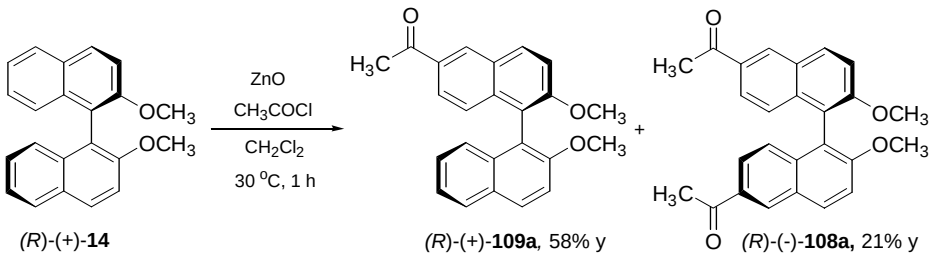
Scheme 43



Accordingly, we have examined the acylation reaction on 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14** by using ZnO as Lewis acid. When we used 1:1.2:3 equiv. ratio of 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14**, ZnO and CH_3COCl at 30 ^oC for 1 h, the mono acylated product, 6-acetyl-1,1′-bi-2-naphthyl methyl ether **109a** was obtained in 58% yield along with the diacylated product **108a** in 21% yield and 15% of the starting reactant (*R*)-(+)-**14** remained unreacted (Scheme 44).

We have carried out several experiments to optimize conditions for monoacylation of 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14** using different ratios of ZnO and CH_3COCl, but in all the runs, some amount of diacetyl product **108a** was also obtained.

Scheme 44

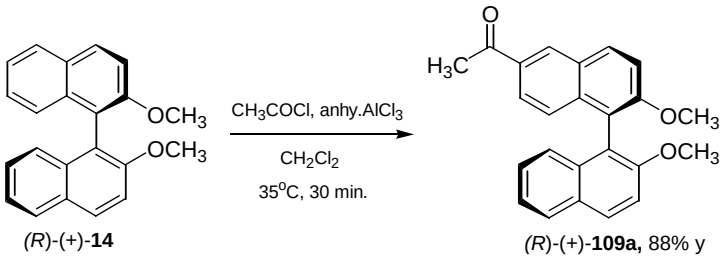


(R)-(+)-**14** *(R)*-(+)-**109a**, 58% y *(R)*-(-)-**108a,** 21% y

When the reaction was carried out using 1:1:1.2 equiv. of 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14**, $AlCl_3$ and acetyl chloride in CH_2Cl_2 solvent at 25 ^oC for 2 h, the 6-acetyl-1,1′-bi-2-naphthyl methyl ether **109a** was obtained in 66% yield along with 6,6′-diacetyl-1,1′-bi-2-naphthyl methyl ether **108a** and unreacted starting material in 15% and 9% yields, respectively. Also, the reaction at -45 ^oC for 1 h gave diacylated product in 27% yield

besides the desired monoacylated product in 54% yield. In a run at 50 ^{o}C for 30 min, gave the monoacylated product **109a** in 62% yield along with diacylated product **108a** in 21% yield (Table 2). Fortunately, when the reaction was carried out by taking 1:1:1.2 equiv. ratio of 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14**, $AlCl_3$ and acetyl chloride in CH_2Cl_2 solvent, the 6-acyl-1,1′-bi-2-naphthyl methyl ether **109a** was obtained in 88% yield and the corresponding diacetyl compound was not formed (Scheme 45).

Scheme 45



(*R*)-(+)-**14** (*R*)-(+)-**109a,** 88% y

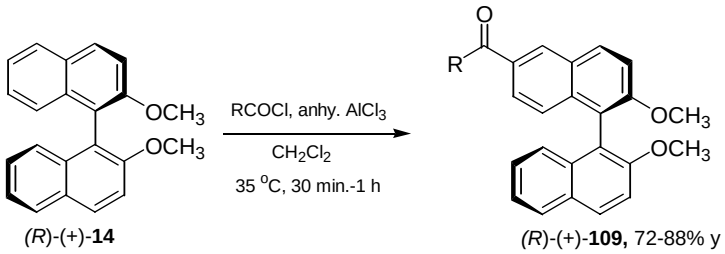
Table 2 : Synthesis of **109a** using various Lewis acids.[a]

No	Lewis acid	Temp	Time	**109a** Yield(%)[b]	**108a** Yield(%)[b]
1	$TiCl_4$	25 ^{o}C	24 h	0	0
2	ZnO	30 ^{o}C	1 h	58	21
3	$AlCl_3$	-45 ^{o}C	1 h	54	27
4	$AlCl_3$	0 ^{o}C	1 h	68	10
5	$AlCl_3$	50 ^{o}C	30 min.	62	21
6	$AlCl_3$	25 ^{o}C	2 h	66	15
7	$AlCl_3$	35 ^{o}C	30 min.	88	trace

[a]All the reactions were carried out using bi-2-naphthyl methyl ether (*R*)-(+)-**14** (5 mmol), anhydrous Lewis acid (5 mmol) and acetyl chloride (6 mmol) in CH_2Cl_2 (40 mL). [b]Yields are of isolated products.

The reaction was also carried out under these optimized conditions using various other acid chlorides. The corresponding monoketones **109a-m** were obtained in good yields (Scheme 46). The results are summarized in Table 3.

Scheme 46



(R)-(+)-**14** *(R)*-(+)-**109,** 72-88% y

Table 3: Synthesis of **109** using various acid chlorides[a]

S.No	R	Time	Product	Yield (%)[b]
1	CH_3	30 min	**109a**	88
2	CH_3CH_2	30 min	**109b**	87
3	$CH_3CH_2CH_2$	30 min	**109c**	84
4	$(CH_3)_2CH$	30 min	**109d**	78
5	$BrCH_2$	30 min	**109e**	75
6	$O_2NC_6H_4$	1 h	**109f**	72
7	C_6H_5	30 min	**109g**	81
8	$H_3CC_6H_4$	1 h	**109h**	77
9	$H_3COC_6H_4$	1 h	**109i**	74
10	Naphthoyl	1 h	**109j**	75
11	BrC_6H_4	1 h	**109k**	77
12	$C_6H_5CH_2$	1 h	**109l**	82
13	$C_2H_5CO_2$	1 h	**109m**	85

[a]All the reactions were carried out using bi-2-naphthyl methyl ether (*R*)-(+)-**14** (5 mmol), anhydrous $AlCl_3$ (5 mmol) and acid chloride (6 mmol) in CH_2Cl_2 (40 mL) at 35 °C. [b]The product was identified by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR, MASS) and the yields are of isolated products.

The reaction using propionyl chloride and butyroyl chloride gave the monoacyl products **109b** and **109c** in 87% and 84% yields, respectively. Reactions using isobutyroyl chloride, bromoacetyl chloride and phenacyl chloride gave the products **109d, 109e** and **109l** in 78%, 75% and 82% yields, respectively. When the reaction was carried out using benzoyl chloride and 1-naphthoyl chloride, the corresponding monoacyl products **109g** and **109j** were obtained in 81% and 75% yields, respectively. With substrates containing electron donating substituents like 4-methylbenzoyl chloride and 4-methoxybenzoyl chloride, the corresponding monoacyl products **109h** and **109i** were obtained in 77% and 74% yields, respectively. Substrates with electron withdrawing substituents like 4-nitrobenzoyl chloride and 4-bromobenzoyl chloride gave the corresponding monoacyl products **109f** and **109k** in 72% and 77% yields respectively. Also, the reaction using ethyl chlorooxoacetate gave the monoacyl acetate product **109m** in 85% yield. Again, there is not much difference in the reactivity when the benzoyl chloride was substituted with either electron donating groups or electron withdrawing groups.

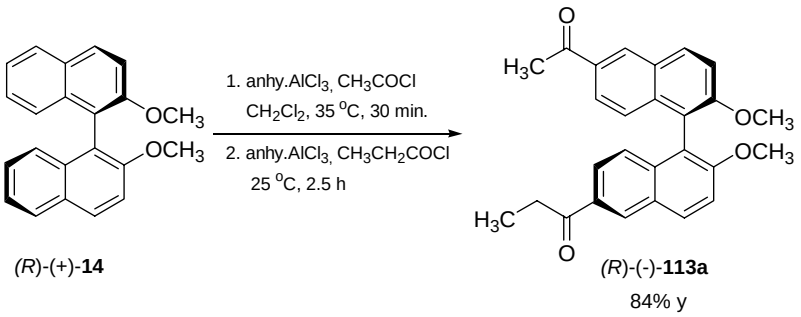
2.1.3 Synthesis of unsymmetrical chiral 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ethers

After successfully developing a procedure for the synthesis of 6-monoacyl-1,1′-bi-2-naphthyl methyl ether derivatives **109** in good yields, we turned our attention on the development of a method of synthesis of unsymmetrical 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ether derivatives **113** in a single pot reaction by using two different acid chlorides.

Accordingly, we have examined the reaction of 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14** (1 equiv.), $AlCl_3$(1 equiv.) and acetyl chloride (1.2 equiv.) in CH_2Cl_2 at 35 ^oC for 30

min.. To this one more equiv. of $AlCl_3$ was added followed by slow addition of propionyl chloride (2 equiv.). To our delight, in this run, the expected unsymmetrical 6-acetyl,6′-propionyl-1,1′-bi-2-naphthyl methyl ether **113a** was obtained in 84% yield (Scheme 47).

Scheme 47

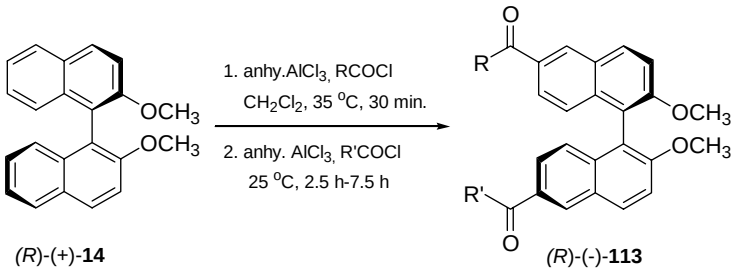


(R)-(+)-**14** *(R)*-(-)-**113a**
84% y

We have generalized the above reaction by using different acid chloride combinations (Table 4). The unsymmetrical 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ethers **113** were obtained in 75% to 84% yields (Scheme 48).

The reaction using the combination of acetyl chloride followed by propionyl chloride under reaction conditions for 3 h gave the unsymmetrical diacylated product **113a** in 84% yield. Reaction using acetyl chloride and butyroyl chloride combination gave the diacylated product **113b** in 82% yield. Also, the one pot reaction of acetyl chloride and bromoacetyl chloride combination gave the desired product **113c** in 75% yield. The reactions of acetyl chloride in combination with benzoyl chloride, 4-chlorobenzoyl chloride and 4-methoxybenzoyl chloride under the same reaction conditions gave the unsymmetrical diacylated products **113d**, **113f** and **113g** in 78%, 75% and 78% yields, respectively. The combination of propionyl chloride and benzoyl chloride gave the desired product **113e** in 77% yield.

Scheme 48



(R)-(+)-**14** *(R)*-(-)-**113**
75-84% y

Table 4 : Synthesis of **113** using various Acid Chlorides[a]

S.No	R	R′	Product	Yield(%)[b]
1	CH_3	CH_3CH_2	**113a**	84
2	CH_3	$CH_3CH_2CH_2$	**113b**	82
3	CH_3	$BrCH_2$	**113c**	75
4	CH_3	C_6H_5	**113d**	78
5	CH_3CH_2	C_6H_5	**113e**	77
6	CH_3	4-ClC_6H_4	**113f**	75
7	CH_3	4-$OMeC_6H_4$	**113g**	78

[a]All the reactions were carried out using bi-2-naphthyl methyl ether (*R*)-(+)-**14** (5 mmol), anhydrous $AlCl_3$ (10 mmol), RCOCl (6 mmol) and R′COCl (10 mmol) in CH_2Cl_2 (40 mL) at 35 °C. [b]The product was identified by spectral data (IR, ^{1}H-NMR, ^{13}C-NMR, MASS) and the yields are of isolated products.

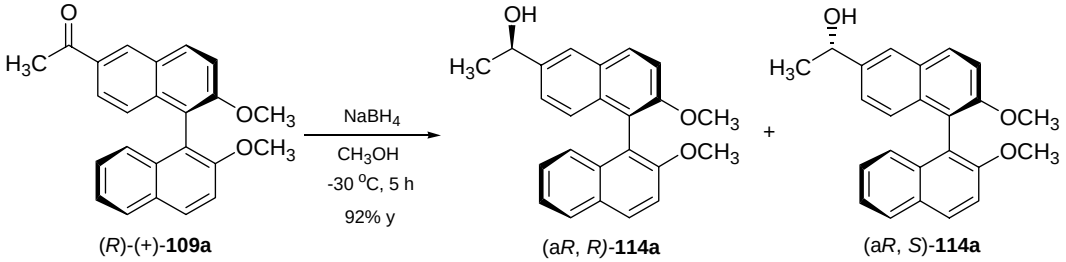
2.2.1 Reduction of 6-acyl-1,1′-bi-2-naphthyl methyl ether derivatives

Enantiomerism due to axial chirality has been receiving increasing attention in recent years.[53] Biaryl derivatives exhibiting axial chirality can be either configurationally stable or can give raise to stereolabile atropisomers, depending on the extent of the steric effects of

their substituents.

We have chosen the chiral ketone, 6-acetyl-1,1′-bi-2-naphthyl methyl ether, (*R*)-(+)-**109a** for our initial studies. We have observed that the reduction of 6-acetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**109a** with the simple $NaBH_4/CH_3OH$ reagent system gave the corresponding reduced alcohol (-)-**114a** in 92% yield (Scheme 49). However, whether the product is a single diastereomer or a mixture could not be deduced based on TLC, HPLC and ^{1}H-NMR analysis. When the methyl[(*R*)-1,1′-bi-2-naphthyl methyl ether]carbinol, (-)-**114a,** which was obtained from the $NaBH_4/CH_3OH$ reduction of 6-acetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**109a**, is subjected to HPLC analysis on chiral cell OD-H column, only one peak was observed. Also, no diastereomeric signals were observed in ^{1}H-NMR and ^{13}C-NMR spectra.

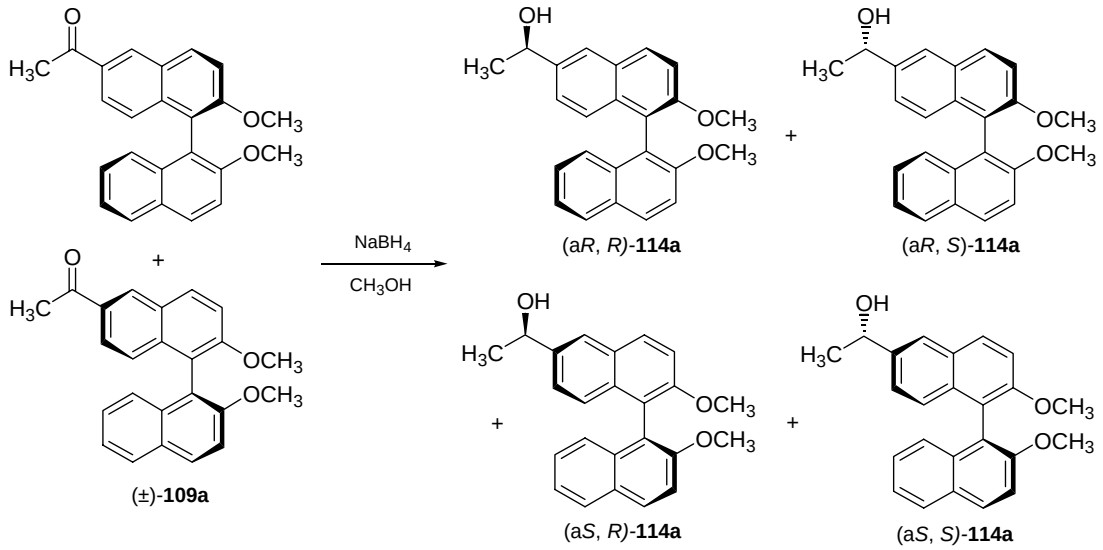
Scheme 49



(*R*)-(+)-**109a** (a*R*, *R)*-**114a** (a*R*, *S*)-**114a**

We have also reduced the racemic 6-acetyl-1,1′-bi-2-naphthyl methyl ether,(±)-**109a** with the $NaBH_4/CH_3OH$ reagent system. The corresponding product alcohol (±)-**114a** exhibited only 2 peaks in HPLC analysis using chiral cell OD-H column (Scheme 50). Also, there is no separation in the ^{1}H-NMR and ^{13}C-NMR spectral signals expected for the four possible stereoisomeric products.

Scheme 50: Possible stereoisomers of alcohol **114a**.



Even the ester derivatives of methyl[(*R*)-1,1′-bi-2-naphthyl methyl ether]carbinol, (-)-**114a** such as **115, 116** and **117** (Figure 5) did not show any diastereomeric signals in the ^{1}H-NMR and ^{13}C-NMR spectra.

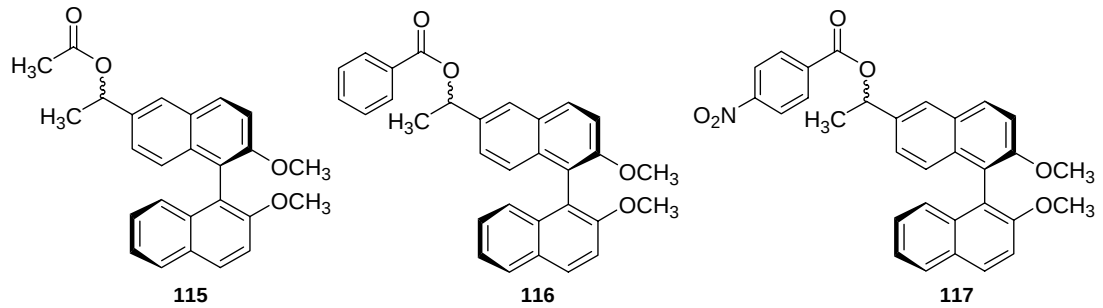
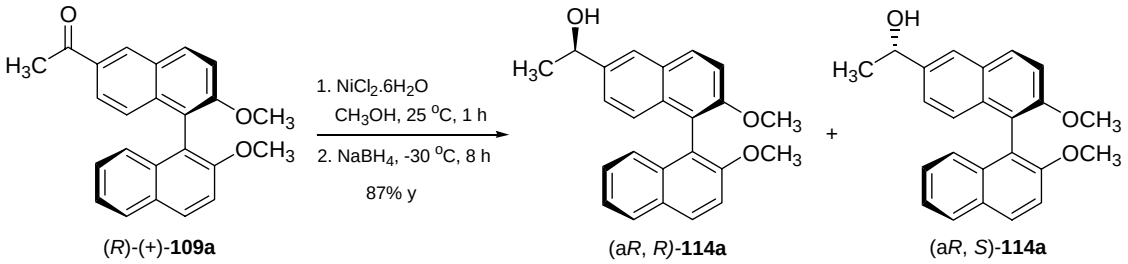


Figure 5

However, the HPLC and ^{1}H-NMR analysis of the chiral α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) ester derivative of (-)-**114a** exhibited two resolved peaks in 50:50 ratio, indicating that the bi-2-naphthyl chirality does not influence the $NaBH_4$ reduction of the 6-acetyl group.

We have also carried out the reduction of 6-acetyl-1,1′-bi-2-naphthyl methyl ether (+)-**109a** with the $NiCl_2{\cdot}6H_2O/NaBH_4/CH_3OH$ reagent system. The product **114a** was obtained in 87% yield (Scheme 51). The HPLC analysis of the *R*-MTPA ester of the alcohol product indicated 55:45 diastereoselectivity in this reaction.

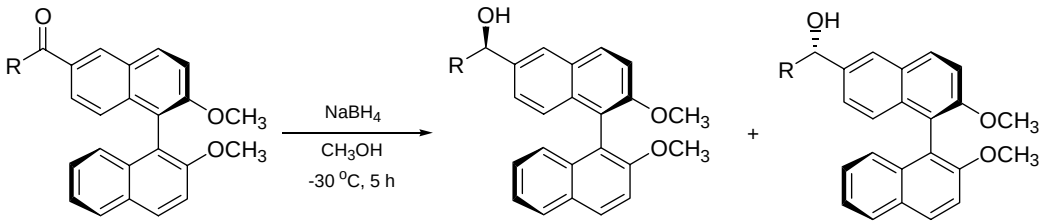
Scheme 51



(*R*)-(+)-**109a** (a*R*, *R*)-**114a** (a*R*, *S*)-**114a**

We have then carried out the reduction of other 6-acyl-1,1′-bi-2-naphthyl methyl ether derivatives (**109b-109c**) with the $NaBH_4/CH_3OH$ reagent system to examine the effect of other alkyl groups. Unfortunately, no chiral induction was observed in the corresponding product alcohols (**114b-114c**) (Scheme 52).

Scheme 52



(*R*)-(+)-**109** (a*R*, *R*)-**114** (a*R*, *S*)-**114**

R	Product	Yield (%)	dr(%)
CH_3	**114a**	92%	50:50
CH_2CH_3	**114b**	91%	52:48
$CH(CH_3)_2$	**114c**	88%	50:50

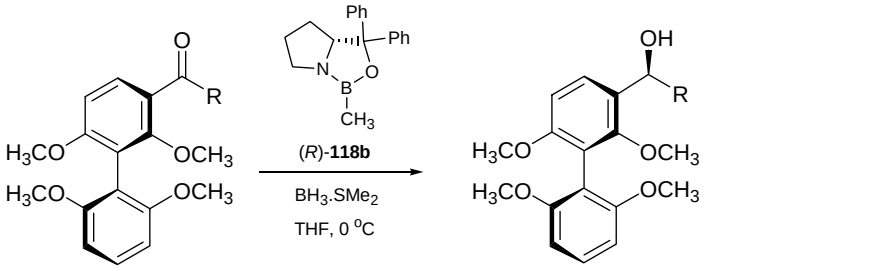
Furthermore, the reduction of 6-acetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**109a** using the BH_3:THF, $NaBH_4/I_2$ and $PhN(Et_2):BH_3$ reagent systems also gave the alcohol products only in 50:50 diastereomeric ratio as revealed by ^{1}H-NMR analysis of the corresponding *R*-MTPA ester.

2.2.2 Asymmetric reduction of prostereogenic carbonyl compounds

Surprisingly, reports are not available for the asymmetric reduction of bi-2-naphthyl alkyl ketones. However, asymmetric reduction of configurationally flexible biphenyl alkyl ketones were reported by chemical[54] as well as enzymatic[55] methods.

For instance, Delogu *et al*.[56,57] reported the stereoselective oxazaborolidine (*R*)-**118b** (CBS) reduction of non-planar biphenyl alkyl ketones **119a-b** to obtain the alcohol products **120a-b** in 93-95% ee (Scheme 53).

Scheme 53

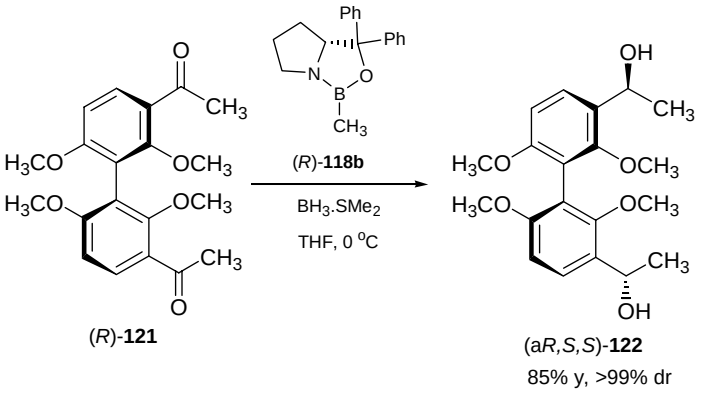


(*R*)-**119a** R = CH_3
(*R*)-**119b** R = ^{t}Bu

(a*R*,*S*)(-)-**120a** R = CH_3 85% y, >95%ee
(a*R*,*S*)(-)-**120b** R = ^{t}Bu 83% y, >93%ee

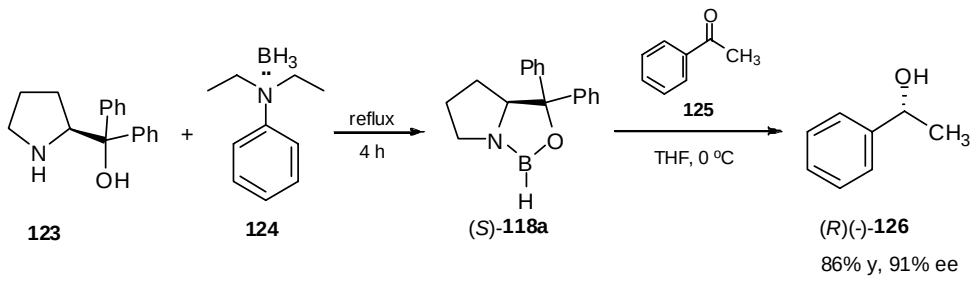
The CBS reduction of the diacetyl derivative **121** using the oxazaborolidine catalyst (*R*)-**118b** gave the corresponding diol **122** in 85% yield with >99% diastereomeric ratio (Scheme 54).

Scheme 54



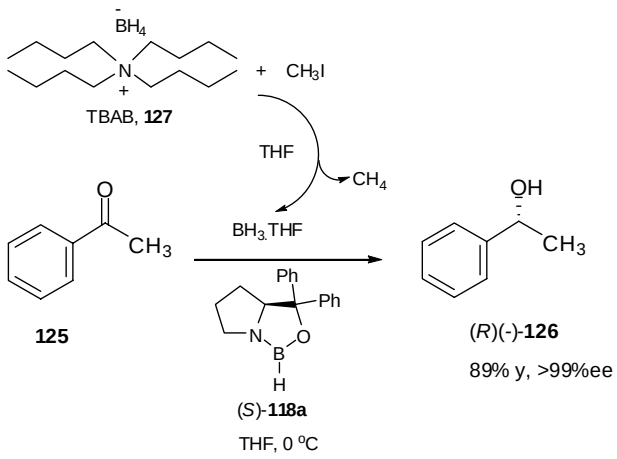
Previously, it was reported from this laboratory that the oxazaborolidine catalyzed asymmetric reduction of acetophenone with $H_3B{:}N(C_2H_5)_2Ph$ gave the corresponding alcohol with 91% ee (Scheme 55).[58]

Scheme 55



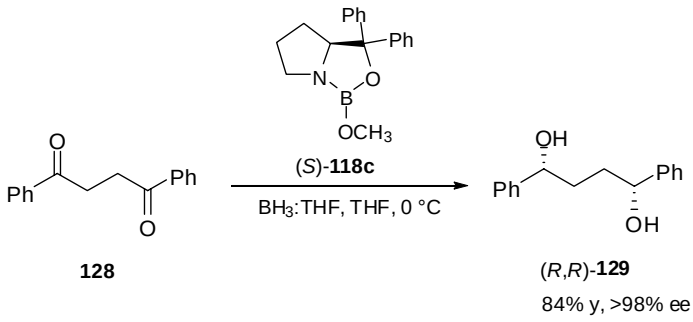
Very recently, it was reported from this laboratory that the asymmetric reduction of prochiral ketones gives the corresponding alcohols in up to 99% ee by using chiral oxazaborolidine catalyst which is readily prepared *in situ* in THF using (*S*)-2-diphenylpyrrolidinemethanol and borane generated from tetrabutylammonium borohydride **127**/CH_3I or I_2 reagent system (Scheme 56).[59]

Scheme 56



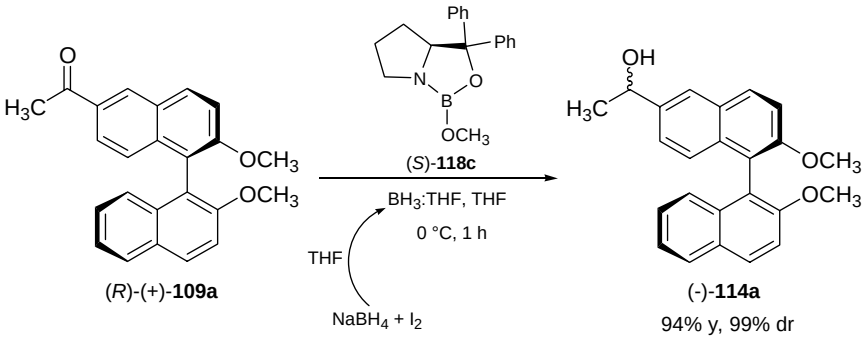
It was also reported from this laboratory that the asymmetric reduction of 1,4-diphenylbutane-1,4-dione **128** to the corresponding diol **129** was achieved in 98% ee using chiral oxazaborolidine (*S*)-**118c** (Scheme 57).[60]

Scheme 57



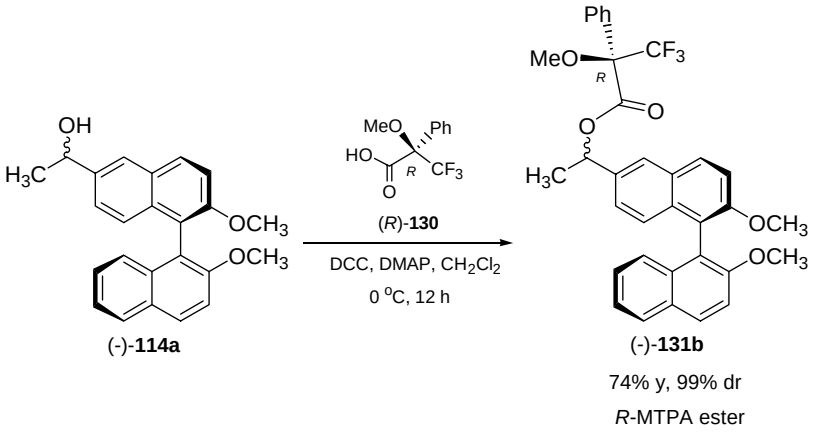
We have carried out the reaction of 6-acetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**109a** with BH_3:THF by using 30 mol% oxazaborolidine catalyst in THF solvent at 0 °C for 1 h (Scheme 58). The expected methyl[(*R*)-1,1′-bi-2-naphthyl methyl ether]carbinol (-)-**114a** was obtained in 94% yield.

Scheme 58

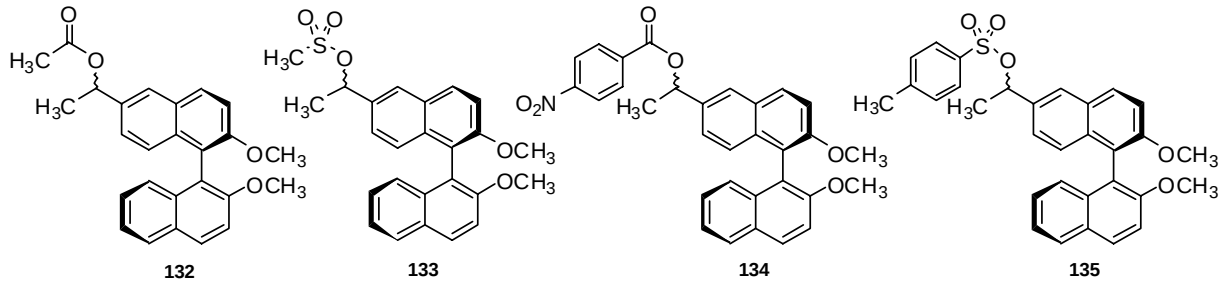


The product (-)-**114a** was obtained in 94% yield with 99% dr by HPLC analysis (OD-H column) of the *R*-MTPA ester of alcohol (-)-**114a** (Scheme 59).

Scheme 59



Though, we have achieved high diastereoselectivity in the chiral oxazaborolidine reduction, the configuration of the newly formed stereogenic centre is not known. We have prepared various derivatives **132, 133, 134** and **135** using the compound (-)-**114a** (Figure 6) to obtain single crystals suitable for X-ray diffraction analysis. Unfortunately, crystals suitable for single crystal X-ray analysis could not be obtained by crystallization of the derivatives **132-135** in various solvents.



132 **133** **134** **135**

Figure 6

Therefore, we looked for other methods for assigning the stereochemistry of new stereogenic centre in the compound **114a**.[61] Several methods are available for assigning configuration of compounds with unknown configuration such as correlation with compounds of known configuration by synthetic interconversions, comparison of optical rotation by polarimetric methods, optical rotary dispersion, circular dichroism and various empirical methods based on NMR spectroscopy.[62] A most frequently used method is NMR spectral analysis of the corresponding Mosher ester.[63-66] Accordingly, we decided to analyze the ^{1}H-NMR data of the Mosher esters **131** for assignment of the configuration of the newly formed stereogenic centre in (-)-**114a**.

2.2.3 Assigning the configuration of unknown stereogenic secondary alcohols

The Mosher ester analytical method relies on the fact that the protons in diastereomeric α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) esters derived from the carbinol display different chemical shifts (δs) in their ^{1}H-NMR spectra. The protocol consists preparation of each of the diastereomeric *S*- and *R*-MTPA esters and determination of the $\Delta\delta^{SR}$ values of the ^{1}H-NMR spectral data of these two esters as described here for assigning configuration in the case of 1-phenylethanol **136**.

The most stable conformations of *S*-MTPA and *R*-MTPA esters of enantiomers of 1-phenylethanol **136** are depicted in Figure 7.[63]

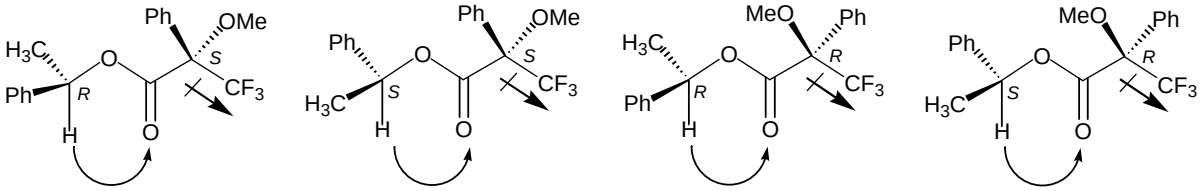
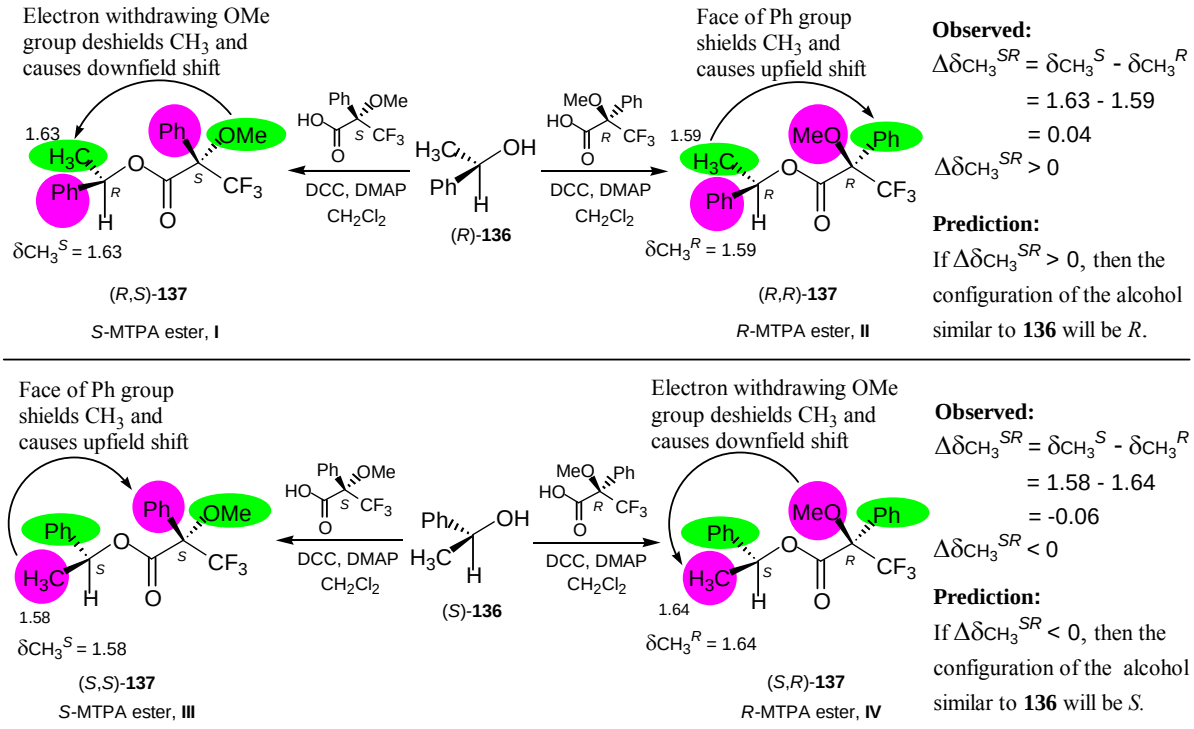


Figure 7: Preferred conformations of MTPA esters of 1-phenylethanol.

By analyzing the sign of the difference in chemical shifts for analogous pairs of protons (the set of $\Delta\delta^{SR}$ values) for CH_3 hydrogens in the diastereomeric esters prepared from 1-phenylethanol **136**, the absolute configuration of its stereocenter can be reliably assigned (Scheme 60).

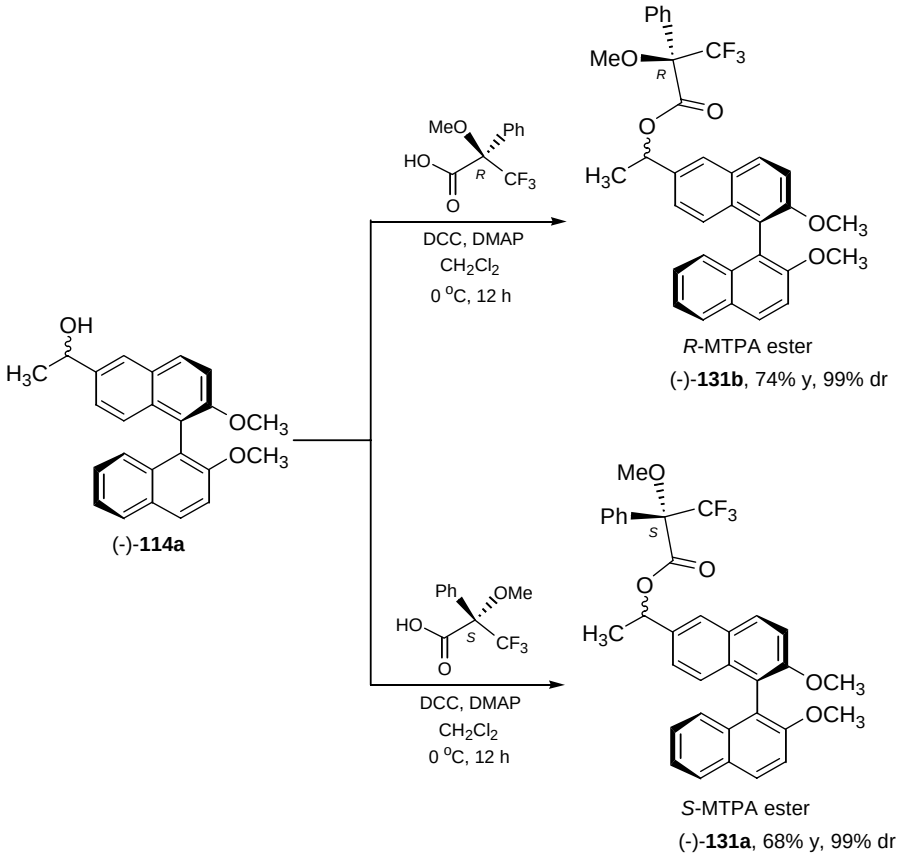
Scheme 60



Accordingly, we have prepared the *R*-Mosher ester **131b** using methyl[(*R*)-1,1′-bi-2-naphthyl methyl ether]carbinol (-)-**114a,** (*R*)-(+)-α-methoxy-α-trifluoromethylphenylacetic acid **130** (*R*-MTPAOH), DCC and DMAP in CH_2Cl_2 solvent at 0 ^oC for 12 h in 74% yield (Scheme 61).

We have also prepared the corresponding *S*-Mosher ester derivative **131a** in 68% yield using methyl[(*R*)-1,1′-bi-2-naphthyl methyl ether]carbinol (-)-**114a,** (*S*)-(-)-α-methoxy-α-trifluoromethylphenylacetic acid **130** (*S*-MTPAOH), DCC and DMAP in CH_2Cl_2 solvent at 0 ^oC for 12 h (Scheme 61).

Scheme 61



The ^{1}H-NMR data of the *S*-MTPA and *R*-MTPA esters of (-)-**114a** have been analyzed following the protocol of analysis in the case of 1-phenylethylalcohol as outlined in Scheme **60** and the results are presented in Figure 8.

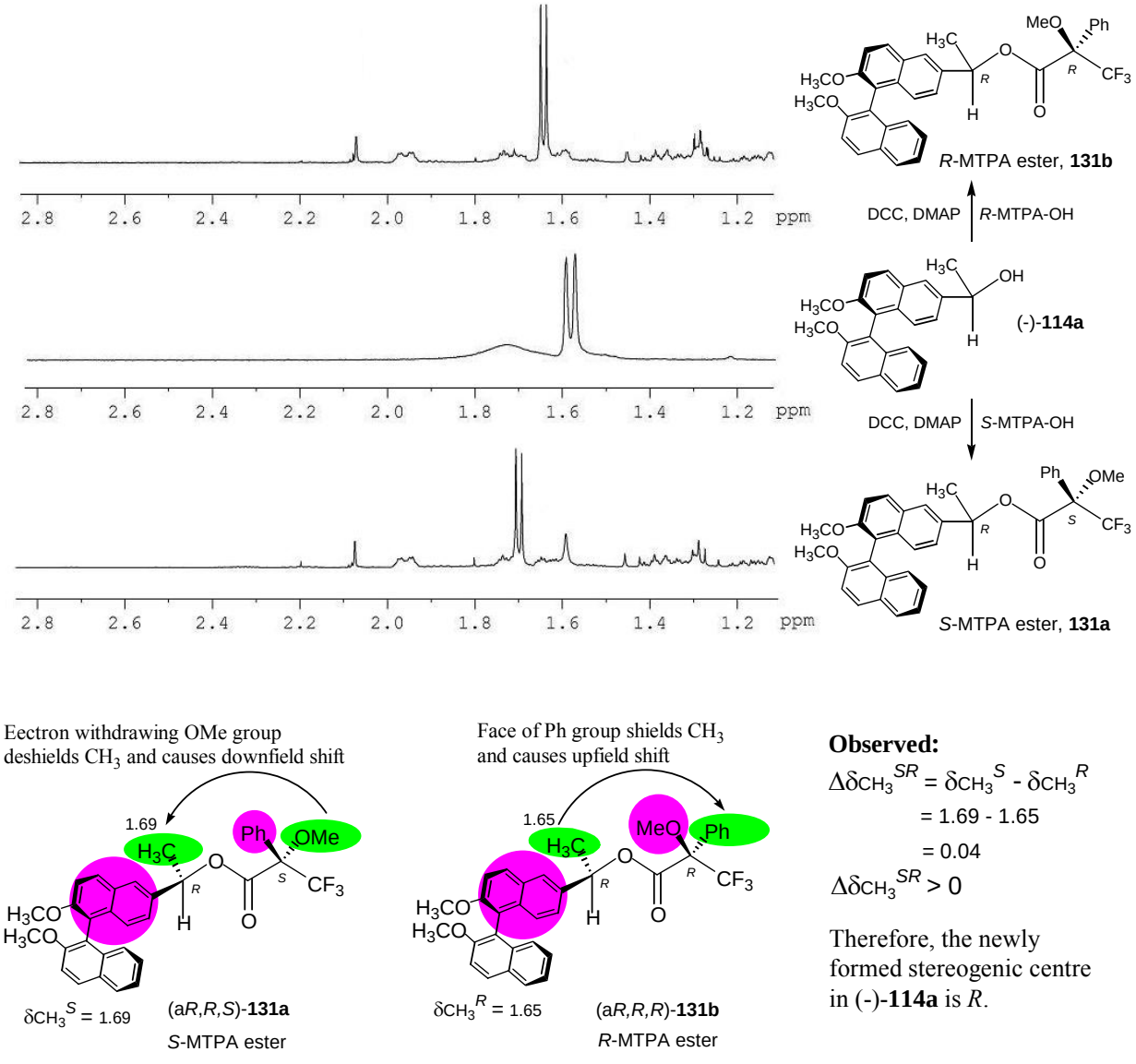


Figure 8: ^{1}H-NMR analysis of the MTPA esters of (-)-**114a** for assignment of configuration at the newly formed stereogenic centre.

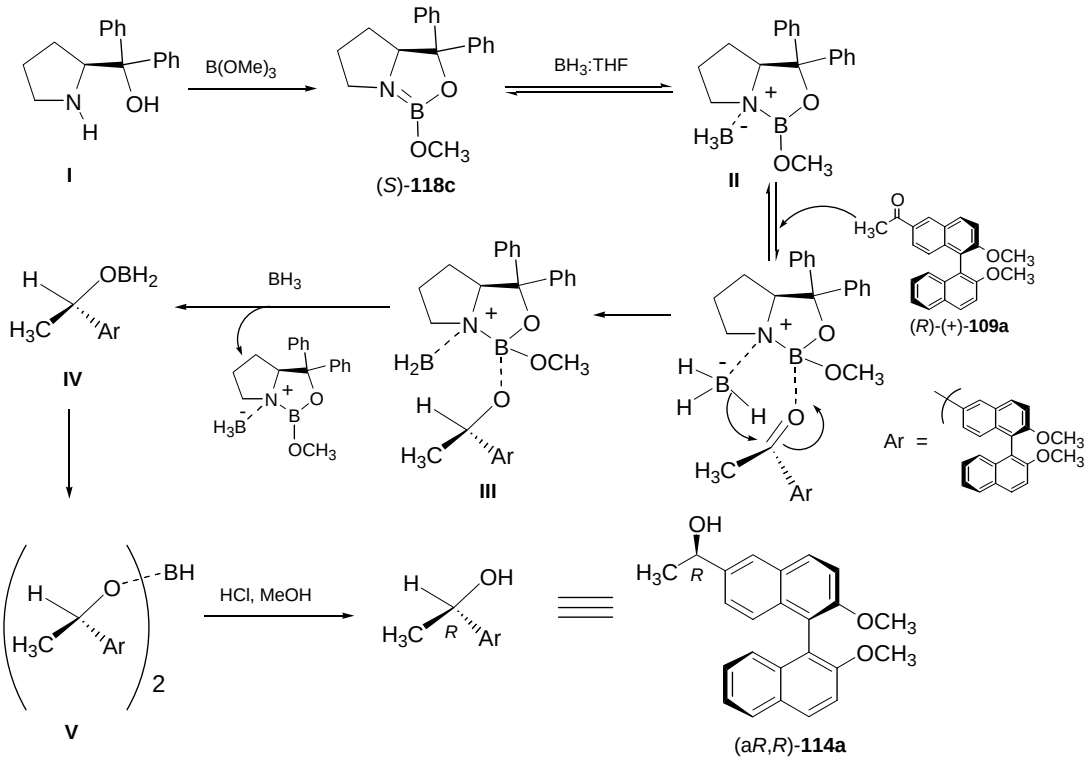
The results clearly indicate that the configuration of the newly formed stereogenic centre of the product (-)-**114a** obtained in the CBS reduction (Scheme 58) is '*R*'.

As discussed in the next section, this configurational assignment is as expected on the basis of the CBS reduction mechanism, indicating that the chiral bi-2-naphthyl moiety does not have any influence in this oxazaborolidine catalyzed borane reduction.

2.2.4 Proposed mechanism for the reduction of prostereogenic ketones using oxazaborolidine catalyst

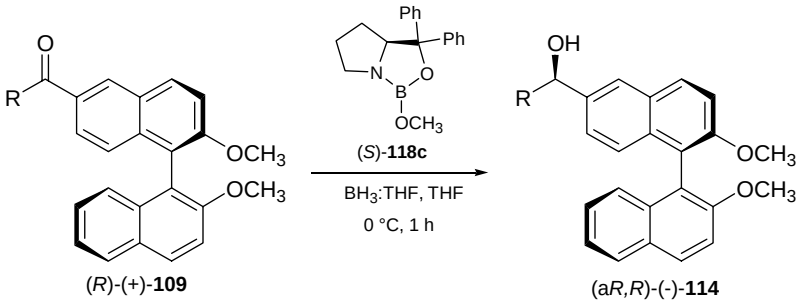
The new stereogenic centre is also expected to be *R* on the basis of the mechanism proposed for the oxazaborolidine reduction of aryl methyl ketones (Scheme 62).[67]

Scheme 62



We have also carried out the asymmetric reduction of other 6-acyl-1,1′-bi-2-naphthyl methyl ether derivatives **109b-109c** using 30 mol% oxazaborolidine catalyst. The corresponding alcohol derivatives **114b-114c** were obtained with high >99 dr (Scheme 63).

Scheme 63



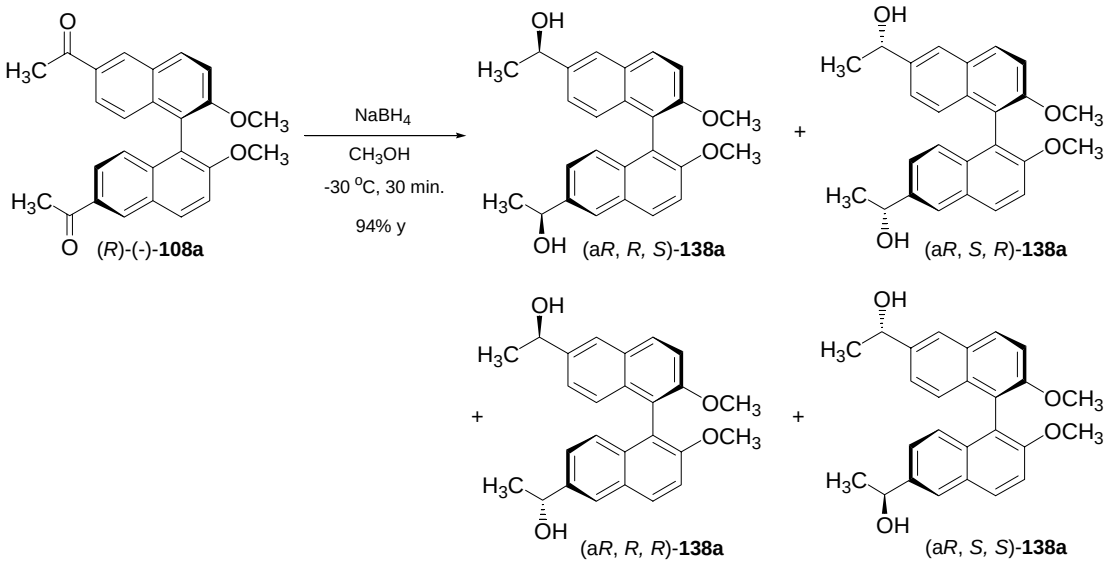
R	Product	Yield (%)	dr(%)
CH_2CH_3	**114b**	91%	99
$CH(CH_3)_2$	**114c**	88%	99

2.2.5 Diastereoselective reduction of 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ether derivatives

The borohydride reduction of 6,6′-diacetyl-1,1′-bi-2-naphthyl methyl ether, (*R*)-(-)-**108a** is expected to give four diastereomeric products (Scheme 64). Among these, the products (a*R*,*R*,*S*)-**138a** and (a*R*,*S*,*R*)-**138a** would be the same. Hence, the products are expected to form in the 2:1:1 ratio if the chiral bi-2-naphthyl skeleton does not have any influence on the diastereoselectivity of the borohydride reaction.

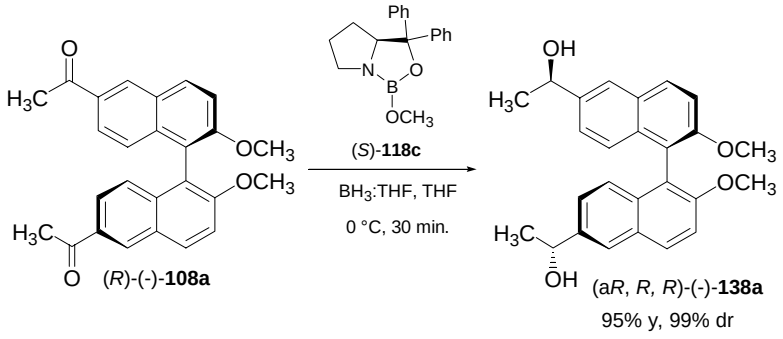
We have observed that the reduction of 6,6′-diacetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(-)-**108a** using the $NaBH_4/CH_3OH$ reagent system at -30 ^oC for 30 min. gave the corresponding diol **138a** in 94% yield with 2:1:1 diastereomeric ratio confirming that the chiral bi-2-naphthyl moiety does not have any influence on the diastereoselectivity in this reaction (Scheme 64).

Scheme 64



Since there is no diastereoselectivity observed from the simple $NaBH_4/CH_3OH$ reduction of 6,6′-diacetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(-)-**108a,** we have turned our attention on the asymmetric reduction using the oxazaborolidine catalyst. Accordingly, we have then carried out the reaction of 6,6′-diacetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(-)-**108a** with 30 mol% oxazaborolidine catalyst (*S*)-**118c** at 0 °C for 30 min. (Scheme 65). The corresponding diol **138a** was obtained in 95% yield with >99% diastereomeric ratio which was also confirmed by HPLC analysis of the corresponding MTPA ester of the diol (-)-**138a**.

Scheme 65



Again, all the efforts towards obtaining suitable single crystals for X-ray analysis from either (-)-**138a** or its derivatives such as **139**, **140** and **141** (Figure 9) were not successful.

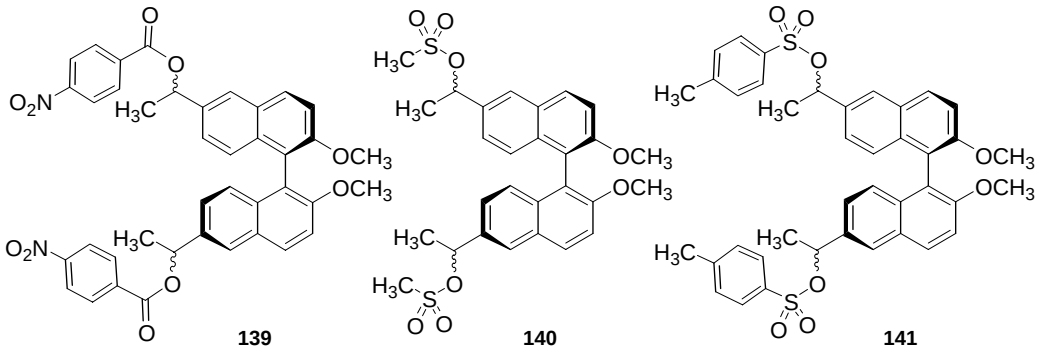
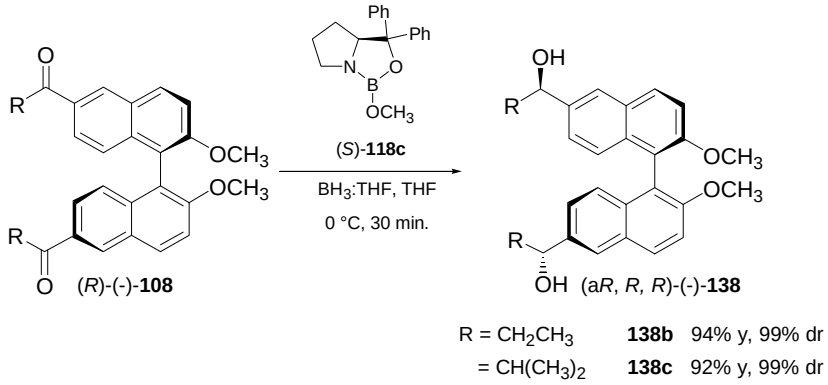


Figure 9

The configuration of newly formed stereogenic centres of methyl[(*R*)-1,1′-bi-2-naphthyl methyl ether]carbinol (-)-**138a** was assigned as *R,R* on the basis of the CBS reduction mechanism outlined in Scheme 62.

We have also examined the asymmetric reduction of some other 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ether derivatives (*R*)-(-)-**108b-c** with 30 mol% oxazaborolidine catalyst. The corresponding diols (-)-**138b-c** were obtained with >99% dr (Scheme 66).

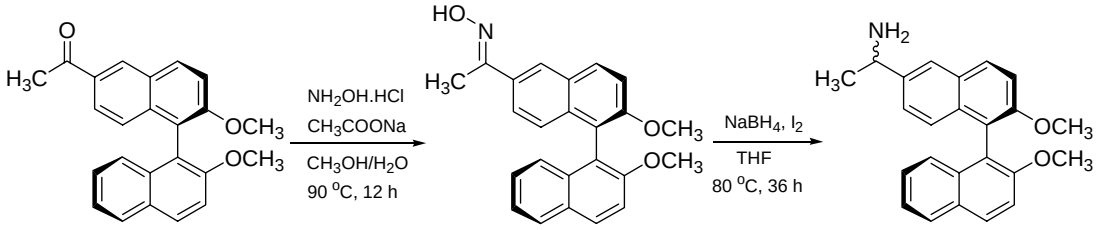
Scheme 66



2.3 Asymmetric reductive amination of 6-acyl-1,1′-bi-2-naphthyl methyl ether derivatives

We have also examined the reductive amination of 6-acetyl-1,1′-bi-2-naphthyl methyl ether derivative (*R*)-(+)-**109a,** *via* preparation of the corresponding oximes. Accordingly, we have carried out the reaction of 6-acetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**109a,** hydroxylamine hydrochloride and CH_3COONa in CH_3OH/H_2O (1:1) solvent at 90 ^oC for 12 h. The corresponding ketoxime **142a** was obtained in 83% yield (Scheme 67).

Scheme 67

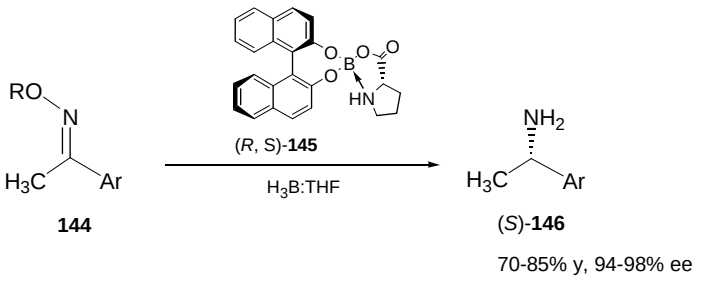


(*R*)-(+)-**109a** (*R*)-(+)-**142a,** 83% y (-)-**143a** 47% y, 1:1 dr

The ketoxime **142a** undergoes reduction with $NaBH_4/I_2$ in THF solvent at 80 ^oC to give the amine **143a** in 47% yield. In this reaction, about 30% of ketoxime **142** remained unreacted even after 36 h. Unfortunately, the amine product **143a** was obtained only in 1:1 diastereomeric ratio as indicated by ^{1}H-NMR analysis.

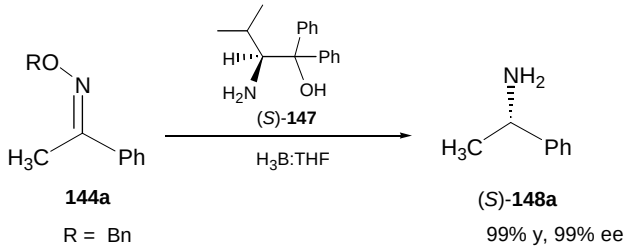
Chu *et al.*[69] reported that the asymmetric reduction of ketoxime ethers **144** using chiral spiroborate esters **145** give the amine product **146** in 70-85% yields with 94-98% ee (Scheme 68).

Scheme 68



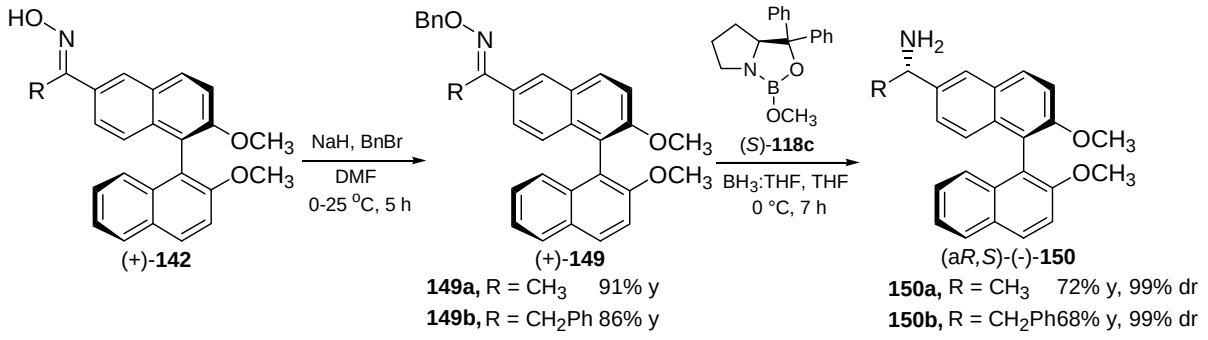
Itsuno *et al.*[70b] reported that the asymmetric reduction of ketoxime ethers by chiral valinol **147** and BH_3:THF reagent system gives the product in 99% yield and 99% ee (Scheme 69).

Scheme 69



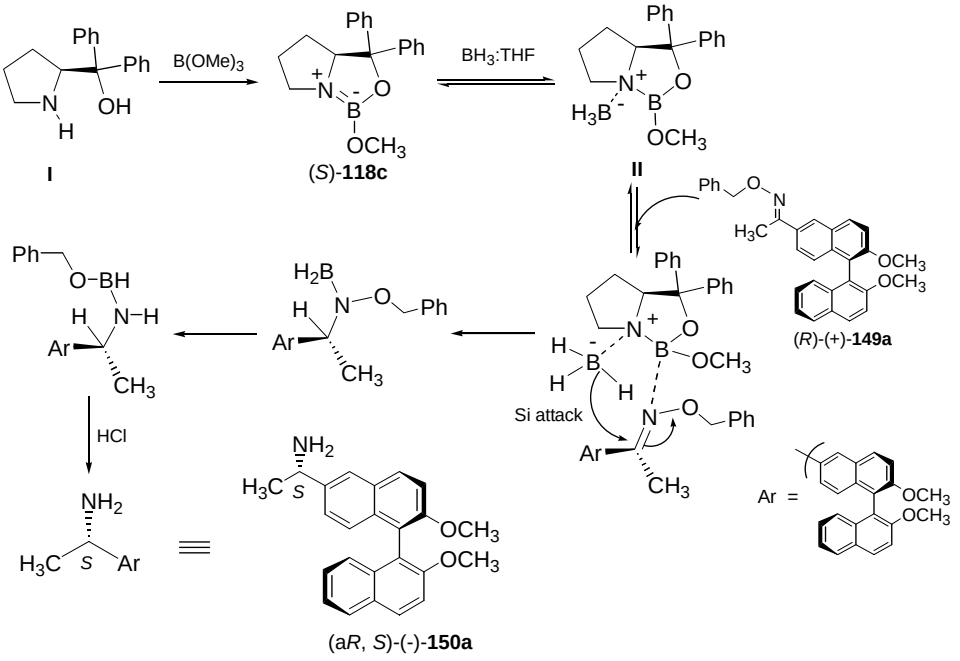
These literature reports prompted us to examine this methodology for the asymmetric reduction of the corresponding ketoxime ether. Accordingly, we have prepared the benzyl ether of the ketoxime **149** by the reaction of the oxime **142** with benzyl bromide in DMF solvent followed by slow addition of sodium hydride at 0 ^{o}C for 5 h. The ketoxime ether was then subjected to asymmetric reduction using 30 mol% oxazaborolidine catalyst and BH_3:THF. The corresponding chiral amine **150a** was obtained in 72% yield with >99% diastereoselectivity (Scheme 70).

Scheme 70



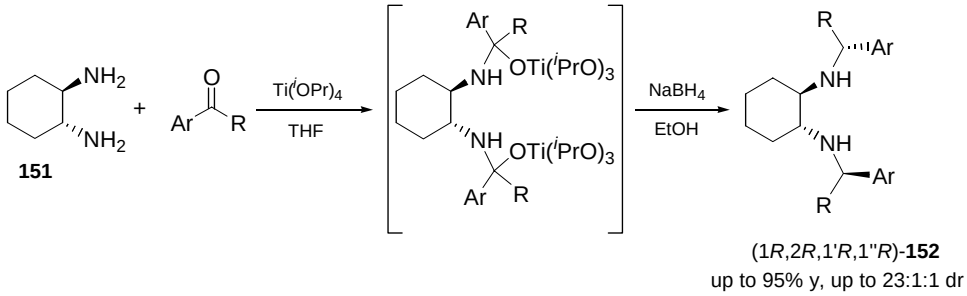
The configuration of the amine **150a** was assigned as *S* by considering the mechanism proposed for oxazaborolidine reduction of oxime ethers (Scheme 71).[70a] In contrast to the oxazaborolidine reduction of methyl ketones where stereochemical outcome is controlled by the chiral catalyst,the geometry of the oxime ether plays a role in the stereochemical outcome of the asymmetric reduction of oxime ethers and leads to delivering of the hydride from the *Si*-face of the *anti*-isomer of oxime ether **149a** resulting in the formation of the *S* amine **150a**.

Scheme 71



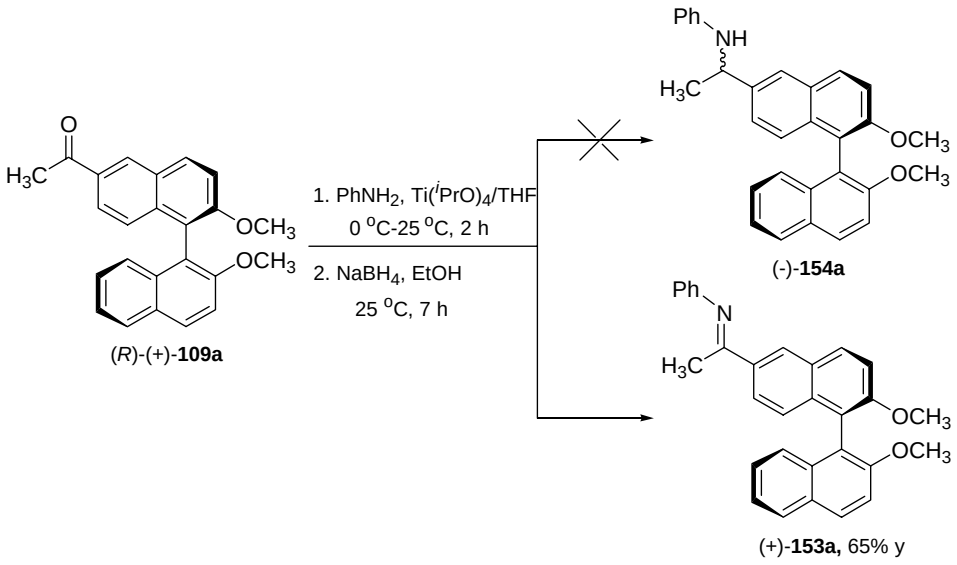
Recently, it was reported from this laboratory that reductive amination of ketones with chiral cyclohexyl diamines and the Ti(^{i}OPr)$_4$/NaBH$_4$ reagent system gave high diastereoselectivities (Scheme 72).[68]

Scheme 72



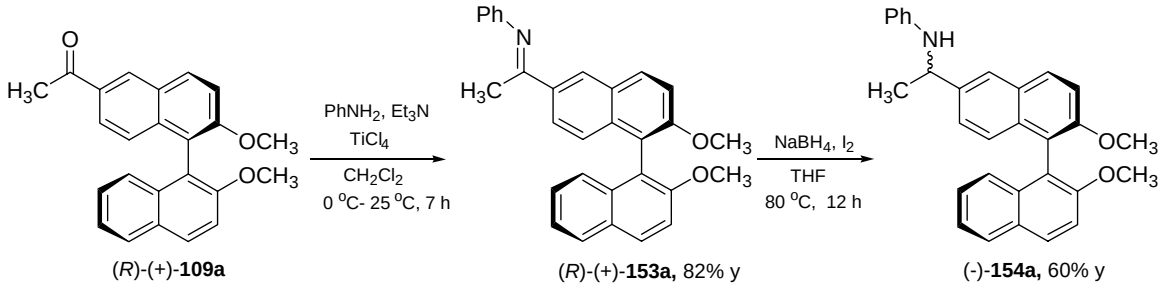
Accordingly, we have carried out the reductive amination of 6-acetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**109a,** aniline using the Ti(^{i}PrO)$_4$/NaBH$_4$ reagent system. However, only the corresponding ketimine (*R*)-(+)-**153a** was obtained in this run (Scheme 73).

Scheme 73



We have observed that the imine (*R*)-(+)-**153a** is also formed in 82% yield by the reaction of 6-acetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**109a** with $TiCl_4$, aniline and Et_3N (Scheme 74).

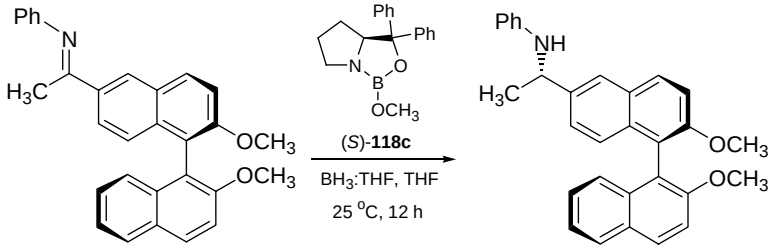
Scheme 74



(*R*)-(+)-**109a** (*R*)-(+)-**153a,** 82% y (-)-**154a,** 60% y

Unfortunately, reduction of the imine **153a** using the $NaBH_4/I_2$ reagent system in THF at 80 °C gave the amine **154a** in 60% yield but only with 50:50 diastereomeric ratio. We have then carried out the asymmetric reduction of ketimine **153a** with the oxazaborolidine catalyst. When 30 mol% of oxazaborolidine catalyst and BH_3:THF was used, the expected amine **154a** was obtained with 60:40 diastereomeric ratio (Scheme 75). When the oxazaborolidine was used in stoichiometric quantities, the diastereomeric ratio improved to 68:32.

Scheme 75



(*R*)-(+)-**153a** (-)-**154a,** 72% Y
68:32 dr

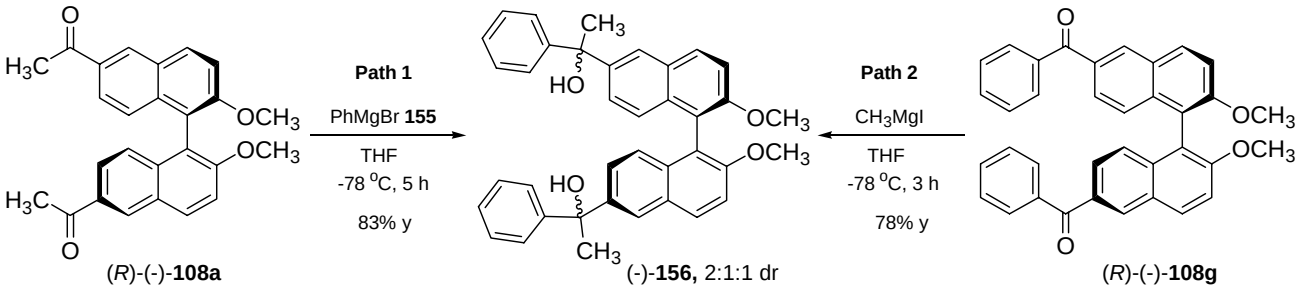
The diastereoselectivity was poor in the case of oxazaborolidine reduction of ketimine **153a** unlike that realized in oxime ether reduction. Presumably, this may be due to faster uncatalyzed reduction of the ketimine **153a** over oxazaborolidine catalyzed reduction[70b] because of low electrophilicity of the imine carbon. Also, if the ketimine **153a** exists as *E* and *Z* mixture undergoing fast inversion, it would lead to lower selectivity.[70c-e]

2.4 Towards the diastereoselective Grignard additions of 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ether derivatives

We have also undertaken efforts to examine the addition of simple Grignard reagents to the chiral diketone 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(-)-**108** (Scheme 76). When we have carried out the reaction of 6,6′-diacetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(-)-**108a** with phenyl magnesium bromide in THF solvent at -78 ^{o}C for 5 h (Path 1), the corresponding nucleophilic addition product (-)-**156** was obtained in 83% yield as a 2:1:1 mixture of diastereomers (HPLC analysis, chiral OD-H column).

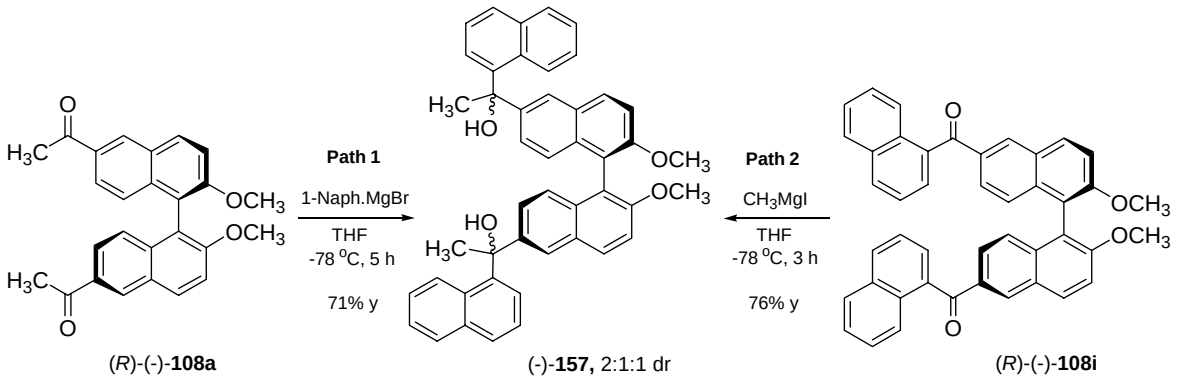
The nucleophilic addition product (-)-**156** was also obtained starting from the 6,6′-dibenzoyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(-)-**108g** *via* Path 2 in 78% yield in 2:1:1 ratio again without any diastereoselectivity (Scheme 76).

Scheme 76



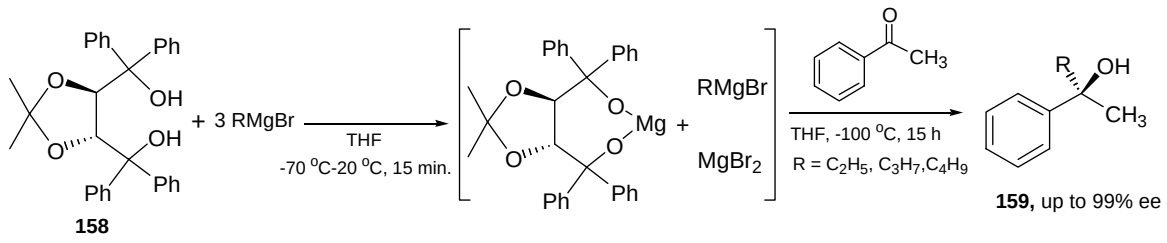
We have also examined the Grignard reaction of 6,6′-diacetyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(-)-**108a** for the preparation of the naphthyl derivative, (*R*)-1,1'-(2,2'-dimethoxy-1,1'-bi-2-naphthyl-6,6'-diyl)bis(1-(naphthalen-1-yl)ethanol) (-)-**157** (Scheme 77). Unfortunately, there was no diastereoselectivity observed in these reactions as well.

Scheme 77



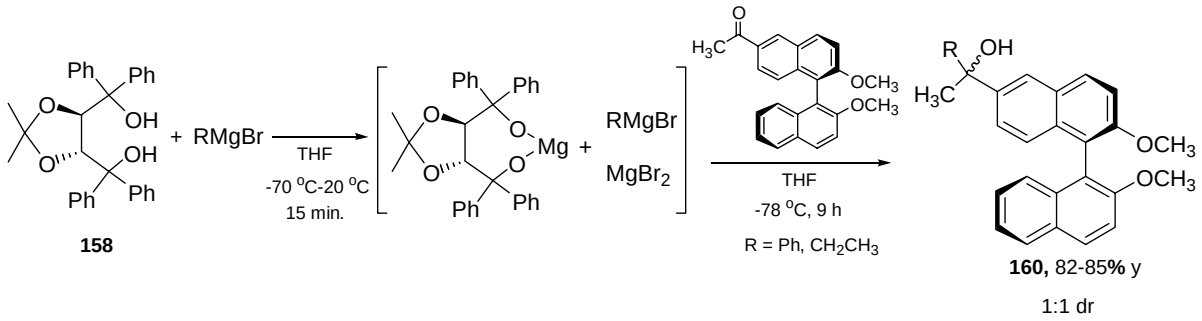
It has been reported that the diaryl substituted carbinol **158** (TADDOL) is useful for enantioselective Grignard reagent addition to ketones (Scheme 78).[71]

Scheme 78



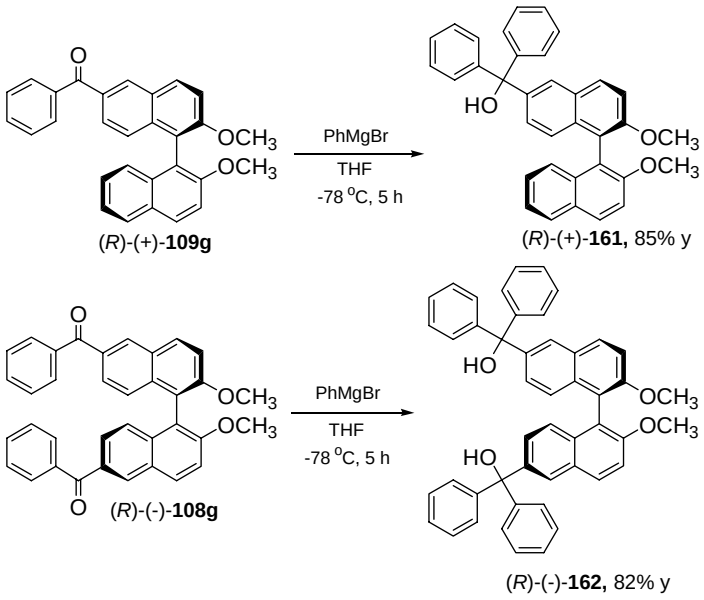
Accordingly, we have examined the TADDOL assisted addition reaction of 6-acetyl-1,1′-bi-2-naphthyl methyl ether derivative, (*R*)-(+)-**109a** (Scheme 79). Unfortunately, only a 1:1 mixture of diastereomers was observed in this reaction as indicated by HPLC (Chiralcel OD-H column) analysis.

Scheme 79



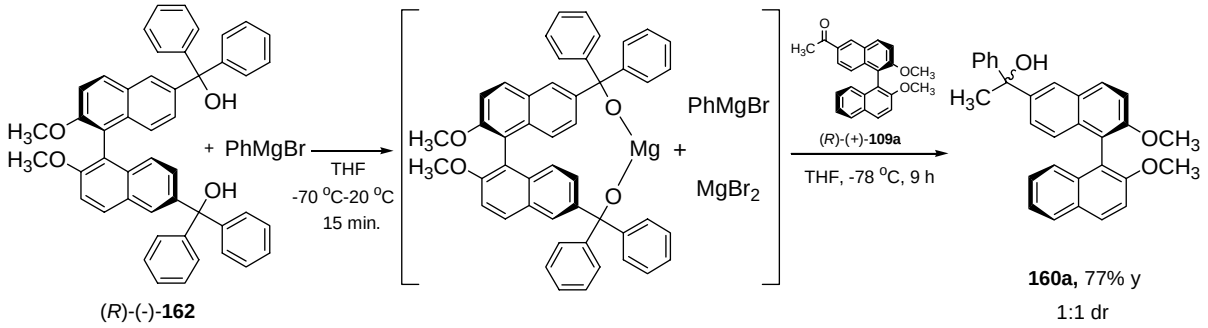
We have also carried out the reaction of phenylmagnesium bromide with 6-benzoyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**109g** and 6,6′-dibenzoyl-1,1′-bi-2-naphthyl methyl ether (*R*)-(-)-**108g** in THF solvent at -78 °C for 5 h. The corresponding triaryl substituted carbinols (*R*)-(-)-**161** and (*R*)-(-)-**162** were obtained in 85% and 82% yields, respectively (Scheme 80).

Scheme 80



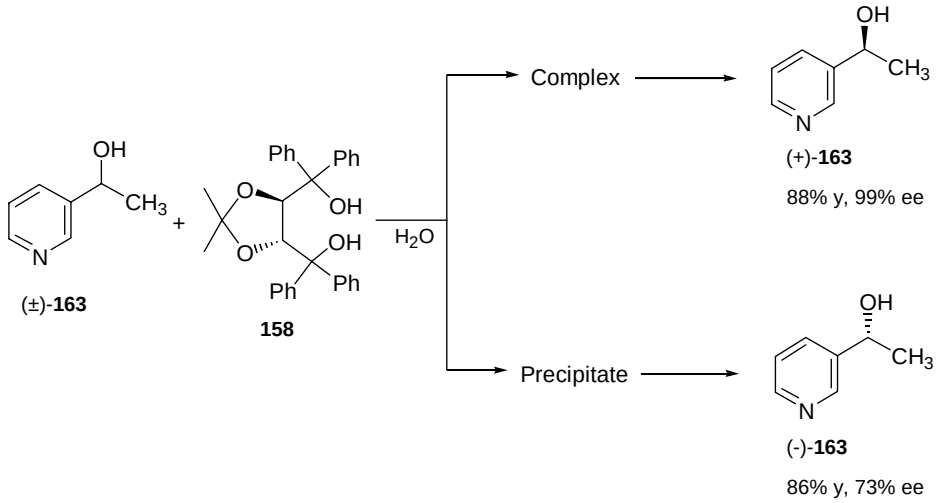
It was also of interest to examine the use of the triaryl substituted carbinol (*R*)-(-)-**162** for the asymmetric Grignard addition to 6-acetyl-1,1′-bi-2-naphthyl methyl ether derivative (*R*)-(+)-**109a.** Again, only 1:1 mixture of diastereomers was obtained (Scheme 81).

Scheme 81



It has been reported that the carbinols like TADDOL are useful in the preparation of chiral inclusion complexes and also in molecular recognition studies. F. Toda *et al.*[72] reported a one pot preparation of optically active compounds by a combination of synthesis and inclusion complexation with a chiral host TADDOL **158** in aqueous medium (Scheme 82).

Scheme 82

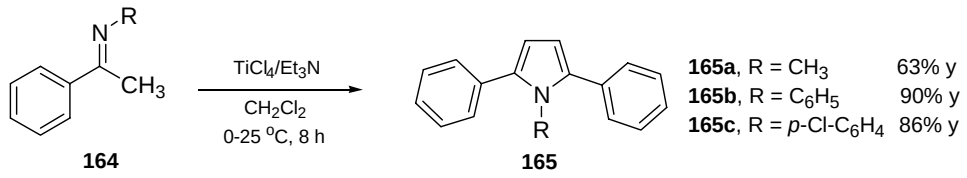


Systematic studies on the use of the triaryl carbinols like **161** and **162** for such applications are expected to give fruitful results.

2.5 Synthesis of polymers containing bi-2-naphthyl moiety

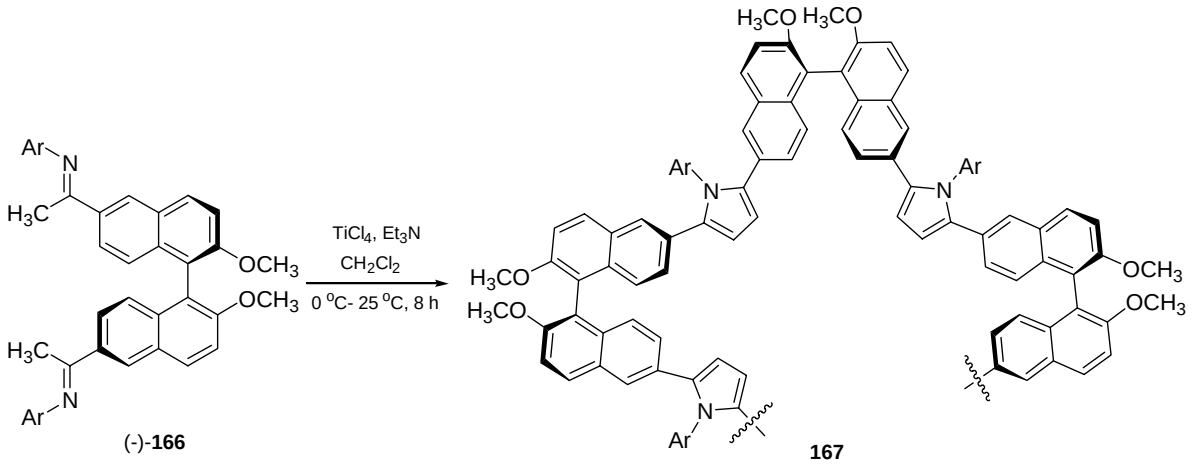
In 1999, a new protocol for the synthesis of 2,5-diarylpyrrole derivatives was reported from this laboratory. For example, the arylmethyl ketimines **164** react with the $TiCl_4/Et_3N$ reagent system to give the corresponding 1,2,5-trisubstituted pyrroles **165** (Scheme 83).[75]

Scheme 83



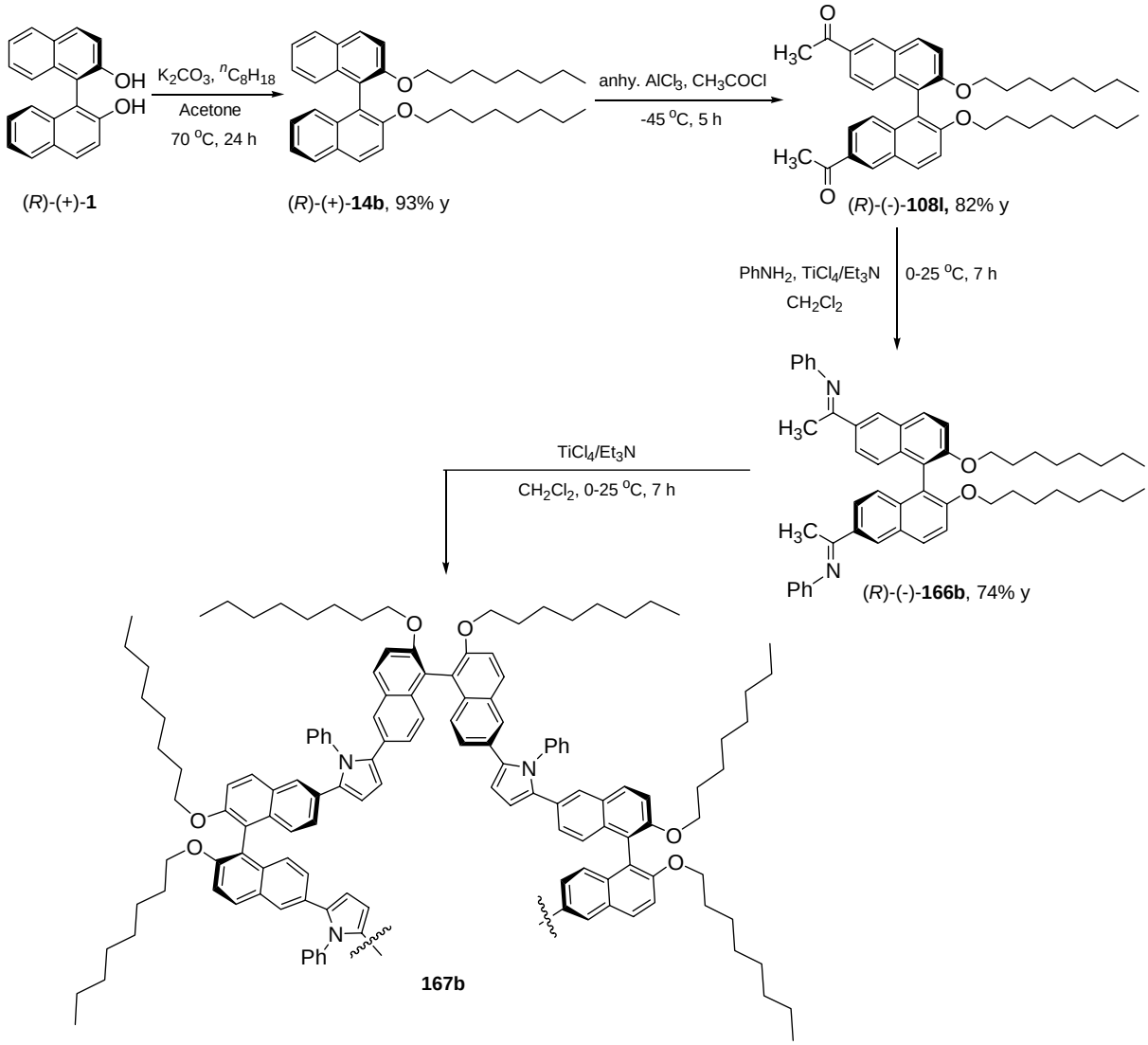
Previously, it was also reported from this laboratory that the reaction of the ketimine **166** with the $TiCl_4/Et_3N$ reagent system gave the poly-1,1′-bi-2-naphthyl derivatives **167** containing pyrrole spacers (Scheme 84).[74] The polymeric bi-2-naphthyls with *N*-aryl pyrrole spacers **167** could not be characterized as they are insoluble. We have undertaken efforts to synthesize chiral bi-2-naphthyl substituted polymers with pyrrole spacers having long chain alkyl groups in order to obtain soluble chiral bi-2-naphthyl polymers with pyrrole spacers.

Scheme 84



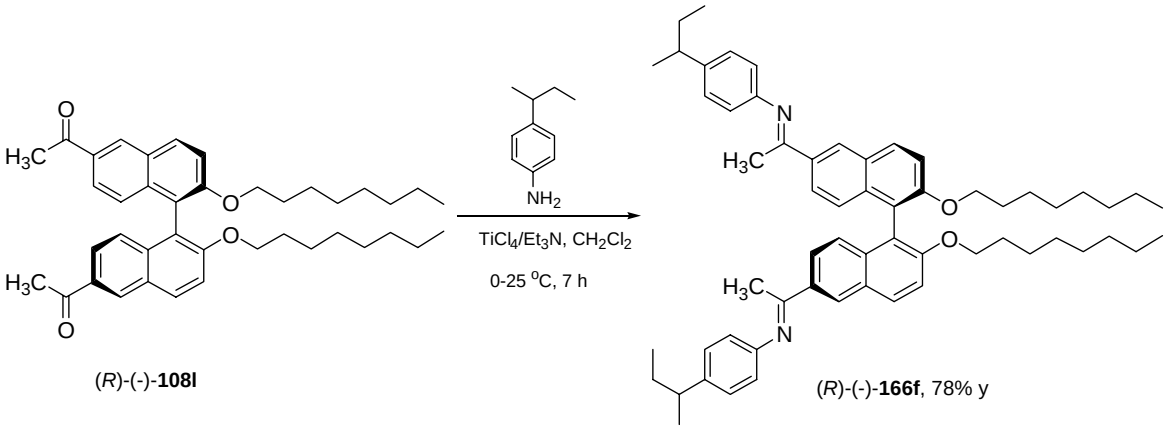
Accordingly, we have synthesized the *n*-octyl-bi-2-naphthyl ether **14b** in 93% yield from bi-2-naphthol, *n*-octyl bromide using K_2CO_3 in acetone solvent at 70 ^oC for 24 h. The corresponding diketone **108l** was obtained in 82% yield under acylation conditions. Subsequent ketimine **166b** formation followed by treatment with the $TiCl_4/Et_3N$ reagent system gave the chiral pyrrole polymer **167b**. Unfortunately, this polymeric product **167b** was also found to be insoluble in all organic solvents (Scheme 85).

Scheme 85

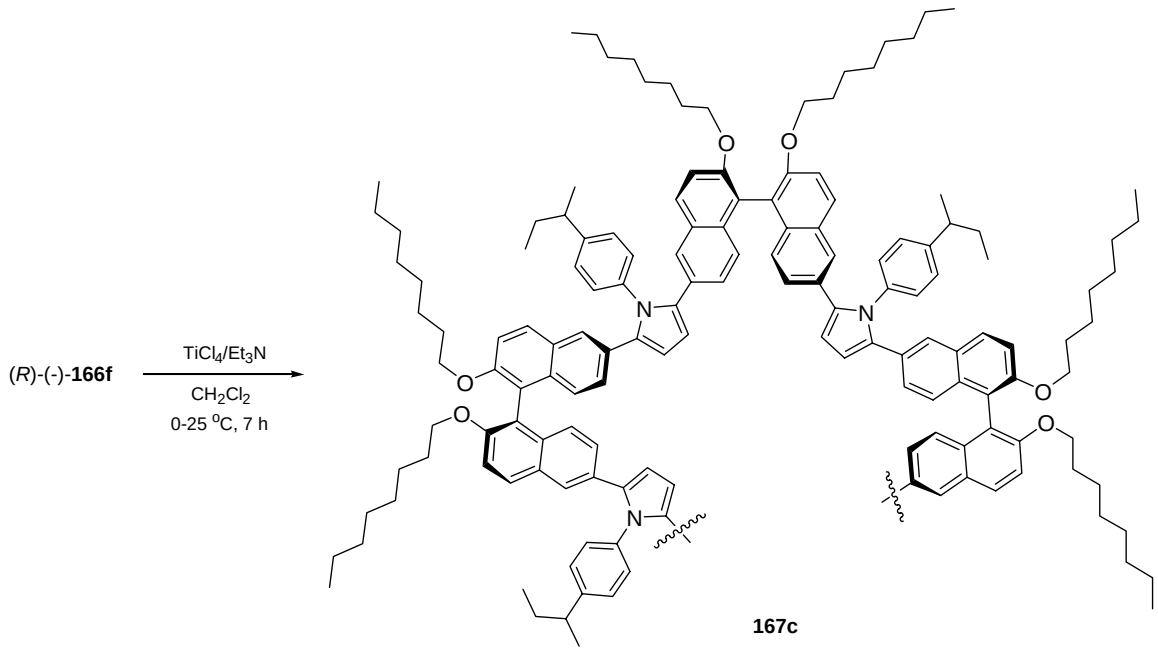


It was thought that introduction of another alkyl group on the phenyl group of the aniline along with *O*-alkyl group would facilitate the solubility of the corresponding polymeric pyrrole product.

Scheme 86



(*R*)-(-)-**108l** (*R*)-(-)-**166f**, 78% y



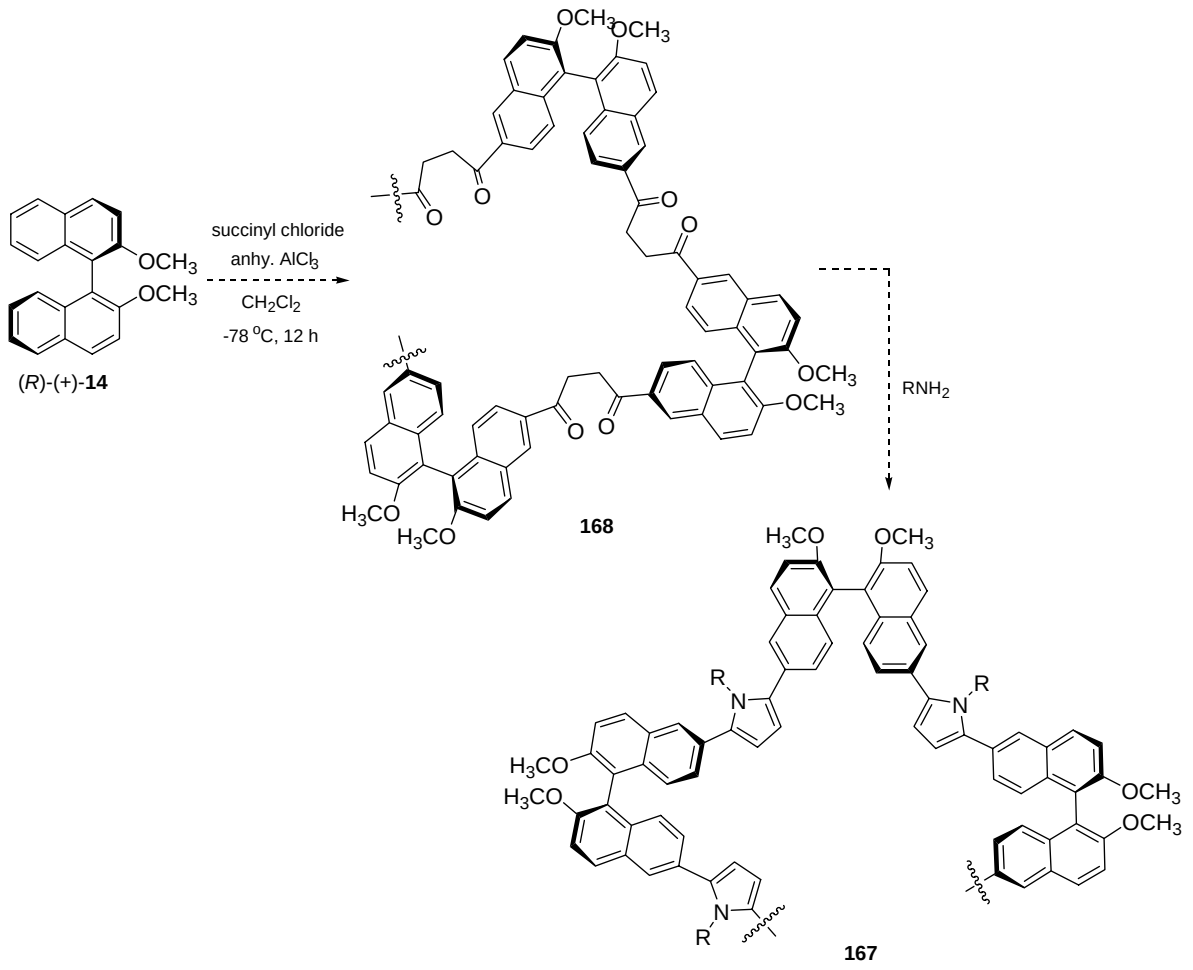
167c

Accordingly, we have examined the reaction of the diketone **108l** with 4-isobutylaniline using the $TiCl_4/Et_3N$ reagent system at 0-25 ^oC for 7 h. The reaction did not

proceed beyond the ketimine stage under these conditions. Only, the diketimine **166f** was isolated in 78% yield. Presumably, the ketimine **166f** formed *in situ* may be in a complexed form. However, further reaction of the ketimine **166f** with the $TiCl_4/Et_3N$ reagent system at 0-25 ^oC for 7 h gave the chiral pyrrole polymer **167c**. Unfortunately, this polymeric product **167c** is also insoluble in all organic solvents (Scheme 86).

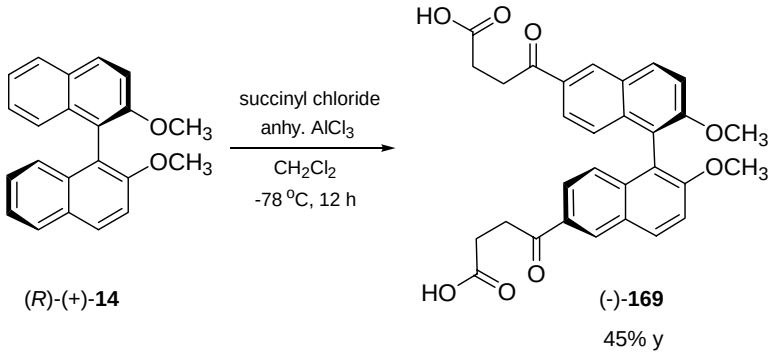
It was then thought that a more conventional protocol involving initial preparation of the polymeric 1,4-diketones **168** would lead to polymeric *N*-alkyl pyrrole upon reaction with RNH_2 (Scheme 87).

Scheme 87



Accordingly, we have carried out the reaction of 1,1′-bi-2-naphthyl methyl ether (*R*)-(+)-**14**, $AlCl_3$ and succinyl chloride to access the corresponding polymeric 1,4-diketone **168**. The reaction was carried out under different conditions but the expected 1,4-diketone polymer **168** was not formed. Instead, the reaction gave only the diketoacid (-)-**169** (Scheme 88).

Scheme 88



(*R*)-(+)-**14** (-)-**169**

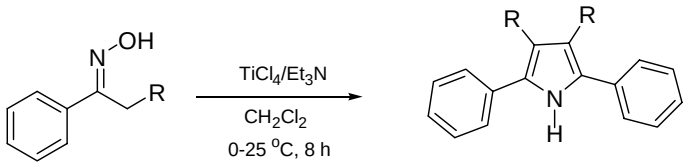
45% y

Though, we did not succeed in the preparation of the polymeric 1,4-diketone **168**, the 6,6′-diketoacid (-)-**169** itself is a valuable synthon. Further studies on the use of this ketoacid for the synthesis of polymeric ketones and heterocycles would lead to more fruitful results.

2.6 Synthesis of 2,5-di(bi-2-naphthyl methyl ether) substituted Chiral Pyrrole derivatives

It was previously observed in this laboratory that the ketoximes **170** give the corresponding 2,3,4,5-tetrasubstituted pyrroles **171** upon reaction with the $TiCl_4/Et_3N$ reagent system at 0-25 °C (Scheme 89).[76]

Scheme 89



170 **171**

171a, R = C_6H_5 81% y

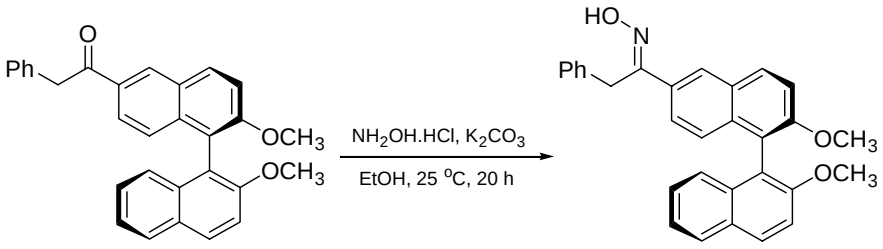
171b, R = CH_3 90% y

171c, R = C_2H_5 86% y

This methodology (Scheme 89) prompted us to examine the synthesis of new C_2-symmetric chiral 2,5-bi-2-naphthyl substituted pyrroles by using 6-aryl-1,1′-bi-2-naphthyl methyl ether derivative (*R*)-(+)-**109l** as starting material.

Accordingly, we have converted the 6-phenylacetyl-1,1′-bi-2-naphthyl methyl ether, (*R*)-(+)-**109l** into its oxime **172a** in 97% yield (Scheme 90).

Scheme 90

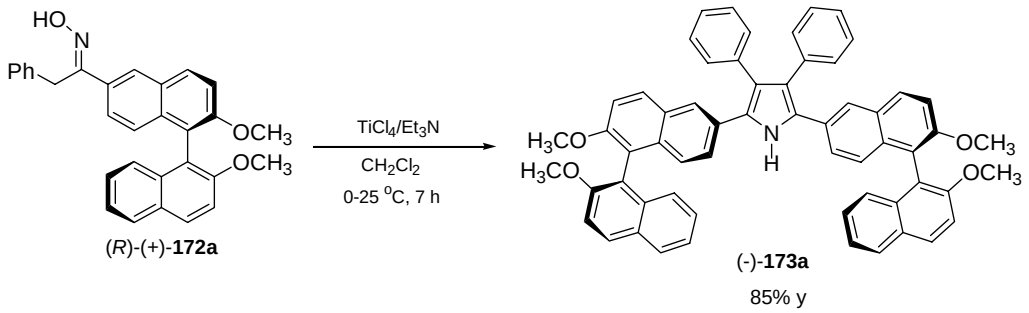


(*R*)-(+)-**109l** (*R*)-(+)-**172a**

97% y

We have then carried out the reaction of this ketoxime (*R*)-(+)-**172a** with the $TiCl_4/Et_3N$ reagent system in CH_2Cl_2 at 0-25 °C (Scheme 91). We have observed that the corresponding chiral 2,3,4,5-tetrasubstituted pyrrole **173a** was obtained in 85% yield under the reaction conditions.

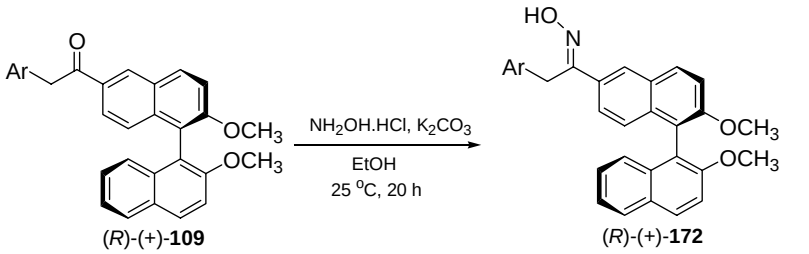
Scheme 91



(*R*)-(+)-**172a** (-)-**173a** 85% y

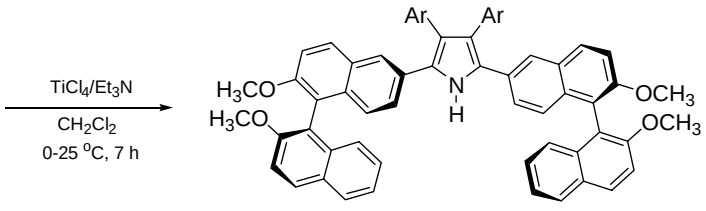
We have then examined the generality of this transformation with some other bi-2-naphthyl ketoxime derivatives **172** using the $TiCl_4/Et_3N$ reagent system. The transformation was found to be smooth and the corresponding chiral pyrroles **173** were obtained in good yields (Scheme 92).

Scheme 92



(*R*)-(+)-**109** (*R*)-(+)-**172**

Ar = C_6H_4	**172a**	97% y
Ar = *p*-BrC_6H_4	**172b**	92% y
Ar = *p*-$OMeC_6H_4$	**172c**	95% y

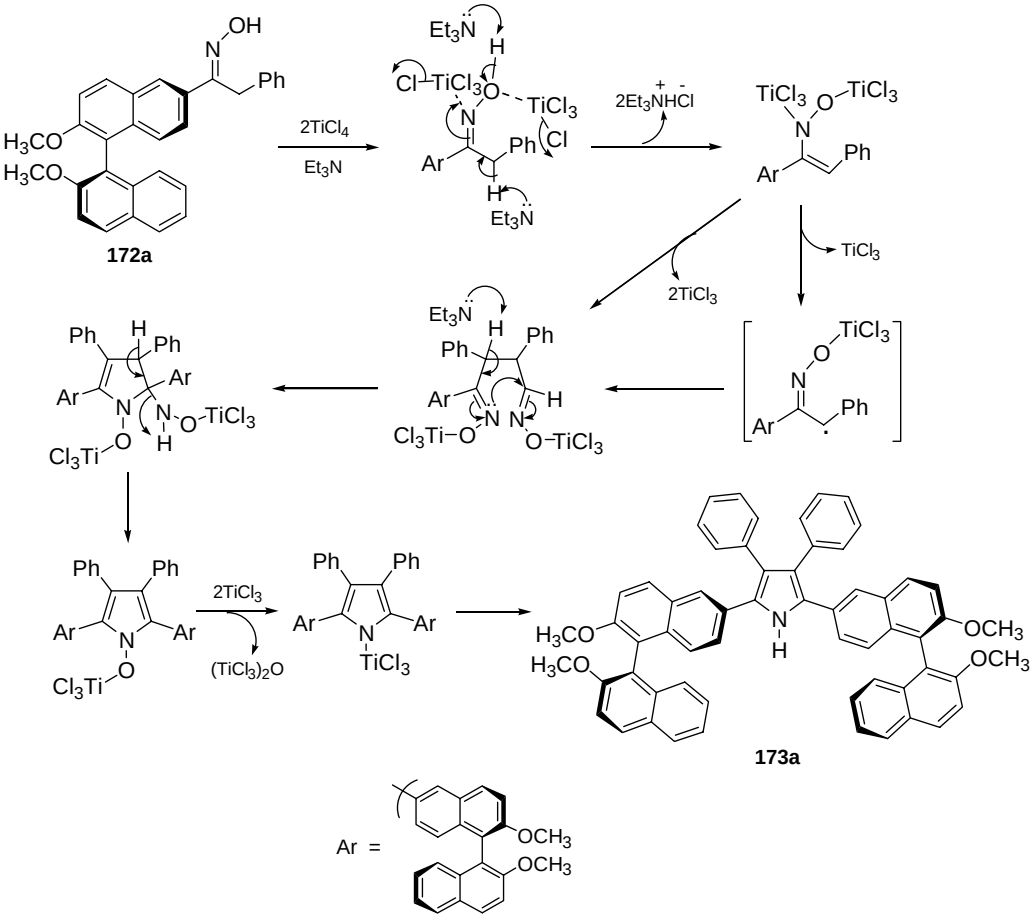


(-)-**173**

Ar = C_6H_4	**173a**	85% y
Ar = *p*-BrC_6H_4	**173b**	78% y
Ar = *p*-$OMeC_6H_4$	**173c**	82% y

The conversion of ketoximes **172** to pyrroles **173** using the $TiCl_4/Et_3N$ reagent system can be explained by considering a mechanism involving oxidative coupling and cyclization (Scheme 93).[76]

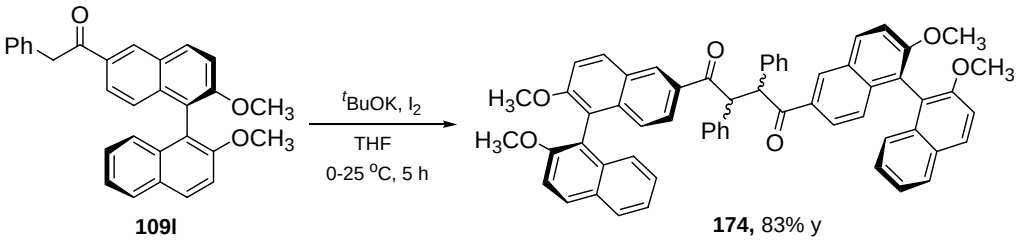
Scheme 93



There are no reports available in the literature for the synthesis of C_2-symmetric chiral bi-2-naphthyl substituted pyrroles. As these novel chiral pyrroles are readily accessed using readily accessible reagents, these derivatives have good potential for further exploitation.

We have also examined the synthesis of C_2-symmetric chiral 2,3,4,5-tetrasubstituted pyrrole **173a** by first making 1,4-diketone **174** followed by cyclization with ammonium acetate. When the 6-phenylacetyl-1,1′-bi-2-naphthyl methyl ether **109k** was reacted with ^{t}BuOK and I_2 at 0 ^{o}C for 5 h, the required 1,4-diketone **174** was obtained in 83% yield (Scheme 94).

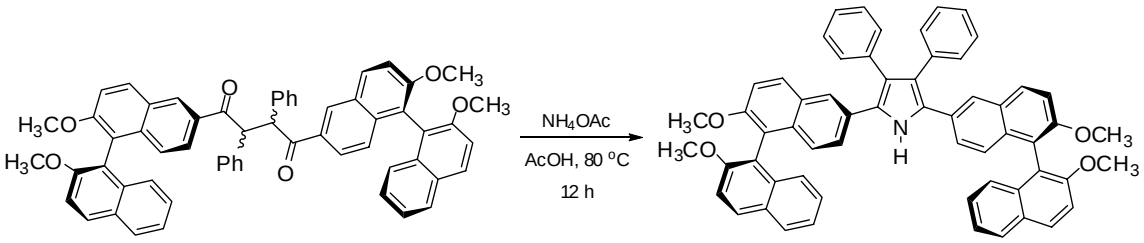
Scheme 94



109l **174,** 83% y

The chiral pyrrole **173a** was obtained in 88% yield by the reaction of 1,4-diketone, 1,4-bis[(*R*)-2,2'-dimethoxy-1,1'-binaphthyl-6-yl]-2,3-diphenylbutane-1,4-dione **174** with ammonium acetate using acetic acid as solvent at 80 ^{o}C (Scheme 95).

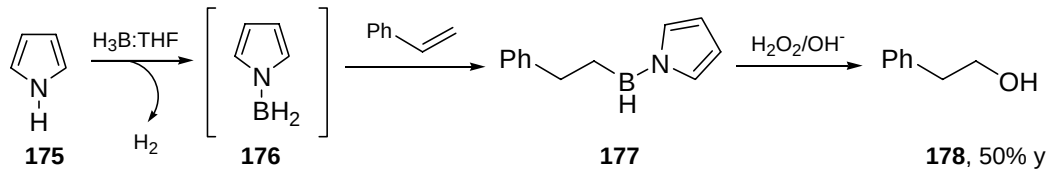
Scheme 95



174 **173a,** 88% y

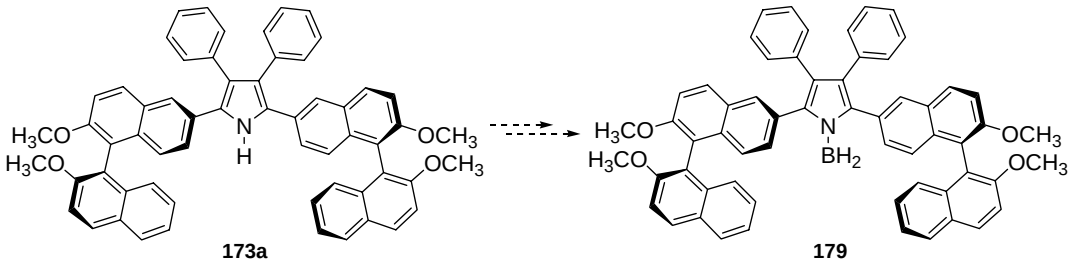
It has been reported that the pyrroloborane derivative **176** is useful for hydroboration of olefins under ambient conditions (Scheme 96).[77]

Scheme 96



However, the unsubstituted pyrroloborane **176** is not stable under ambient conditions, limiting its synthetic potential (Scheme 97).

Scheme 97

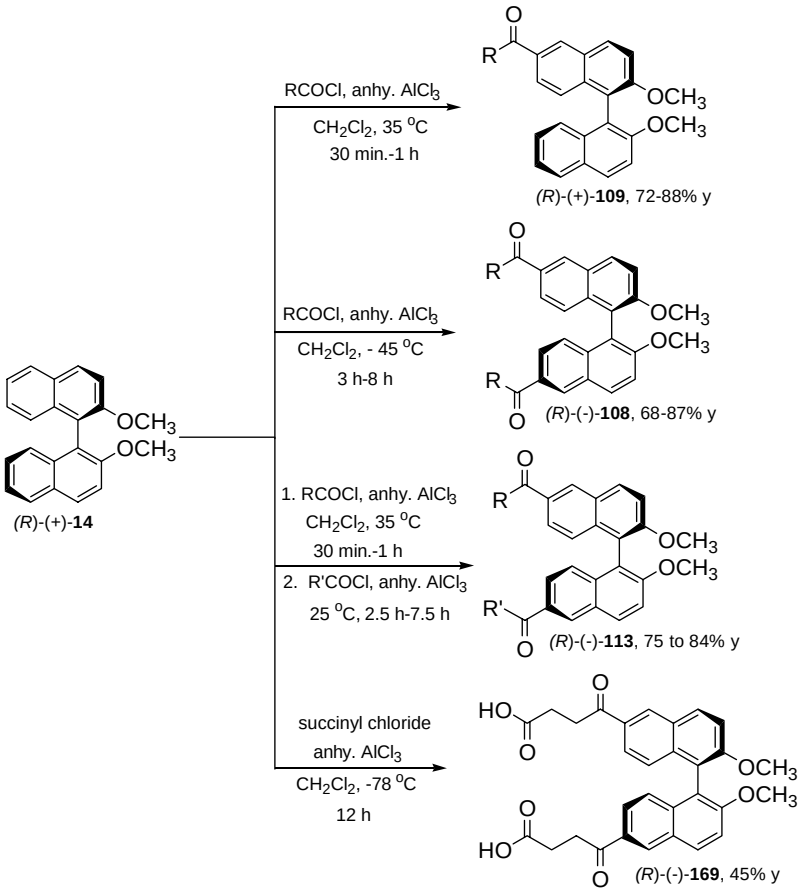


The borane derivative of the 2,5-di-bi-2-naphthyl pyrrole **179** is expected to be more stable and hence has potential for such applications.

Summary and Outlook

Methods have been developed for acylation of (*R*)-(+)-1,1′-bi-2-naphthyl methyl ether. The corresponding monoacyl, symmetrical diacyl and unsymmetrical diacyl derivatives were prepared in good yields (Scheme 98).

Scheme 98

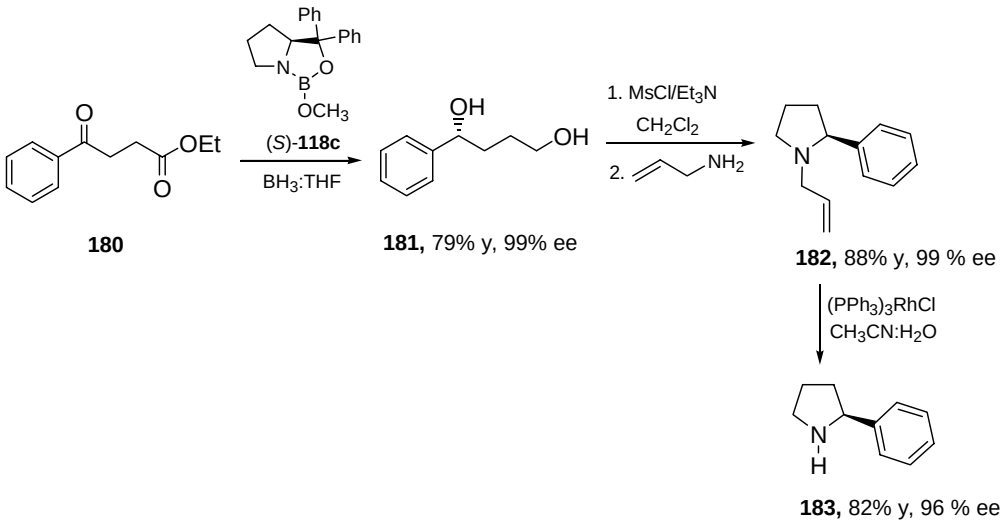


There are no reports available in the literature to access axially chiral unsymmetrical diketones (*R*)-(-)-**113** and therefore this is a good methodology to access such diacyl compounds in a single pot synthetic operation.

Method has been developed for asymmetric reduction of (*R*)-(+)-6-acyl-1,1′-bi-2-naphthyl methyl ethers using 30 mol% oxazaborolidine catalyst to obtain the corresponding alcohol with >99% diastereoselectivity.

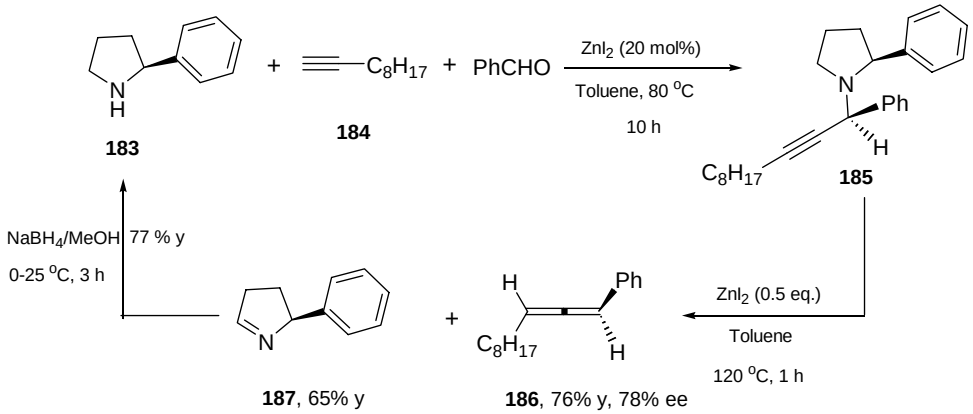
Recently, it was reported from this laboratory that the chiral diols prepared using the ketoester **180** is useful for the synthesis of chiral 2-substituted pyrrolidines (Scheme 99).[78]

Scheme 99



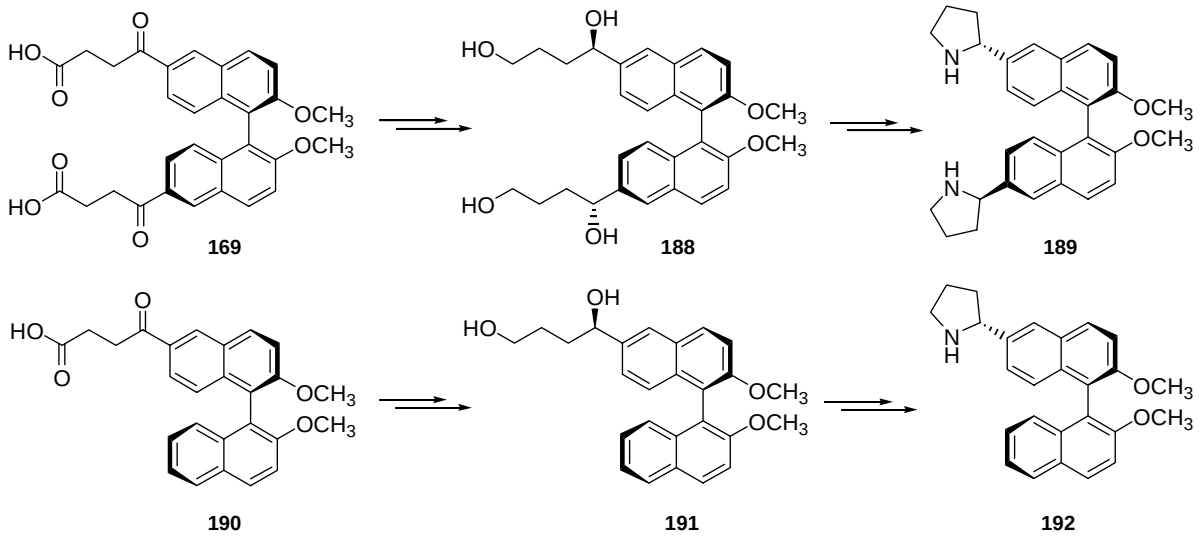
Such pyrrolidine derivatives are useful in some asymmetric transformations (Scheme 100).[78]

Scheme 100



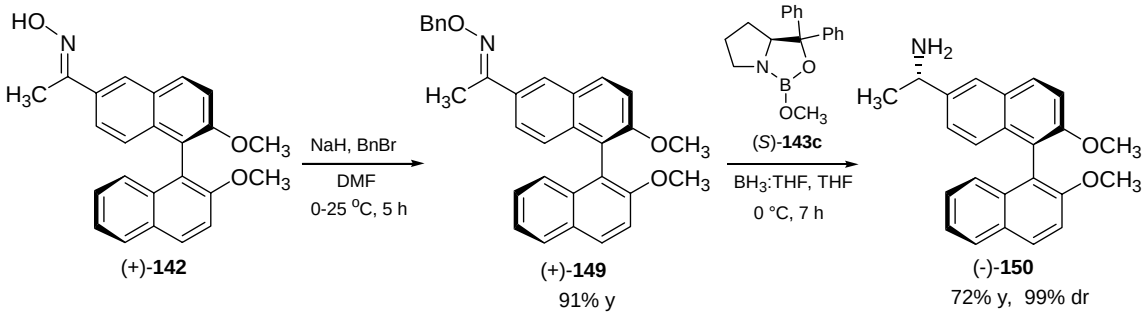
Similar chiral pyrrolidines containing bi-2-naphthyl moiety are expected to be readily accessed using the chiral bi-2-naphthyl derivatives reported here (Scheme 101).

Scheme 101



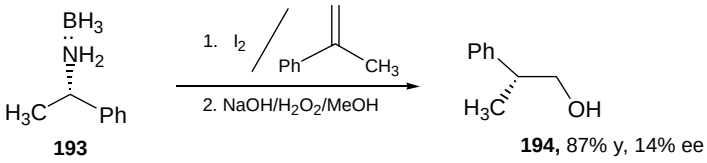
The asymmetric reduction of bi-2-naphthyl based ketoxime ethers **149** using 30 mol% oxazaborolidine catalyst gave the corresponding chiral amine **150** in good yields with upto 99% dr (Scheme 102).

Scheme 102



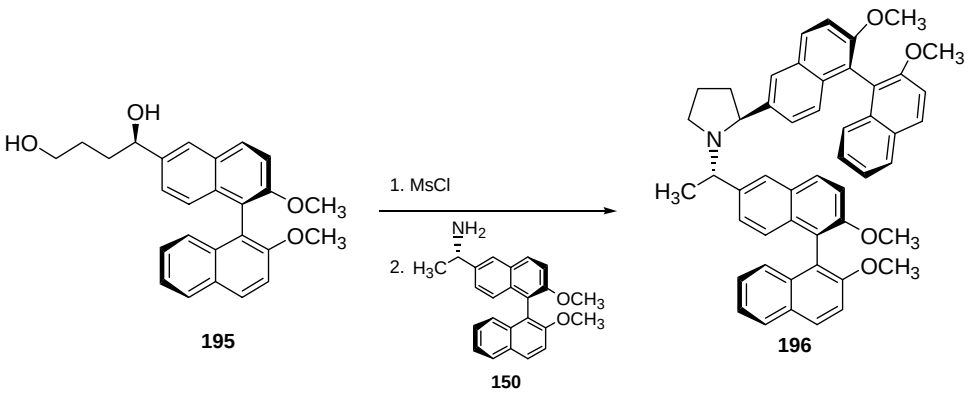
Previously, it was reported from this laboratory that the chiral amine boranes promote asymmetric hydroboration reactions (Scheme 103).[79,80]

Scheme 103



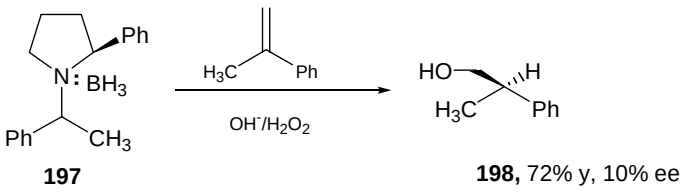
The chiral amine **150** readily accessible from the method described in this thesis (Scheme 102), should find useful in such applications. An obvious extension is synthesis of the corresponding pyrrolidine derivative **196** (Scheme 104).

Scheme 104

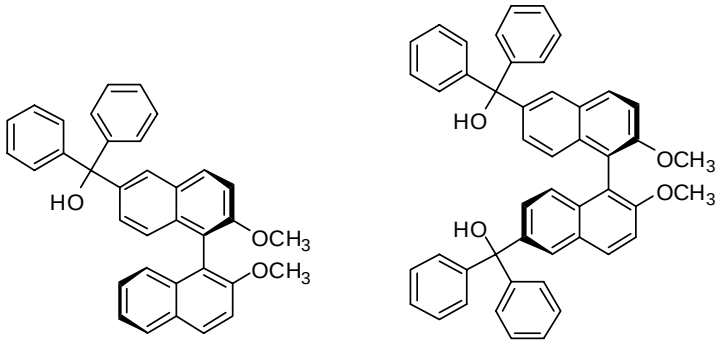


The pyrrolidine derivative **197** is useful for asymmetric hydroboration studies as outlined in Scheme 105.[78] Similar studies using the amine-borane complex prepared using the chiral bi-2-naphthyl containing pyrrolidine **196** are expected to give interesting results.

Scheme 105



Methods have been described in this thesis for the synthesis of chiral triaryl carbinols containing bi-2-naphthyl moiety **161** and **162** (Figure 10).

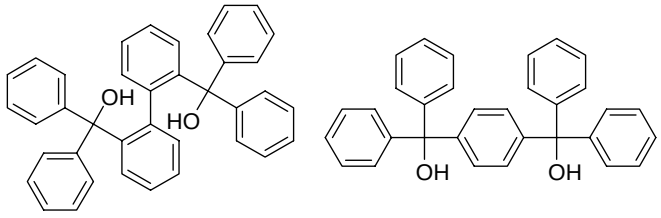


(*R*)-(+)-**161** (*R*)-(-)-**162**

Figure 10

Previously, Toda *et al.*[73] reported that triaryl carbinols **199** and **200** are useful for the preparation of certain inclusion complexes. Such studies using the chiral triaryl carbinols **161** and **162** would lead to fruitful results (Scheme 106).

Scheme 106



199 **200**

Methods have been developed for the synthesis of 2,5-di-(*R*)-(+)-bi-2-naphthyl methyl ether substituted chiral pyrroles. As outlined under Section 2.6, such chiral pyrrole derivatives should be useful in the preparation of stable pyrroloborane complexes which have potential for use in asymmetric hydroboration of olefins.

Chapter 3

Experimental Section

3. Experimental Section

General Information

Melting points reported in this thesis are uncorrected and were determined using a superfit capillary point apparatus. IR (KBr) spectra were recorded on JASCO FT-IR spectrophotometer model 5300. The neat IR spectra were recorded on JASCO FT-IR spectrophotometer model 5300 and SHIMADZU FT-IR spectrophotometer model 8300 with polystyrene as reference. ^{1}H-NMR (400 MHz) and ^{13}C-NMR (100 MHz) spectra were recorded on Bruker-Avance-400 spectrometer with chloroform-d as solvent and TMS as reference (δ = 0 ppm). The chemical shifts are expressed in δ downfield from the signal of internal TMS. Elemental analyses were carried out using a Perkin-Elmer elemental analyzer model-240C and Thermo Finnigan analyzer series Flash EA 1112. Mass spectral analyses were carried out on VG 7070H mass spectrometer using EI technique at 70 eV.

Analytical thin layer chromatographic tests were carried out on glass plates (3 x 10 cm) coated with 250 mμ acme's silica gel-G and GF_{254} containing 13% calcium sulfate as binder. The spots were visualized by short exposure to iodine vapour or UV light. Column chromatography was carried out using acme's silica gel (100-200 mesh).

All the glassware were pre-dried at 140 ºC in an air-oven for 4 h, assembled in hot condition and cooled under a stream of dry nitrogen. Unless, otherwise mentioned, all the operations and transformations of reagents were carried out using standard syringe, septum technique recommended for handling air sensitive organometallic compounds. Reagents

prepared *in situ* in solvents were transferred using a double-ended stainless steel (Aldrich) needle under a pressure of nitrogen whenever required.

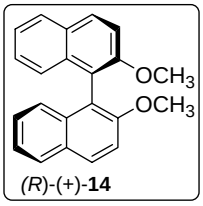
In all experiments, a round bottom flask of appropriate size with a side arm, a side septum, a magnetic stirring bar, a condenser and a connecting tube attached to a mercury bubbler were used. The outlet of the mercury bubbler was connected by a long tube to the atmosphere. All dry solvents and reagents (liquids) used were distilled from appropriate drying agents. As a routine practice, all organic extracts were washed with saturated sodium chloride solution (brine) and dried over anhydrous $MgSO_4$ or Na_2SO_4 and concentrated on Büchi-EL-rotary evaporator. All yields reported are of isolated materials adjudged homogeneous by TLC, IR and NMR spectroscopy. Dichloromethane, 1,2-dichloroethane and chloroform were distilled over CaH_2 and stored over KOH pellets. Titanium tetrachloride, supplied by Spectrochem Ltd., India was used. It was used as 1:1 $TiCl_4$:CH_2Cl_2 stock solution.

Dichloromethane was distilled over CaH_2 and dried over molecular sieves. Methanol and ethanol supplied by Ranbaxy were distilled over CaO before use. Toluene and THF supplied by E-Merck, India were kept over sodium-benzophenone ketyl and freshly distilled before use. Titanium tetrachloride and Aniline were supplied by E-Merck, India. Triethylamine was distilled over CaH_2 and stored over KOH pellets. Thionyl chloride, acetyl chloride, propionyl chloride, butyryl chloride, benzoyl chloride, phenylacetyl chloride were supplied by E-Merck (India) and were distilled before use. $NaBH_4$ and carbon disulfide were supplied by E-Merck (India). Racemic-bi-2-naphthol, (*R*)-(+)-bi-2-naphthol, (*S*)-(-)-bi-2-naphthol and (*S*)-DPP were supplied by Gerchem Labs (India).

3.1 Procedure for the preparation of 1,1'-bi-2-naphthyl methyl ether

A suspension of (*R*)-(+)-bi-2-naphthol (5.0 g, 17.4 mmol) **1** was heated at 40°C in acetone (150 mL) to give a homogeneous solution. To this solution stirred under N_2 was added K_2CO_3 (8.0 g, 58 mmol) and CH_3I (5.3 mL, 84 mmol) and the mixture was refluxed for 24 h. An additional portion of CH_3I (1.7 mL, 28 mmol) was added and the mixture was further refluxed for an additional 12 h. The solvent was removed and 150 mL of water was added. The mixture was allowed to stir for 8 h, filtered and the solid was dissolved in CH_2Cl_2 (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2 X 25 mL). The combined CH_2Cl_2 solution was successively washed with water, brine and dried over anhydrous Na_2SO_4. The solvent was evaporated and the desired product (*R*)-(+)-**14** was obtained as a white powder.

(*R*)-(+)-**14:**



(*R*)-(+)-**14**

Yield 5.3 g (97%)

Mp 204-206 °C

IR (KBr) (cm^{-1}) 2955, 2837, 1618, 1249, 1147, 1089

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.97 (d, *J* = 9.2 Hz, 2H), 7.85 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 9.2 Hz, 2H), 7.33-7.19 (m, 4H), 7.10 (d, *J* = 8.2 Hz, 2H), 3.76 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.0, 134.0, 131.1, 129.8, 129.4, 128.2, 119.6, 114.2, 56.9.

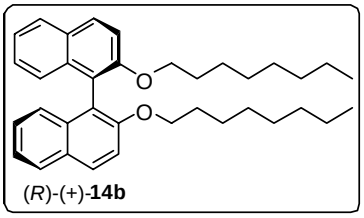
LCMS *m/z* 315 (M+1)

$[\alpha]_D^{25}$ +57.54 (*c* 1, $CHCl_3$).

Procedure for the preparation of 1,1'-bi-2-naphthyl methyl ether

A suspension of (*R*)-(+)-bi-2-naphthol (5.0 g, 17.4 mmol) in acetonitrile (50 mL) solution stirred under N_2 was added K_2CO_3 (6.0 g, 43.5 mmol) and $C_8H_{15}Br$ (6.5 mL, 52.2 mmol) and the mixture was refluxed at 85°C for 24 h. The solvent was removed under vacuum, and the mixture was diluted with CH_2Cl_2 (30 mL). The organic layer was further washed with water, brine and dried over anhydrous Na_2SO_4. After removal of the solvent, the residue was purified by column chromatography on silica gel eluted with 97:3 hexane/EtOAc mixture. The product (*R*)-(+)-**14b** was obtained as a viscous liquid.

(*R*)-(+)-**14b**



(*R*)-(+)-**14b**

Yield 8.25 g (93%)

IR (Neat) (cm^{-1}) 2930, 2868, 1622, 1593, 1145, 1086

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.96 (d, *J* = 8.8 Hz, 2H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.44 (d, *J* = 8.9 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.22-7.19 (m, 4H), 3.98-3.94 (m, 4H), 1.41-1.39 (m, 8H), 1.07-0.95 (m, 16H), 0.78 (t, *J* = 7.2 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 156.7, 136.5, 132.3, 131.3, 130.6, 127.9, 125.5, 124.3, 119.6, 115.6, 69.2, 29.7, 29.2, 28.9, 27.8, 26.4, 22.1, 13.0.

LCMS *m/z* 469 (M+1)

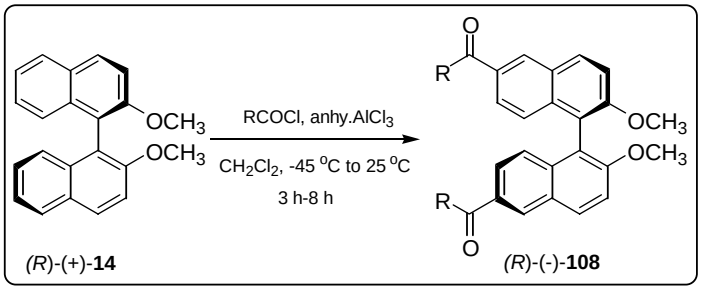
$[\alpha]_D^{25}$ +53.7 (*c* 0.6, $CHCl_3$)

Analytical data calculated for $C_{36}H_{46}O_2$: C, 84.66; H, 9.08; O, 6.27.

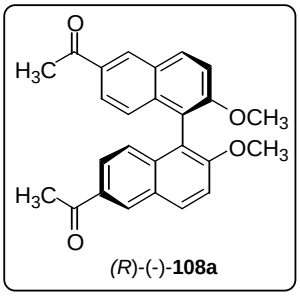
Found: C, 84.64; H, 9.12; O, 6.25.

3.1.1 General procedure for the diacylation of 1,1′-bi-2-naphthyl methyl ethers using acid chlorides and $AlCl_3$

Anhydrous $AlCl_3$ (2.66 g, 20 mmol) and acid chloride (20 mmol) were added to CH_2Cl_2 (30 mL) at 0°C. To this mixture, 2,2′-bis(methoxy) bi-2-naphthyl (1.57 g, 5 mmol) **14** was added, and the mixture was stirred at -45 °C for 3 h. The reaction mixture was poured into ice cold water, and was shaken with CH_2Cl_2 (25 mL). The aqueous layer was extracted in CH_2Cl_2 (2 X 25 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using 80:20 hexane/EtOAc mixture to obtain the 6,6′-bis(acyl)-2,2′-bis(methoxy) bi-2-naphthyl **108**.



(*R*)-(-)-**108a:**



Yield 1.73 g (87%)

Mp 184-186 °C

IR (KBr) (cm^{-1}) 2935, 2837, 1666, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): (s, 2H), 8.13 (d, *J* = 9.2 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.12 (d, *J* = 9.2 Hz, 2H), 3.80 (s, 6H), 2.68 (s, 6H). (Spectrum No. 1)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 197.9, 157.1, 136.3, 132.5, 131.7, 130.7, 128.0, 125.3, 124.6, 118.8, 114.4, 56.5, 26.6. (Spectrum No. 2)

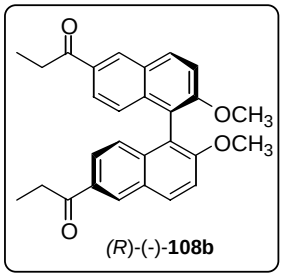
LCMS *m/z* 399 (M+1)

$[\alpha]_D^{25}$ -100.3 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{26}H_{22}O_4$: C, 78.37; H, 5.57; O, 16.06.

Found: C, 78.25; H, 5.53; O, 16.21.

(*R*)-(-)-**108b:**



(R)-(-)-**108b**

Yield 0.67 g (78%)

Mp 156-158 °C

IR (KBr) (cm^{-1}) 2966, 2839, 1678, 1616, 1172, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.55 (s, 2H), 8.15 (d, *J* = 8.8 Hz, 2H), 7.81 (d, *J* = 8.8 Hz, 2H), 7.55 (d, *J* = 8.8 Hz, 2H), 7.14 (d, *J* = 8.8 Hz, 2H), 3.83 (s, 6H), 3.12 (q, *J* = 7.2 Hz, 4H), 1.28 (t, *J* = 7.2 Hz, 6H). (Spectrum No. 3)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 200.6, 157.1, 136.3, 132.3, 131.7, 130.1, 128.1, 125.4, 124.7, 118.9, 114.5, 56.7, 31.8, 8.6. (Spectrum No. 4)

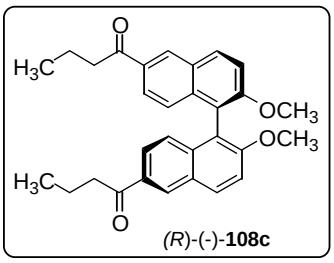
LCMS *m/z* 427 (M+1)

$[\alpha]_D^{25}$ -86.4 (*c* 0.5, $CHCl_3$)

Analytical data calculated for $C_{28}H_{26}O$: C, 78.85; H, 6.14; O, 15.01.

Found: C, 78.73; H, 6.15; O, 15.12.

(*R*)-(-)-**108c:**



(R)-(-)-**108c**

Yield 0.67 g (78%)

Mp 156-158 °C

IR (KBr) (cm^{-1}) 2966, 2839, 1678, 1616, 1172, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.52 (s, 2H), 8.01 (d, *J* = 9.2 Hz, 2H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 9.2 Hz, 2H), 3.81 (s, 6H), 3.05 (t, *J* = 6.8 Hz, 4H), 1.82 (m, *J* = 6.8 Hz, 4H), 1.04 (t, *J* = 6.4 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 200.6, 157.0, 136.2, 132.3, 131.6, 130.0, 128.6, 125.4, 124.6, 118.9, 114.4, 56.8, 31.4, 18.1, 14.1.

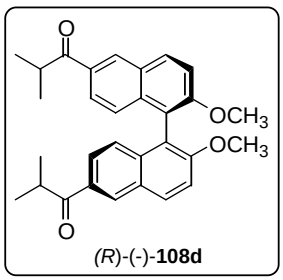
LCMS *m/z* 455 (M+1)

$[\alpha]_D^{25}$ -86.4 (*c* 0.5, $CHCl_3$)

Anal. Calcd for $C_{28}H_{26}O_4$: C, 78.85; H, 6.14; O, 15.01.

Found: C, 78.73; H, 6.15; O, 15.12.

(*R*)-(-)-**108d:**



(R)-(-)-**108d**

Yield 0.68 g (75%)

Mp 126-128 °C

IR (KBr) (cm^{-1}) 2968, 2841, 1674, 1616, 1271, 1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.55 (s, 2H), 8.16 (d, *J* = 9.0 Hz, 2H), 7.80 (d, *J* = 8.9 Hz, 2H), 7.55 (d, *J* = 9.0 Hz, 2H), 7.15 (d, *J* = 8.9 Hz, 2H), 3.83 (s, 6H), 3.75-3.68 (m, 2H), 1.28 (d, 12H). (Spectrum No. 5)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 204.2, 157.1, 136.2, 131.7, 131.6, 130.3, 128.2, 125.5, 118.9, 114.4, 56.7, 35.3, 19.4. (Spectrum No. 6)

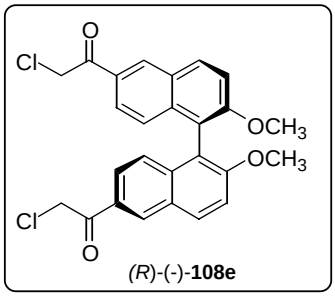
LCMS *m/z* 455 (M+1)

$[\alpha]_D^{25}$ -90.6 (*c* 0.5, $CHCl_3$).

Analytical data calculated for $C_{30}H_{30}O_4$: C, 79.27; H, 6.65; O, 14.08.

Found: C, 79.34; H, 6.77; O, 13.89.

(*R*)-(-)-**108e:**



(R)-(-)-**108e**

Yield 0.67 g (72%)

Mp 178-180 °C

IR (KBr) (cm^{-1}) 2935, 2841, 1695, 1682, 1616, 1350

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.50 (s, 2H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.56 (dd, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H), 4.79 (s, 4H), 3.79 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 193.6, 155.5, 134.6, 129.6, 128.1, 127.9, 126.8, 125.7, 124.8, 123.6, 114.3, 56.7, 50.6.

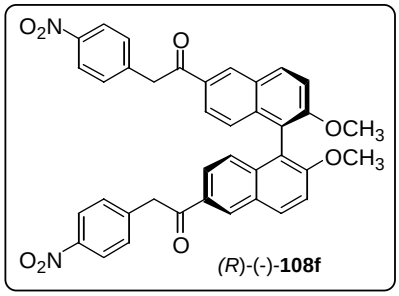
LCMS *m/z* 468 (M+1)

$[\alpha]_D^{25}$ -42.0 (*c* 0.2, $CHCl_3$)

Analytical data calculated for $C_{26}H_{20}Cl_2O_4$: C, 66.82; H, 4.31; Cl, 15.17; O, 13.69.

Found: C, 66.79; H, 4.33; Cl, 15.09; O, 13.78.

(*R*)-(-)-**108f:**



(R)-(-)-**108f**

Yield 0.87 g (68%)

Mp 156-158 °C

IR (KBr) (cm^{-1}) 2939, 2839, 1674, 1606, 1514, 1344

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.62 (s, 2H), 8.2-7.06 (m, 16H), 4.51 (s, 4H), 3.82 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 195.6, 157.5, 154.9, 147.0, 142.4, 136.7, 133.7, 131.4, 129.2, 128.1, 126.5, 124.8, 123.7, 119.7, 118.4, 114.7, 56.9, 51.7.

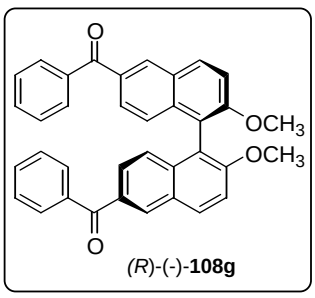
LCMS *m/z* 641 (M+1)

$[\alpha]_D^{25}$ -54.2 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{38}H_{28}N_2O_8$: C, 71.24; H, 4.41; N, 4.37; O, 19.98.

Found: C, 71.20; H, 4.45; N, 4.39; O, 19.96.

(*R*)-(-)-**108g:**



(R)-(-)-**108g**

Yield 0.78 g (75%)

Mp 152-154 °C

IR (KBr) (cm^{-1}) 2935, 2835, 1718, 1653, 1616, 1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.33 (s, 2H), 8.10 (d, *J* = 8.9 Hz, 2H), 7.86 (d, *J* = 8.2 Hz, 4H), 7.73 (d, *J* = 8.7 Hz, 2H), 7.60 (t, *J* = 7.7 Hz, 2H), 7.55-7.49 (m, 6H), 7.19 (d, *J* = 8.9 Hz, 2H), 3.83 (s, 6H). (Spectrum No. 7)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 196.3, 156.9, 142.9, 135.9, 135.4, 133.0, 132.3, 131.5, 130.3, 129.0, 127.8, 126.5, 125.3, 118.9, 114.4, 56.6. (Spectrum No. 8)

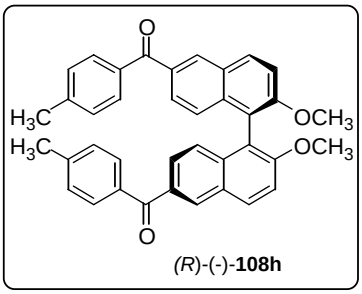
LCMS *m/z* 523 (M+1)

$[\alpha]_D^{25}$ -52.3 (*c* 0.6, $CHCl_3$)

Analytical data calculated for $C_{36}H_{26}O_4$: C, 82.74; H, 5.01; O, 12.25.

Found: C, 82.59; H, 5.04; O, 12.36.

(*R*)-(-)-**108h:**



(R)-(-)-**108h**

Yield 0.79 g (72%)

Mp 128-130 °C

IR (KBr) (cm^{-1}) 2935, 2843, 1763, 1651, 1616, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.96 (d, 4H), 7.47-7.43 (m, 4H), 7.33-7.17 (m, 6H), 7.03 (d, 2H), 7.01 (d, 2 H), 3.77 (s, 6H), 2.03 (s, 6H). (Spectrum No. 9)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 196.3, 156.9, 142.9, 135.9, 135.4, 133.0, 132.3, 131.5, 130.3, 129.0, 127.8, 126.5, 125.3, 118.9, 114.4, 56.6, 21.7. (Spectrum No. 10)

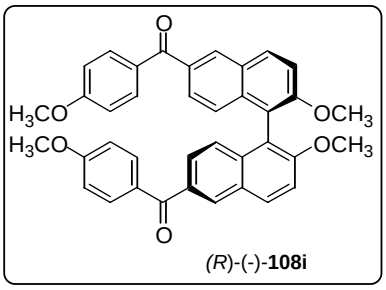
LCMS *m/z* 551 (M+1)

$[\alpha]_D^{25}$ -67.2 (*c* 0.6, $CHCl_3$)

Analytical data calculated for $C_{38}H_{30}O_4$: C, 82.89; H, 5.49; O, 11.62.

Found: C, 82.65; H, 5.42; O, 11.92.

(*R*)-(-)-**108i:**



(R)-(-)-**108i**

Yield 0.81 g (70%)

Mp 132-134 °C

IR (KBr) (cm^{-1}) 2964, 2847, 1762, 1645, 1597, 1021

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.32 (s, 2H), 8.11 (d, *J* = 9.0 Hz, 2H), 7.91 (d, *J* = 8.6 Hz, 4H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.56 (d, *J* = 9.0 Hz, 2H), 7.21 (d, *J* = 8.8 Hz, 2H), 7.01 (d, *J* = 8.6 Hz, 4H), 3.92 (s, 6H), 3.85 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 195.4, 163.1, 156.8, 135.8, 133.3, 131.8, 131.3, 130.7, 127.9, 126.5, 125.2, 119.0, 114.5, 113.6, 56.7, 55.5.

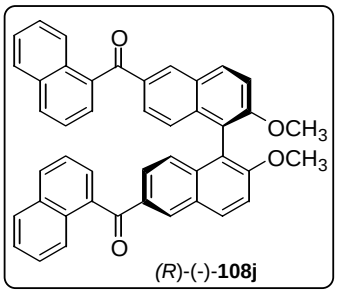
LCMS *m/z* 583 (M+1)

$[\alpha]_D^{25}$ -65.2 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{38}H_{30}O_6$: C, 78.33; H, 5.19; O, 16.48.

Found: C, 78.39; H, 5.12; O, 16.49.

(*R*)-(-)-**108j:**



(R)-(-)-**108j**

Yield 0.88 g (71%)

Mp 138-140 °C

IR (KBr) (cm^{-1}) 2937, 2843, 1768, 1685, 1602, 1265

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.29 (s, 2H), 8.28-7.26 (m, 22 H), 3.74 (s, 6H)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 173.0, 156.2, 143.9, 134.6, 134.0, 133.7, 132.9, 131.8, 130.9, 130.4, 129.6, 129.1, 128.6, 128.3, 127.9, 127.6, 127.2, 126.6, 118.7, 118.6, 114.6, 56.7.

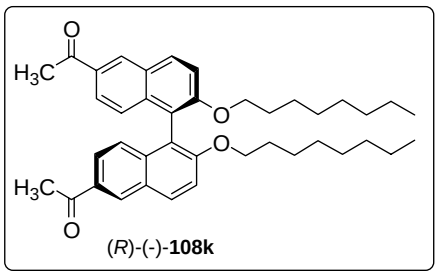
LCMS *m/z* 623 (M+1)

$[\alpha]_D^{25}$ -52.4 (*c* 0.6, $CHCl_3$)

Analytical data calculated for $C_{44}H_{30}O_4$: C, 84.87; H, 4.86; O, 10.28.

Found: C, 84.65; H, 4.89; O, 10.46.

(*R*)-(-)-**108k:**



(*R*)-(-)-**108k**

Yield 0.97 g (82%)

IR (Neat) (cm^{-1}) 3063, 2953, 1682, 1618, 1273, 1051

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.50 (s, 2H), 8.07 (d, *J* = 8.8 Hz, 2H), 7.76 (d, *J* = 8.8 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.16 (d, *J* = 8.8 Hz, 2H), 4.01-3.92 (m, 4H), 2.66 (s, 6H), 1.43-1.40 (m, 8H), 1.04 -0.88 (m, 16H), 0.63 (t, *J* = 6.8 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 197.9, 156.7, 136.5, 132.3, 131.3, 130.6, 127.9, 125.5, 124.3, 119.6, 115.6, 69.2, 29.7, 28.9, 27.8, 26.6, 22.1, 17.3, 13.6, 8.4.

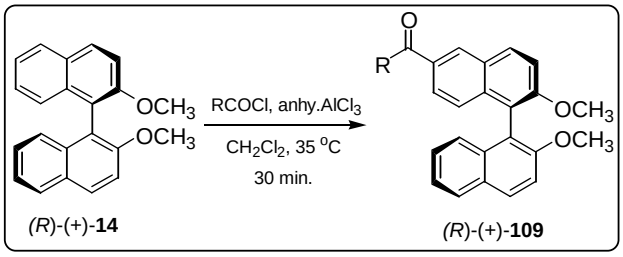
LCMS *m/z* 511 (M+1)

Analytical data calculated for $C_{40}H_{50}O_4$: C, 80.77; H, 8.47; O, 10.76

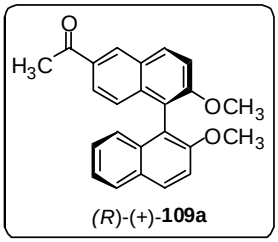
Found: C, 80.68; H, 8.52; O, 10.80.

3.1.2 General procedure for the monoacylation of 1,1′-bi-2-naphthyl methyl ethers using acid chlorides and $AlCl_3$

To the solution of 2,2′-bis(methoxy)-bi-2-naphthyl (1.57 g, 5 mmol) **14** in CH_2Cl_2 (30 mL) was added anhydrous $AlCl_3$ (0.66 g, 5 mmol) followed by acid chloride (6 mmol) at 25 °C. The reaction mixture was allowed to stir at 35 °C for 30 min. The reaction mixture was poured into ice cold water, and was shaken with CH_2Cl_2 (25 mL). The aqueous layer was extracted in CH_2Cl_2 (2 X 25 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using 80:20 hexane/EtOAc mixture to obtain the 6-acyl-2,2′-bis(methoxy) bi-2-naphthyl **109**.



(*R*)-(+)-**109a:**



Yield 1.56 g (88%)

Mp 192-194 °C

IR (KBr) (cm^{-1}) 2935, 2837, 1668, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.53 (s, 1H), 8.12 (d, *J* = 9.2 Hz, 1H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.99 (d, *J* = 9.2 Hz, 1H), 7.76 (d, *J* = 8.2 Hz, 1H), 7.52 (d, 2H), 7.34 (t, *J* = 8.6 Hz, 1H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 2.69 (s, 3H). (Spectrum No. 11)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 198.0, 157.2, 155.0, 136.5, 134.0, 132.4, 131.4, 131.0, 129.8, 129.4, 129.2, 128.1, 128.0, 126.5, 125.7, 124.9, 124.4, 123.6, 119.7, 118.7, 114.5, 56.8, 56.6, 26.6. (Spectrum No. 12)

LCMS *m/z* 357 (M+1)

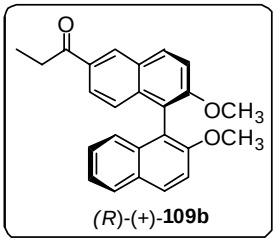
$[\alpha]_D^{25}$ +140.3 (*c* 1.00, $CHCl_3$)

Anal. Calcd for $C_{24}H_{20}O_3$: C, 80.88; H, 5.66; O, 13.47.

Found: C, 80.92; H, 5.59; O, 13.50.

(*R*)-(+)-**109b:**

Yield 0.64 g (87%)



(*R*)-(+)-**109b**

Mp 168-170 °C

IR (KBr) (cm^{-1}) 2966, 2839, 1678, 1616, 1172, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.54 (s, 1H), 8.11 (d, *J* = 8.8 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.50 (d, *J* = 9.2 Hz, 2H), 7.33 (t, *J* = 7.2 Hz, 1H), 7.24 (t, 1H), 7.16 (d, *J* = 9.2 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.10 (q, *J* = 7.2 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H). (Spectrum No. 13)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 200.7, 157.0, 154.9, 136.4, 133.8, 132.1, 131.3, 129.9, 129.7, 129.2, 128.1, 126.5, 125.7, 124.9, 124.4, 123.8, 123.6, 119.6, 118.8, 114.5, 114.1, 56.8, 31.7, 8.5. (Spectrum No. 14)

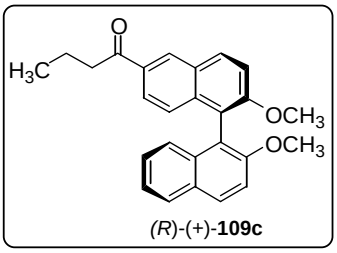
LCMS *m/z* 371 (M+1)

$[\alpha]_D^{25}$ +138.4 (*c* 0.5, $CHCl_3$)

Analytical data calculated for $C_{25}H_{22}O_3$: C, 81.06; H, 5.99; O, 12.96.

Found: C, 81.18; H, 5.95; O, 13.04.

(*R*)-(+)-**109c:**



(*R*)-(+)-**109c**

Yield 0.56 g (72%)

Mp 174-176 °C

IR (KBr) (cm^{-1}) 2939, 2839, 1674, 1606, 1514, 1344

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.52 (s, 1H), 8.11 (d, *J* = 9.2 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.54-7.46 (d, 2H), 7.33 (t, *J* = 8.4 Hz, 1H), 7.22 (t, *J* = 8.4 Hz, 1H), 7.15 (d, *J* = 8.8 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.05 (t, *J* = 6.8 Hz, 2H), 1.82 (m, *J* = 6.8 Hz, 2H), 1.04 (t, *J* = 6.4 Hz, 3H). (Spectrum No. 15)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 200.2, 157.0, 155.0, 136.4, 133.8, 132.3, 131.3, 130.1, 129.7, 129.2, 128.1, 127.6, 126.5, 125.7, 125.0, 124.5, 123.6, 119.6, 118.8, 114.5, 114.1, 56.8, 40.5, 18.1, 14.0. (Spectrum No. 16)

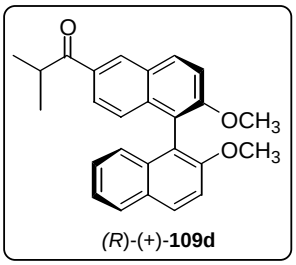
LCMS *m/z* 385 (M+1)

$[\alpha]_D^{25}$ +102.6 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{26}H_{24}O_3$: C, 81.22; H, 6.29; O, 12.48.

Found: C, 81.28; H, 6.31; O, 12.56.

(*R*)-(+)-**109d:**



(R)-(+)-**109d**

Yield 0.60 g (78%)

Mp 136-138 °C

IR (KBr) (cm^{-1}) 2968, 2844, 1672, 1618, 1271, 1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.54 (s, 1H), 8.12 (d, *J* = 8.8 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.77 (d, *J* = 7.2 Hz, 1H), 7.51 (dd, *J* = 9.2 Hz, 2H), 7.33 (t, *J* = 6.8 Hz, 1H), 7.27 (t, 1H), 7.17 (d, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.72-3.69 (M, 1H), 1.27 (d, 6H). (Spectrum No. 17)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 204.3, 157.0, 155.0, 136.4, 133.8, 131.4, 130.2, 129.8, 129.8, 128.1, 126.5, 125.7, 125.0, 124.8, 123.6, 119.6, 118.7, 114.4, 114.0, 56.8, 56.6, 35.2, 19.4. (Spectrum No. 18)

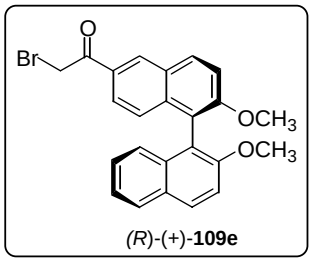
LCMS *m/z* 385 (M+1)

$[\alpha]_D^{25}$ +141.4 (*c* 0.5, $CHCl_3$)

Analytical data calculated for $C_{26}H_{24}O_3$: C, 81.22; H, 6.29; O, 12.48.

Found: C, 81.31; H, 6.27; O, 12.41.

(*R*)-(+)-**109e:**



(R)-(+)-**109e**

Yield 0.59 g (75%)

Mp 184-186 °C

IR (KBr) (cm^{-1}) 2935, 2841, 1695, 1682, 1618, 1351

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.55 (s, 1H), 8.10 (d, *J* = 9.2 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 9.2 Hz, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.53-7.44 (dd, 2H), 7.32 (t, *J* = 8.4 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 8.7 Hz), 1H), 7.05 (d, *J* = 7.6 Hz, 1H), 4.51 (s, 2H), 3.80 (s, 3H), 3.76 (s, 3H). (Spectrum No. 19)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 191.1, 157.6, 154.9, 136.8, 133.8, 131.6, 131.5, 129.9, 129.2, 129.1, 128.1, 127.9, 126.6, 126.1, 124.8, 124.6, 123.7, 119.7, 118.4, 114.7, 114.0, 56.8, 56.6, 31.0. (Spectrum No. 20)

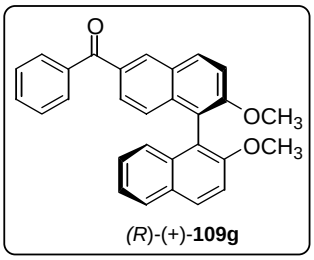
LCMS *m/z* 391 (M+1)

$[\alpha]_D^{25}$ +122.0 (*c* 0.2, $CHCl_3$)

Analytical data calculated for $C_{24}H_{19}BrO_3$: C, 66.22; H, 4.40; Br, 18.36; O, 11.03.

Found: C, 66.31; H, 4.37; Br, 18.28; O, 11.05.

(*R*)-(+)-**109g:**



(R)-(+)-**109g**

Yield 0.63 g (81%)

Mp 165-167 °C

IR (KBr) (cm^{-1}) 2935, 2835, 1718, 1653, 1616, 1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.33 (s, 1H), 8.10 (d, *J* = 8.9 Hz, 1H), 7.86 (d, *J* = 8.2 Hz, 1H), 7.74 (d, *J* = 8.7 Hz, 1H), 7.73 (t, *J* = 8.2 Hz, 1H), 7.68 (t, *J* = 8.7

Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.54 (m, 6H), 7.50 (d, *J* = 7.7 Hz, 1H), 7.20 (d, *J* = 8.9 Hz, 1H), 7.1 (s, 1H), 3.81 (s, 3H), 3.79(s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 196.2, 157.5, 155.1, 147.1, 142.4, 143.6, 138.7, 136.7, 133.4, 131.5, 130.8, 129.9, 129.5, 128.9, 128.4, 127.5, 126.7, 126.6, 125.7, 125.3, 125.2, 124.7, 123.8, 119.4, 114.4, 56.7, 56.5.

LCMS *m/z* 419 (M+1)

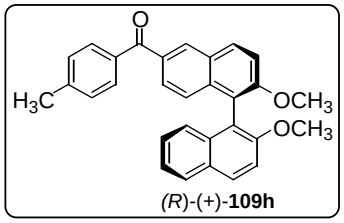
$[\alpha]_D^{25}$ +111.4 (*c* 0.6, $CHCl_3$)

Analytical data calculated for $C_{29}H_{22}O_3$: C, 82.74; H, 5.01; O, 12.25.

Found: C, 82.59; H, 5.04; O, 12.36.

(*R*)-(+)-**109h:**

Yield 0.66 g (77%)



(R)-(+)-**109h**

Mp 134-136 °C

IR (KBr) (cm^{-1}) 2935, 2843, 1763, 1651, 1618, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.51 (s, 1H), 8.34 (d, *J* = 8.6 Hz, 1H), 7.91 (d, *J* = 8.8 Hz, 1H), 7.71 (d, *J* = 8.6 Hz, 1H), 7.75 (t, *J* = 8.8 Hz, 1H), 7.67 (t, *J* = 8.6 Hz, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.52 (m, 5H), 7.50 (d, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 8.6 Hz, 1H), 7.14 (s, 1H), 3.80 (s, 3H), 3.78(s, 3H), 2.41 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 196.8, 157.7, 155.4, 146.3, 144.6, 143.1, 138.3, 136.4, 133.7, 131.2, 130.1, 129.8, 129.2, 128.6, 128.3, 127.1, 126.3, 125.5, 125.7, 125.1, 124.3, 122.5, 119.8, 114.8, 56.8, 56.6, 21.6.

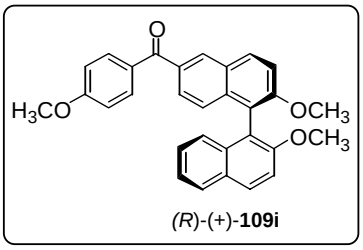
LCMS *m/z* 433 (M+1)

$[\alpha]_D^{25}$ +121.4 (*c* 0.6, $CHCl_3$)

Analytical data calculated for $C_{30}H_{24}O_3$: C, 82.89; H, 5.49; O, 11.62.

Found: C, 82.65; H, 5.42; O, 11.92.

(*R*)-(+)-**109i:**



(*R*)-(+)-**109i**

Yield 0.69 g (74%)

Mp 132-134 °C

IR (KBr) (cm^{-1}) 2965, 2842, 1764, 1647, 1597, 1021

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.32 (s, 1H), 8.21 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 9.2 Hz, 1H), 7.74 (d, *J* = 8.6 Hz, 2H), 7.70 (t, *J* = 9.2 Hz, 1H), 7.66 (t, *J* = 8.2 Hz, 1H), 7.62 (d, *J* = 8.0 Hz, 1H), 7.49 (m, 4H), 7.43 (d, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 8.2 Hz, 1H), 7.08 (s, 1H), 3.92 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 197.4, 156.2, 155.8, 147.1, 145.6, 144.6, 139.1, 135.8, 133.9, 132.6, 130.3, 129.9, 129.4, 129.0, 128.5, 127.3, 126.8, 125.4, 125.1, 124.7, 124.2, 123.8, 119.3, 114.5, 56.7, 56.5, 52.7.

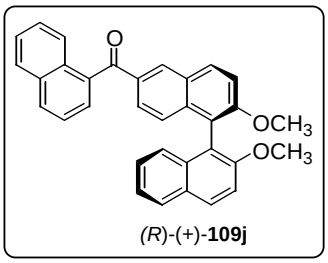
LCMS *m/z* 449 (M+1)

$[\alpha]_D^{25}$ +104.6 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{30}H_{24}O_4$: C, 80.34; H, 5.39; O, 14.27.

Found: C, 80.42; H, 5.46; O, 14.12.

(*R*)-(+)-**109j:**



(R)-(+)-**109j**

Yield 0.70 g (75%)

Mp 154-156 °C

IR (KBr) (cm^{-1}) 2937, 2843, 1768, 1685, 1602, 1265

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.53 (s, 1H), 8.18 (d, *J* = 8.8 Hz, 1H), 7.86-7.66 (m, 4H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.54 (m, 8H), 7.51 (d, *J* = 7.8 Hz, 1H), 7.25 (d, *J* = 8.9 Hz, 1H), 7.13 (s, 1H), 3.78 (s, 3H), 3.76 (s,3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 191.5, 157.4, 143.9, 134.8, 134.2, 133.9, 133.4, 132.7, 131.5, 130.7, 130.1, 129.7, 129.0, 128.8, 128.1, 127.7, 127.4, 127.1, 126.6, 123.4, 121.6, 118.7, 118.6, 114.6, 56.7, 56.5.

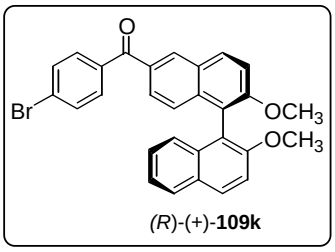
LCMS *m/z* 469 (M+1)

$[\alpha]_D^{25}$ +122.6 (*c* 0.6, $CHCl_3$)

Analytical data calculated for $C_{33}H_{24}O_3$: C, 84.59; H, 5.16; O, 10.24.

Found: C, 84.65; H, 5.21; O, 10.13.

(*R*)-(+)-**109k:**



(R)-(+)-**109k**

Yield 0.67 g (82%)

Mp 165-167 °C

IR (KBr) (cm^{-1}) 2938, 2836, 1715, 1652, 1617, 1064

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.51 (s, 1H), 8.24 (d, *J* = 8.6 Hz, 1H), 7.87 (d, *J* = 9.2 Hz, 1H), 7.79 (d, *J* = 8.6 Hz, 1H), 7.69 (t, *J* = 9.2 Hz, 1H), 7.63 (t, *J* = 8.2

Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.48 (m, 5H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.12 (s, 1H), 3.78 (s, 3H), 3.76 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 196.2, 156.7, 155.2, 147.6, 146.1, 144.9, 138.6, 135.4, 133.4, 132.8, 130.1, 129.9, 129.5, 129.1, 128.5, 127.6, 126.4, 125.7, 125.2, 124.9, 124.1, 123.5, 119.2, 114.9, 56.6, 56.4.

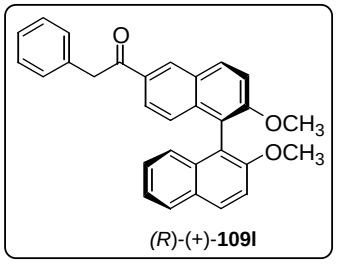
LCMS *m/z* 419 (M+1)

$[\alpha]_D^{25}$ +111.4 (*c* 0.6, $CHCl_3$).

Analytical data calculated for $C_{29}H_{21}BrO_3$: C, 70.03; H, 4.26; Br, 16.07; O, 9.65.

Found: C, 69.96; H, 4.21; Br, 16.11; O, 9.73.

(*R*)-(+)-**109l:**



(R)-(+)-**109l**

Yield 0.65 g (74%)

Mp 146-148 °C

IR (KBr) (cm^{-1}) 2967, 2844, 1767, 1645, 1592, 1021

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.67 (s, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 8.04 (d, *J* = 8.8 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.8 Hz, 1H), 7.50 (d, *J* = 9.2 Hz, 2H), 7.39-7.36 (m, 5H), 7.30-7.26 (m, 3H), 7.15 (d, *J* = 8.4 Hz, 1H), 4.41 (s, 2H), 3.81 (s, 3H), 3.79 (s, 3H). (Spectrum No. 21)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 197.3, 157.2, 136.3, 134.9, 131.9, 131.8, 131.0, 129.5, 128.7, 128.3, 128.0, 126.9, 125.4, 125.0, 118.7, 114.9, 114.3, 56.6, 45.5. (Spectrum No. 22)

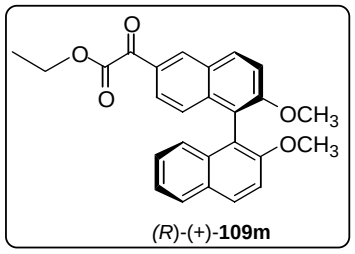
LCMS *m/z* 433 (M+1)

$[\alpha]_D^{25}$ +113.6 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{30}H_{24}O_3$: C, 83.31; H, 5.59; O, 11.10.

Found: C, 83.42; H, 5.64; O, 10.94.

(*R*)-(+)-**109m:**



(R)-(+)-**109m**

Yield 0.64 g (87%)

Mp 168-170 °C

IR (KBr) (cm^{-1}) 2965, 2836, 1678, 1616, 1177, 1043

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.61 (s, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.56-7.46 (d, 2H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 8.2 Hz, 1H), 7.06 (d, *J* = 8.2 Hz, 1H), 4.52 (q, *J* = 8.0 Hz, 2H), 3.83 (s, 3H), 3.77 (s, 3H), 1.47 (t, *J* = 8.0 Hz, 3H). (Spectrum No. 25)

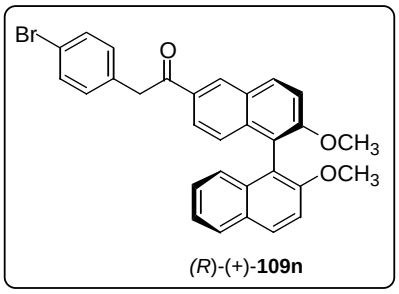
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 186.2, 164.3, 158.1, 154.9, 137.4, 134.0, 133.7, 132.0, 130.0, 129.2, 128.1, 127.8, 127.7, 126.6, 126.2, 124.8, 124.4, 123.7, 119.9, 118.3, 114.6, 114.0, 62.3, 56.7, 56.5, 14.2. (Spectrum No. 26)

LCMS *m/z* 415 (M+1)

Analytical data calculated for $C_{26}H_{22}O_5$: C, 75.35; H, 5.35; O, 19.30.

Found: C, 75.39; H, 5.22; O, 19.39.

(*R*)-(+)-**109n:**



(R)-(+)-**109n**

Yield 0.68 g (67%)

Mp 146-148 °C

IR (KBr) (cm^{-1}) 2968, 2845, 1767, 1646, 1594, 1019

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.59 (s, 1H), 7.94 (d, *J* = 8.6 Hz, 1H), 7.84 (d, *J* = 8.8 Hz, 1H), 7.81 (d, *J* = 8.6 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H), 7.48 (d, 2H), 7.37-7.32 (m, 4H), 7.29-7.24 (m, 3 H), 7.18 (d, *J* = 8.4 Hz, 1H), 4.59 (s, 2H), 3.80 (s, 3H), 3.79 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 197.1, 157.2, 138.1, 135.4, 132.6, 131.6, 130.6, 129.4, 128.6, 128.2, 127.8, 127.2, 125.4, 124.2, 119.3, 114.6, 114.0, 56.6, 56.2.

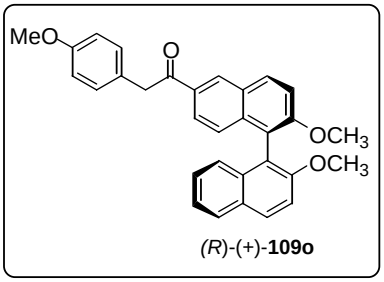
LCMS *m/z* 512 (M+2)

$[\alpha]_D^{25}$ +121.6 (*c* 1.00, $CHCl_3$)

Anal. Calcd for $C_{30}H_{23}BrO_3$: C, 70.46; H, 4.53; Br, 15.62; O, 9.39.

Found: C, 70.58; H, 4.61; Br, 15.70; O, 9.51.

(*R*)-(+)-**109o:**



(R)-(+)-**109o**

Yield 0.70 g (77%)

Mp 152-154 °C

IR (KBr) (cm^{-1}) 2966, 2848, 1766, 1648, 1595, 1018

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.52 (s, 1H), 8.24 (d, *J* = 8.8 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.76 (d, *J* = 8.8 Hz, 1H), 7.72 (t, *J* = 7.8 Hz, 1H), 7.64 (t, *J* = 8.4

Hz, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.53 (m, 5H), 7.46 (d, *J* = 8.2 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.13 (s, 1H), 4.53 (s, 2H), 3.86 (s, 3H), 3.81 (s, 3H), 3.79 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 197.1, 157.4, 156.4, 147.2, 145.4, 144.7, 139.3, 135.5, 134.7, 132.7, 130.4, 129.8, 129.2, 128.9, 128.2, 127.5, 126.3, 125.6, 125.2, 124.6, 124.0, 123.5, 119.7, 114.8, 56.2, 56.0, 52.4.

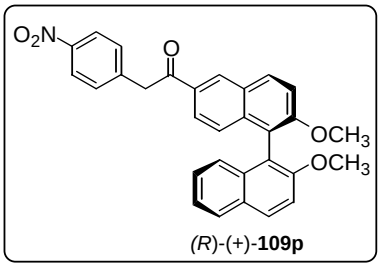
LCMS *m/z* 462 (M+1)

$[\alpha]_D^{25}$ +112.7 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{31}H_{26}O_4$: C, 80.50; H, 5.67; O, 13.83.

Found: C, 80.69; H, 5.57; O, 13.94.

(*R*)-(+)-**109p:**



(R)-(+)-**109p**

Yield 0.67 g (72%)

Mp 146-148 °C

IR (KBr) (cm^{-1}) 2965, 2846, 1765, 1648, 1595, 1021

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.60 (s, 1H), 8.22-8.14 (m, 3H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.90 (d, 1H), 7.79 (d, 1H), 7.57 (d, *J* = 8.8 Hz, 1H), 7.48-7.08 (m, 7H), 4.52 (s, 2H), 3.85 (s, 3H), 3.80 (s, 3H). (Spectrum No.23)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 195.6, 157.5, 155.0, 147.1, 142.4, 136.7, 133.8, 131.5, 131.4, 130.8, 130.6, 129.9, 129.2, 128.1, 127.9, 126.5, 126.1, 124.8,

124.4, 123.8, 123.7, 119.8, 118.5, 114.6, 114.0, 56.8, 56.6, 44.9. (Spectrum No.24)

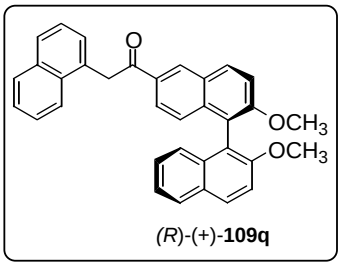
LCMS *m/z* 478 (M+1)

$[\alpha]_D^{25}$ +106.4 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{30}H_{23}NO_5$: C, 75.46; H, 4.85; N, 2. 93; O, 16.75.

Found: C, 75.39; H, 4.98; N, 2.80; O, 16.82.

(*R*)-(+)-**109q:**



(*R*)-(+)-**109q**

Yield 0.61 g (64%)

Mp 144-148 °C

IR (KBr) (cm^{-1}) 2968, 2842, 1764, 1645, 1594, 1023

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.57 (s, 1H), 8.32 (d, *J* = 8.6 Hz, 1H), 7.82-7.66 (m, 4H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.57 (m, 8H), 7.54 (d, *J* = 8.2 Hz, 1H), 7.34 (d, *J* = 8.6 Hz, 1H), 7.14 (s, 1H), 4.21 (s, 2H), 3.79 (s, 3H), 3.77 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 189.2, 154.6, 144.2, 135.3, 134.6, 133.7, 133.1, 132.6, 131.2, 130.7, 130.2, 129.8, 129.3, 128.9, 128.3, 127.8, 127.3, 127.0, 126.7, 125.6, 125.1, 124.8, 123.6, 119.7, 117.6, 114.1, 56.8, 56.5, 42.6.

LCMS *m/z* 483 (M+1)

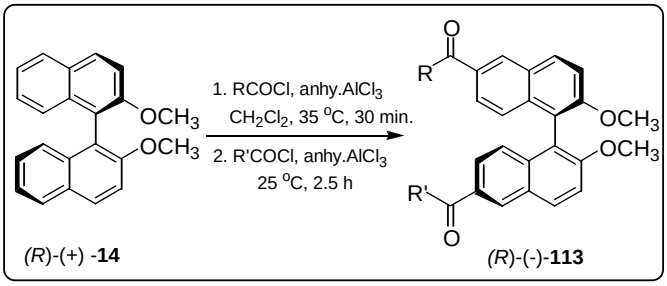
$[\alpha]_D^{25}$ +123.4 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{34}H_{26}O_3$: C, 84.62; H, 5.43; O, 9.95.

Found: C, 84.54; H, 5.37; O, 10.09.

3.1.3 General procedure for the preparation of unsymmetrical diketones by acylation of 1,1′-bi-2-naphthyl methyl ethers using acid chlorides and $AlCl_3$

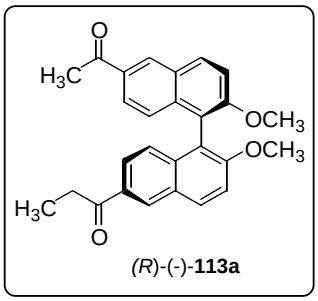
To the solution of 2,2′-bis(methoxy) bi-2-naphthyl (1.57 g, 5 mmol) **14** in CH_2Cl_2 (30 mL) was added anhydrous $AlCl_3$ (0.66 g, 6 mmol) followed by acid chloride (RCOCl, 6 mmol) at 25 °C. The reaction mixture was allowed to stir at 35 °C for 30 min. To this reaction mixture was added anhydrous $AlCl_3$ (0.66 g, 6 mmol) followed by slow addition of acid chloride (R′COCl, 10 mmol) and allowed it to srirr for 2.5 h. The reaction mixture was poured into ice cold water, and was shaken with CH_2Cl_2 (25 mL). The aqueous layer was extracted in CH_2Cl_2 (2 X 25 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using 80:20 hexane/EtOAc mixture to obtain the unsymmetrical 6,6′-diacyl-2,2′-bis(methoxy) bi-2-naphthyl **113**.



(*R*)-(-)-**113a:** (RCOCl = CH_3COCl, R′COCl = CH_3CH_2COCl)

Yield 1.73 g (84%)

Mp 172-174 °C



IR (KBr) (cm^{-1}) 2935, 2837, 1672, 1666, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.57 (s, 2H), 8.14 (d, *J* = 8.8 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.14 (d, *J* = 8.8 Hz, 2H), 3.81 (s, 6H), 3.10 (q, *J* = 8.6 Hz, 2H), 2.69 (s, 3H), 1.12 (t, *J* = 8.6 Hz, 3H).

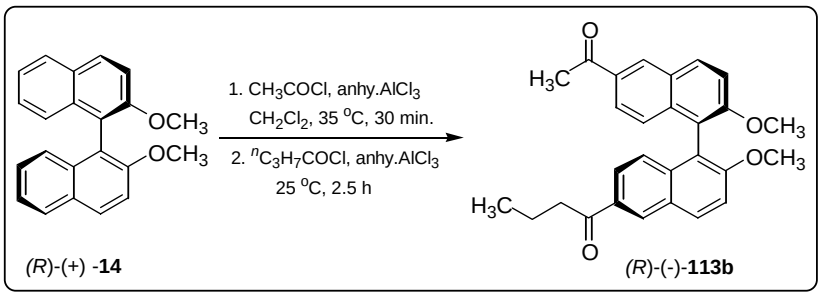
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 200.7, 198.2, 157.3, 157.1, 136.7, 136.5, 132.6, 132.5, 131.9, 131.4, 130.6, 128.1, 127.9, 125.6, 125.3, 124.9, 118.8, 118.2, 114.5, 56.6, 41.2, 28.2, 16.1.

LCMS *m/z* 413 (M+1)

$[\alpha]_D^{25}$ -123.6 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{27}H_{24}O_4$: C, 78.62; H, 5.86; O, 15.52.

Found: C, 78.55; H, 5.74; O, 15.71.



(*R*)-(-)-**113b:**

Yield 0.69 g (82%)

Mp 164-166 °C

IR (KBr) (cm^{-1}) 2968, 2841, 1674, 1668, 1616, 1271,1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.54 (s, 2H), 8.13 (d, *J* = 9.2 Hz, 2H), 7.79 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.11 (d, *J* = 9.2 Hz, 2H), 3.80 (s, 6H), 3.04 (q, *J* = 8.8 Hz, 2H), 2.68 (s, 3H), 1.86-1.77 (m, 2H), 1.03 (t, *J* = 8.8 Hz, 3H). (Spectrum No.27)

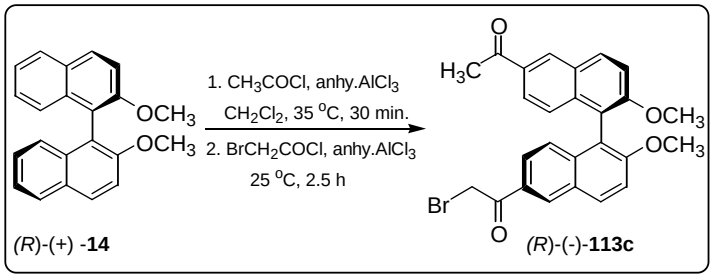
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 200.2, 197.9, 157.1, 157.0, 136.3, 136.2, 132.5, 132.4, 131.7, 130.7, 130.2, 128.0, 127.9, 125.4, 125.3, 124.6, 118.8, 118.7, 114.4, 56.5, 40.4, 26.6, 18.0, 14.0. (Spectrum No.28)

LCMS *m/z* 427 (M+1)

$[\alpha]_D^{25}$ -112.4 (*c* 0.5, $CHCl_3$)

Analytical data calculated for $C_{28}H_{26}O_4$: C, 78.85; H, 6.14; O, 15.01.

Found: C, 78.94; H, 6.27; O, 14.79.



(*R*)-(-)-**113c:**

Yield 0.72 g (75%)

Mp 158-160 °C

IR (KBr) (cm^{-1}) 2937, 2843, 1768, 1685, 1602, 1265

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.54 (s, 2H), 8.13 (d, *J* = 8.8 Hz, 1H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 1H)), 7.73 (d, *J* = 9.2 Hz, 1H), 7.55 (d, *J* = 9.2 Hz, 1H), 7.35 (d, *J* = 6.8 Hz, 1H), 7.20 (d, *J* = 6.8 Hz, 1H), 7.05 (d, *J* = 6.8 Hz, 1H), 4.80 (s, 2H), 3.82 (s, 3H), 3.78 (s, 3H), 1.56 (s, 3H). (Spectrum No. 29)

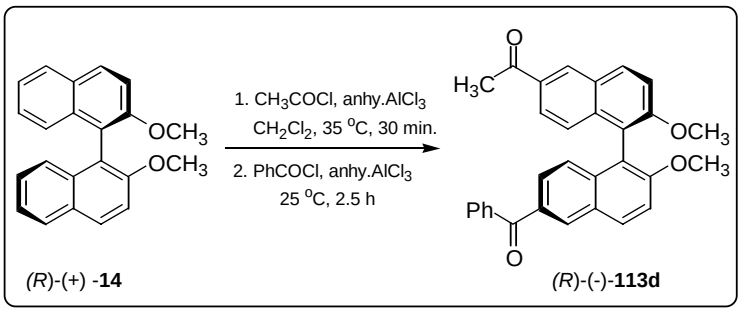
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 198.4, 171.1, 157.2, 155.0, 134.0, 131.4, 130.8, 129.8, 129.4, 129.2, 128.0, 126.4, 125.3, 124.5, 123.7, 119.6, 114.5, 114.3, 56.9, 26.6. (Spectrum No. 30)

LCMS *m/z* 479 (M+2)

$[\alpha]_D^{25}$ -132.6 (*c* 0.6, $CHCl_3$).

Analytical data calculated for $C_{26}H_{21}BrO_4$: C, 65.42; H, 4.43; Br, 16.74; O, 13.41.

Found: C, 65.46; H, 4.39; Br, 16.76; O, 13.39.



(*R*)-(-)-**113d:**

Yield 0.71 g (78%)

Mp 164-166 °C

IR (KBr) (cm^{-1}) 2935, 2841, 1695, 1682, 1616, 1350

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.54 (s, 1H), 8.34 (s, 1H), 8.15 (d, *J* = 9.2 Hz, 1H), 8.09 (d, *J* = 8.8 Hz, 1H), 7.86 (d, *J* = 7.6 Hz, 2H), 7.84 (d, 1H), 7.80 (d, *J* = 7.2 Hz, 1H), 7.73 (t, *J* = 7.2 Hz, 1H), 7.61-7.49 (m, 4H), 7.18-7.15 (m, 2H), 3.83 (s, 3H), 3.81 (s, 3H), 2.69 (s, 3H). (Spectrum No. 31)

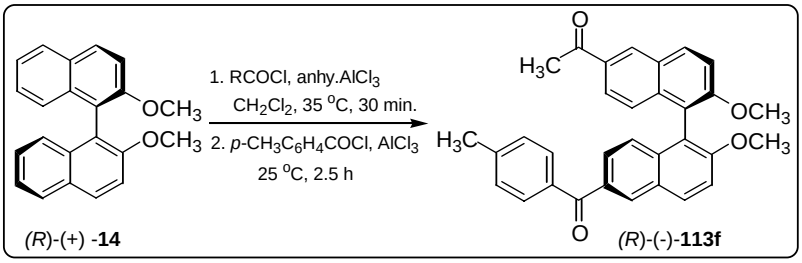
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 197.9, 196.6, 157.1, 157.0, 138.1, 136.3, 136.0, 132.7, 132.6, 132.5, 132.2, 131.7, 131.6, 130.7, 128.0, 127.8, 126.5, 125.4, 125.3, 124.6, 118.8, 114.4, 56.6, 26.6. (Spectrum No. 32)

LCMS *m/z* 461 (M+1)

$[\alpha]_D^{25}$ -146.4 (*c* 0.2, $CHCl_3$)

Analytical data calculated for $C_{31}H_{24}O_4$: C, 80.85; H, 5.25; O, 13.90.

Found: C, 80.79; H, 5.43; O, 12.88.



(*R*)-(-)-**113f:**

Yield 0.71 g (75%)

Mp 148-150 °C

IR (KBr) (cm^{-1}) 2939, 2839, 1674, 1668, 1606,1514, 1344

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.51 (s, 1H), 8.35 (s, 1H), 8.11 (d, *J* = 8.8 Hz, 1H), 8.07 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 8.6 Hz, 2H), 7.88 (d, 1H), 7.79 (d, *J*

= 8.2 Hz, 1H), 7.78 (t, *J* = 8.2 Hz, 1H), 7.56-7.51 (m, 3H), 7.15-7.10 (m, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 2.69 (s, 3H), 2.05 (s, 3H).

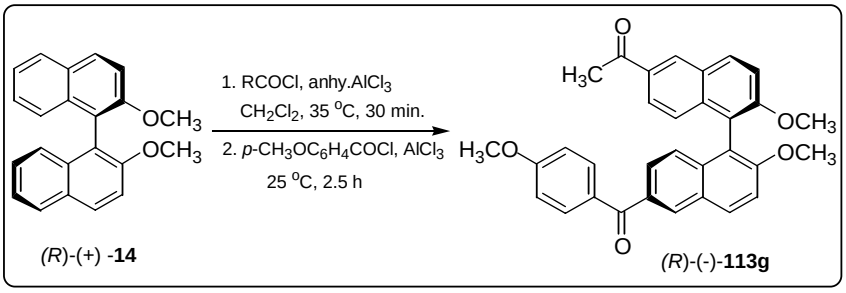
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 195.6, 193.7, 157.5, 154.9, 147.0, 142.4, 136.7, 133.7, 131.4, 129.2, 128.1, 126.5, 124.8, 123.7, 119.7, 118.4, 114.7, 56.7, 44.6, 24.3, 21.8.

LCMS *m/z* 475 (M+1)

$[\alpha]_D^{25}$ -134.6 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{32}H_{26}O_4$: C, 80.99; H, 5.52; O, 13.49.

Found: C, 81.12; H, 5.57; O, 13.31.



(*R*)-(-)-**113g:**

Yield 0.76 g (78%)

Mp 152-154 °C

IR (KBr) (cm^{-1}) 2935, 2835, 1664, 1653, 1616, 1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.53 (s, 1H), 8.32 (s, 1H), 8.09 (d, *J* = 9.2 Hz, 1H), 8.05 (d, *J* = 9.2 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.84 (d, 1H), 7.72 (d, *J*

= 8.4 Hz, 1H), 7.69 (t, *J* = 8.6 Hz, 1H), 7.62-7.56 (m, 3H), 7.12-7.06 (m, 2H), 3.84 (s, 3H), 3.80 (s, 3H), 3.79 (s, 3H), 2.67 (s, 3H).

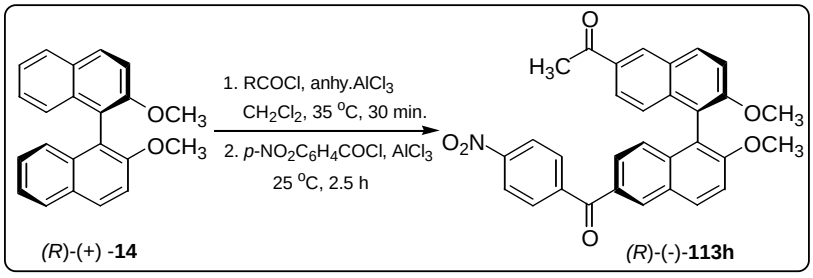
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 196.2, 194.7, 155.1, 143.6, 138.7, 133.4, 129.5, 128.9, 128.4, 127.5, 126.7, 126.6, 125.7, 125.3, 125.2, 119.4, 114.4, 56.2, 54.7, 41.5.

LCMS *m/z* 491 (M+1)

$[\alpha]_D^{25}$ -134.5 (*c* 0.6, $CHCl_3$)

Analytical data calculated for $C_{32}H_{26}O_5$: C, 78.35; H, 5.34; O, 16.31.

Found: C, 78.49; H, 5.43; O, 16.08.



(*R*)-(-)-**113h:**

Yield 0.79 g (72%)

Mp 168-170 °C

IR (KBr) (cm^{-1}) 2935, 2843, 1676, 1651, 1616, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.51 (s, 1H), 8.34 (s, 1H), 8.09 (d, *J* = 8.6 Hz, 1H), 8.05 (d, *J* = 8.6 Hz, 1H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.83 (d, 1H), 7.76 (d, *J*

= 8.4 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.61-7.56 (m, 3H), 7.21-7.16 (m, 2H), 3.82 (s, 3H), 3.81 (s, 3H), 2.68 (s, 3H).

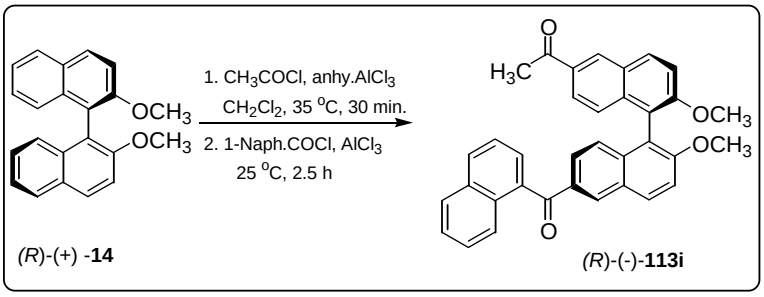
^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 198.4, 197.4, 156.9, 142.8, 135.5, 135.1, 133.9, 132.1, 131.6, 130.8, 128.9, 127.8, 126.5, 125.2, 119.2, 114.3, 56.8, 41.8.

LCMS *m/z* 551 (M+1)

$[\alpha]_D^{25}$ -67.2 (*c* 0.6, $CHCl_3$)

Anal. Calcd for $C_{31}H_{23}NO_6$: C, 73.65; H, 4.59; N, 2.77; O, 18.99.

Found: C, 73.52; H, 4.45; N, 2.92; O, 19.11.



(*R*)-(-)-**113i:**

Yield 0.69 g (68%)

Mp 148-150 °C

IR (KBr) (cm^{-1}) 2964, 2847, 1668, 1643, 1592, 1021

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.32 (s, 1H), 8.30 (s, 1H), 8.01 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 1H), 7.86-7.73 (m, 5H), 7.64-7.51 (m, 6H), 7.21-7.16 (m, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 2.66 (s, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 197.3, 196.7, 157.6, 143.2, 134.5, 134.4, 133.7, 133.2, 132.7, 131.5, 130.6, 130.2, 129.7, 129.2, 128.7, 128.2, 127.6, 127.4, 127.2, 126.8, 123.6, 121.6, 118.7, 118.6, 114.6, 56.7, 42.6.

LCMS *m/z* 511 (M+1)

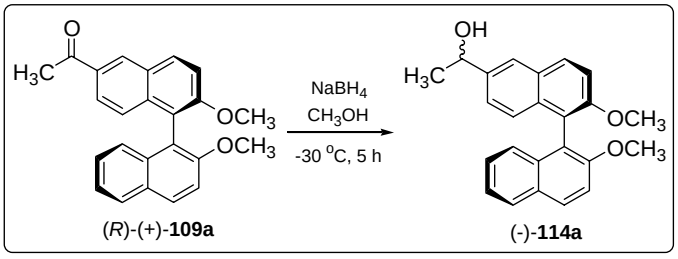
$[\alpha]_D^{25}$ -154.6 (*c* 1.00, $CHCl_3$)

Anal. Calcd for $C_{35}H_{26}O_4$: C, 82.33; H, 5.13; O, 12.53.

Found: C, 82.39; H, 5.23; O, 12.68.

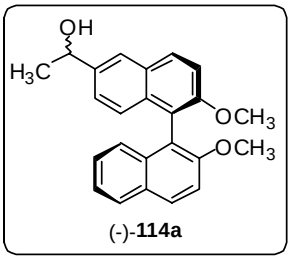
3.2 General procedure for the reduction of 6-acyl-1,1′-bi-2-naphthyl methyl ethers using the $NaBH_4/CH_3OH$ reagent system

To the solution of 6-acetyl-2,2′-bis(methoxy) bi-2-naphthyl **109a** (1.78 g, 5 mmol) in CH_3OH (30 mL) at -30 ^oC was added anhydrous $NaBH_4$ (2.66 g, 20 mmol). The mixture was stirred at -30 °C for 5 h. The solvents were removed and the crude residue was diluted with EtOAc (30 mL) and washed with water. The aqueous layer was extracted in EtOAc (2 X 25 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using 80:20 hexane/EtOAc mixture to obtain the monoalcohol **114a** in 92% yield.



(*R*)-(+)-**109a** (-)-**114a**

(-)-**114a:**



(-)-**114a**

Yield 1.64 g (92%)

Mp 164-166 °C

IR (KBr) (cm^{-1}) 3245, 2935, 2837, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.01 (t, *J* = 8.6 Hz, 2H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.86 (s, 1H), 7.46 (d, *J* = 8.8 Hz, 2H), 7.32 (t, *J* = 8.2 Hz, 1H), 7.23-7.20 (m, 2H), 7.11 (d, *J* = 8. 8 Hz, 2H), 5.01 (q, 1H), 3.78 (s, 6H), 1.91 (s, 1H), 1.54 (d, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.1, 154.9, 140.6, 133.9, 133.5, 129.4, 129.1, 129.0, 127.9, 126.3, 125.7, 125.2, 124.4, 124.0, 123.5, 119.6, 119.5, 114.5, 114.2, 70.5, 56.9, 24.8.

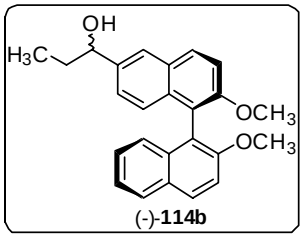
LCMS *m/z* 359 (M+1)

$[\alpha]_D^{25}$ -40.4 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{24}H_{22}O_3$: C, 80.42,; H, 6.19, O, 13.39.

Found: C, 80.51; H, 6.21; O, 13.28.

(-)-**114b:**



(-)-**114b**

Yield 0.67 g (91%)

Mp 144-146 °C

IR (KBr) (cm^{-1}) 3255, 2966, 2839, 1616, 1172, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.32 (s, 1H), 8.15 (d, *J* = 8.8 Hz, 2H), 7.81 (d, *J* = 8.6 Hz, 2H), 7.55 (t, *J* = 8.4 Hz, 1H), 7.36 (t, *J* = 8.4 Hz, 1H), 7.26-7.21 (m, 2H), 7.14 (d, *J* = 8.6 Hz, 2H), 4.93 (t, 1H), 3.81 (s, 6H), 3.11-3.02 (m, 2H), 1.89 (s, 1H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 157.1, 154.4, 136.6, 133.6, 132.4, 131.3, 129.9, 129.6, 129.1, 128.4, 126.4, 125.5, 124.7, 124.1, 123.8, 123.9, 119.4, 118.7, 114.5, 114.1, 68.7, 56.8, 31.7, 8.5.

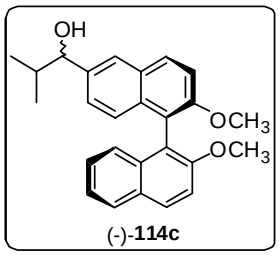
LCMS *m/z* 373 (M+1)

$[\alpha]_D^{25}$ -56.4 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49; O, 12.89.

Found: C, 80.73; H, 6.53; O, 12.75.

(-)-**114c:**



(-)-**114c**

Yield 0.68 g (88%)

Mp 134-136 °C

IR (KBr) (cm^{-1}) 3312, 2968, 2841, 1616, 1271, 1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.31 (s, 1H), 8.16 (d, *J* = 8.8 Hz, 2H), 7.80 (d, *J* = 8.6 Hz, 2H), 7.55 (d, *J* = 8.8 Hz, 2H), 7.32-7.29 (m, 2H), 7.15 (d, *J* = 8.6 Hz, 2H), 5.09 (d, 1H), 3.83 (s, 6H), 3.72 (m, 1H), 1.93 (s, 1H), 1.28 (d, *J* = 7.4 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 157.6, 155.3, 136.5, 133.9, 132.3, 131.2, 130.1, 129.7, 129.2, 128.1, 127.5, 126.5, 125.7, 125.3, 124.7, 123.8, 120.0, 118.9, 114.5, 114.1, 68.7, 56.8, 40.5, 18.2.

LCMS *m/z* 387 (M+1)

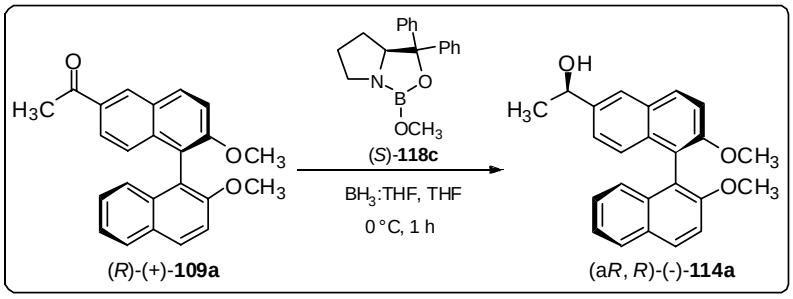
$[\alpha]_D^{25}$ -44.6 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{26}H_{26}O_3$: C, 80.80; H, 6.78; O, 12.42.

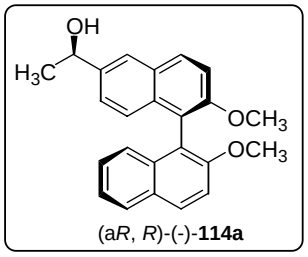
Found: C, 80.72; H, 6.62; O, 12.56.

3.2.1 General procedure for the reduction of 6-acyl-1,1′-bi-2-naphthyl methyl ethers using the 30 mol% oxazaborolidine/BH_3:THF reagent system

To the solution of 6-acetyl-2,2′-bis(methoxy) bi-2-naphthyl **109a** (1.78 g, 5 mmol) in THF (30 mL) at 0 ^oC was added 30 mol% oxazaborolidine (prepared *in situ* by the reaction of (*S*)-DPP and trimethyl borate in THF solvent at 25 ^oC for 2 h) followed by the addition of BH_3:THF (1 mL, 5 mmol). The mixture was stirred at 0 °C for 30 min. The reaction mixture was poured into water, and was shaken with EtOAc (25 mL). The aqueous layer was extracted in EtOAc (2 X 25 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using 80:20 hexane/EtOAc mixture to obtain the alcohol product **114a**.



(a*R*, *R*)-(-)-**114a:**



Yield 1.68 g (94%)

Mp 186-188 °C

IR (KBr) (cm^{-1}) 3214, 2935, 2837, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.98 (t, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.84 (s, 1H), 7.47 (d, *J* = 8.8 Hz, 2H), 7.35 (t, *J* = 8.0 Hz, 1H), 7.24-7.20 (m, 2H), 7.11 (d, *J* = 8.8 Hz, 2H), 5.01 (q, 1H), 3.77 (s, 6H), 1.90 (s, 1H), 1.55 (d, 3H). (Spectrum 33)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.1, 154.9, 140.7, 134.0, 133.6, 129.5, 129.4, 129.2, 129.0, 128.0, 126.4, 125.8, 125.2, 124.4, 124.0, 123.5, 119.6, 119.5, 114.5, 114.2, 70.5, 56.9, 24.9. (Spectrum 34)

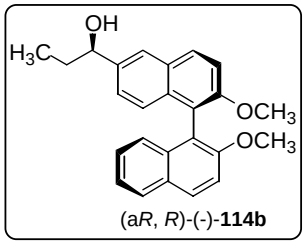
LCMS *m/z* 359 (M+1)

$[\alpha]_D^{25}$ -184.6 (*c* 1.00, $CHCl_3$) (dr was estimated by chiral HPLC analysis on Chiralcel-OD-H column, hexane/2-propanol = 80:20, flow rate: 0.5 mL/min.)

Analytical data calculated for $C_{24}H_{22}O_3$: C, 80.42; H, 6.19; O, 13.39.

Found: C, 80.58; H, 6.27; O, 13.63.

(a*R*, *R*)-(-)-**114b:**



(a*R*, *R*)-(-)-**114b**

Yield 0.67 g (91%)

Mp 166-168 °C

IR (KBr) (cm^{-1}) 3217, 2966, 2839, 1616, 1172, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.31 (s, 1H), 8.16 (d, *J* = 8.8 Hz, 2H), 7.84 (d, *J* = 8.4 Hz, 2H), 7.56 (t, *J* = 8.4 Hz, 1H), 7.35 (t, *J* = 8.4 Hz, 1H), 7.31-7.26 (m, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 5.06 (t, 1H), 3.80 (s, 6H), 3.12-3.04 (m, 2H), 1.93 (s, 1H), 1.29 (t, *J* = 6.8 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 157.4, 155.0, 136.5, 133.8, 132.1, 131.3, 129.9, 129.7, 129.2, 128.1, 126.5, 125.7, 124.9, 124.4, 123.8, 123.6, 119.6, 118.8, 114.5, 114.1, 68.4, 56.9, 31.8, 8.7.

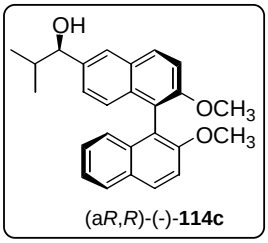
LCMS *m/z* 373 (M+1)

$[\alpha]_D^{25}$ -181.2 (*c* 1.00, $CHCl_3$) (dr was estimated by chiral HPLC analysis on Chiralcel-OD-H column, hexane/2-propanol = 80:20, flow rate: 0.5 mL/min.)

Anal. Calcd for $C_{25}H_{24}O_3$: C, 80.62; H, 6.49; O, 12.89.

Found: C, 80.77; H, 6.58; O, 13.13.

(a*R*, *R*)-(-)-**114c:**



(a*R*,*R*)-(-)-**114c**

Yield 0.59 g (75%)

Mp 146-148 °C

IR (KBr) (cm^{-1}) 3211, 2968, 2841, 1616, 1271, 1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.32 (s, 1H), 8.21 (d, *J* = 9.2 Hz, 2H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.53 (d, *J* = 9.2 Hz, 2H), 7.27-7.22 (m, 2H), 7.09 (d, *J* = 8.8 Hz, 2H), 5.11 (d, 1H), 3.81 (s, 6H), 3.70 (m, *J* = 7.4 Hz, 1H), 1.91 (s, 1H), 1.24 (d, *J* = 7.4 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 157.2, 155.1, 136.3, 133.7, 132.3, 131.3, 130.1, 129.7, 129.2, 128.1, 127.8, 126.5, 125.7, 125.1, 124.4, 123.5, 120.1, 118.7, 114.7, 114.2, 68.9, 56.7, 40.6, 18.3.

LCMS *m/z* 388 (M+1)

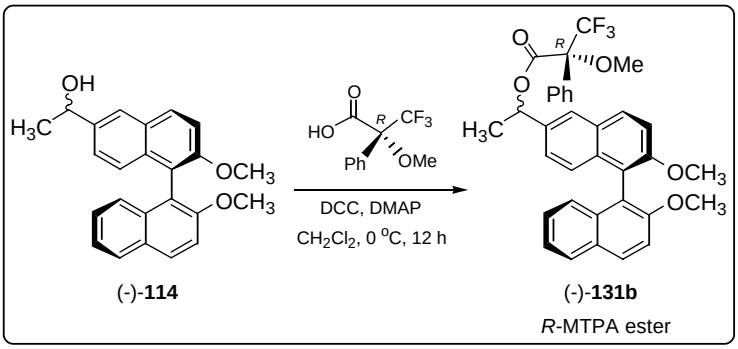
$[\alpha]_D^{25}$ -105.6 (*c* 0.5, $CHCl_3$) (dr was estimated by chiral HPLC analysis on Chiralcel-OD-H column, hexane/2-propanol = 80:20, flow rate: 0.5 mL/min.)

Analytical data calculated for $C_{26}H_{26}O_3$: C, 80.80; H, 6.78; O, 12.42.

Found: C, 80.68; H, 6.59; O, 12.73.

3.2.2 General procedure for the synthesis of MTPA ester 131b of methyl(1,1′-bi-2-naphthyl methyl ether)carbinols 114a.

To the solution of alcohol **114** (0.1 g, 0.36 mmol), (*R*)-MTPA-OH acid (1 mmol) in CH_2Cl_2 (3 mL) under N_2, was added Et_3N (0.14 mL, 1 mmol) and DCC (0.08 mL, 1 mmol) followed by catalytic amount of DMAP (5 mg) and was allowed to stir for 12 h. The reaction mixture was poured into water, and was shaken with CH_2Cl_2 (10 mL). The aqueous layer was extracted in CH_2Cl_2 (2 X 10 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using 90:10 hexane/EtOAc mixture to obtain the (*R*)-MTPA-ester **131b** of alcohol **114a.**

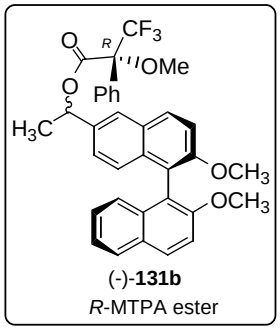


(-)-**131b**:

Yield 0.68 g (72%)

Mp 184-186 °C

IR (KBr) (cm^{-1}) 2935, 2834, 1738, 1618, 1172, 1055



^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.51 (s, 1H), 8.12 (d, *J* = 9.2 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.57-7.53 (m, 4H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.36 (m, 3H), 7.11 (d, *J* = 9.2 Hz, 2H), 3.75 (s, 6H), 3.56 (s, 3H), 1.65 (d, 3H).

$[\alpha]_D^{25}$ -183.3 (*c* 1.00, $CHCl_3$) (dr was estimated by chiral HPLC analysis on Chiralcel-OD-H column, hexane/2-propanol = 80:20, flow rate: 0.5 mL/min.)

LCMS *m/z* 575 (M+1)

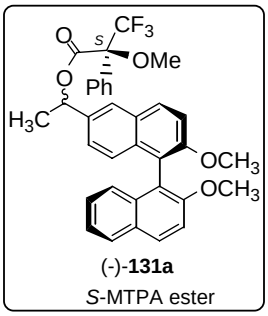
(-)-**131a**:

Yield 0.14 g (68%)

Mp 180-182 °C

IR (KBr) (cm^{-1}) 2935, 2837, 1731, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.52 (s, 1H), 8.13 (d, *J* = 9.2 Hz, 2H), 7.76 (d, *J* = 8.2 Hz, 2H), 7.59-7.54 (m, 4H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.39 (m, 3H), 7.14 (d, *J* = 9.2 Hz, 2H), 3.80 (s, 6H), 3.59 (s, 3H), 1.69 (d, 3H).



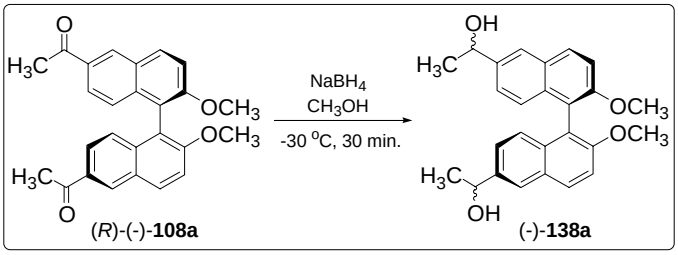
(-)-**131a**
S-MTPA ester

$[\alpha]_D^{25}$ -167.3 (*c* 1.00, $CHCl_3$). (dr was estimated by chiral HPLC analysis on Chiralcel-OD-H column, hexane/2-propanol = 80:20, flow rate: 0.5 mL/min.)

LCMS *m/z* 575 (M+1)

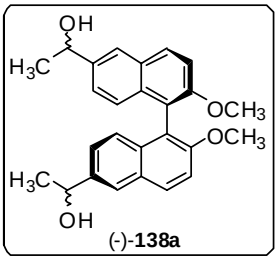
3.2.3 General procedure for the reduction of 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ethers using the $NaBH_4/CH_3OH$ reagent system

To the solution of 6,6′-diacyl-2,2′-bis(methoxy) bi-2-naphthyl **108** (2.0 g, 5 mmol) in THF ((30 mL) at -30 ^oC was added anhydrous $NaBH_4$ (2.66 g, 20 mmol). The mixture was stirred at -30 °C for 5 h. The reaction mixture was poured into water, and was shaken with EtOAc (25 mL). The aqueous layer was extracted in EtOAc (2 X 25 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using 80:20 hexane/EtOAc mixture to obtain the diol product **138a**.



(*R*)-(-)-**108a** (-)-**138a**

(-)-**138a**:



(-)-**138a**

Yield 1.74 g (87%)

Mp 184-186 °C

IR (KBr) (cm^{-1}) 3258, 2935, 2837, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.92 (d, *J* = 8.8 Hz, 2H), 7.80 (s, 2H), 7.41 (d, *J* = 9.2 Hz, 2H), 7.24-7.19 (m, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 4.97-4.94 (m, 2H), 3.72 (s, 6H), 1.98 (bs, 2H), 1.52 (d, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 154.9, 140.7, 133.5, 129.4, 129.0, 125.6, 124.3, 123.9, 119.5, 114.4, 70.3, 56.6, 24.8.

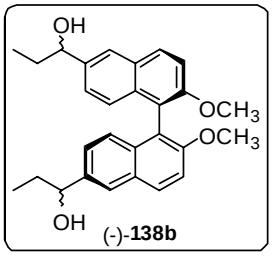
LCMS *m/z* 403 (M+1)

$[\alpha]_D^{25}$ -100.3 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{26}H_{26}O_4$: C, 77.59; H, 6.51; O, 15.90.

Found: C, 78.25; H, 5.53; O, 16.21.

(-)-**138b**:



(-)-**138b**

Yield 0.68 g (78%)

Mp 156-158 °C

IR (KBr) (cm^{-1}) 3246, 2966, 2839, 1616, 1172, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.01 (d, 2H), 7.82 (s, 2H), 7.49 (d, 2H), 7.28-7.21 (m, 2H), 7.12 (d, 2H), 4.74 (m, 2H), 3.81 (s, 6H), 1.89-1.81 (m, 4H), 1.59 (bs, 2H), 0.98 (t, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 154.9, 140.6, 133.4, 129.3, 128.9, 125.6, 124.3, 123.9, 119.5, 114.4, 56.8, 40.0, 26.5, 19.8.

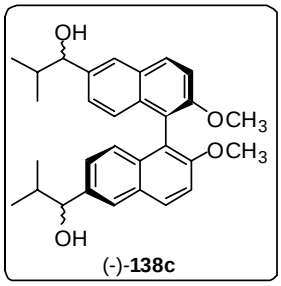
LCMS *m/z* 431 (M+1)

$[\alpha]_D^{25}$ -86.4 (*c* 0.5, $CHCl_3$)

Analytical data calculated for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02; O, 14.86.

Found: C, 78.32; H, 6.95; O, 14.72.

(-)-**138c**:



(-)-**138c**

Yield 0.68 g (75%)

Mp 126-128 °C

IR (KBr) (cm^{-1}) 3237, 2968, 2841, 1616, 1271,1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.51 (s, 2H), 8.11 (d, *J* = 8.8 Hz, 2H), 7.83 (dd, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 8.8 Hz, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 4.42 (m, 2H), 3.81 (s, 6H), 3.71-3.66 (m, 2H), 1.52 (bs, 2H), 1.28 (d, 12H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 154.9, 140.6, 133.4, 129.3, 128.9, 125.6, 124.3, 123.9, 119.5, 114.4, 56.8, 40.4, 24.8, 19.3.

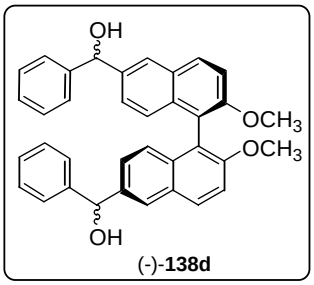
LCMS *m/z* 459 (M+1)

$[\alpha]_D^{25}$ -90.6 (*c* 0.5, $CHCl_3$)

Analytical data calculated for $C_{30}H_{34}O_4$: C, 78.57; H, 7.47; O, 13.96.

Found: C, 78.44; H, 7.55; O, 14.01.

(-)-**138d**:



(-)-**138d**

Yield 0.68 g (75%)

Mp 126-128 °C

IR (KBr) (cm^{-1}) 3237, 2968, 2841, 1616, 1271, 1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.96 (d, *J* = 9.2 Hz, 2H), 7.88 (d, *J* = 6.4 Hz, 2H), 7.46-7.42 (m, 6H), 7.35-7.32 (m, 4H), 7.25 (d, *J* = 7.2 Hz, 2H), 7.18-7.15 (m, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 5.95 (s, 2H), 3.75 (s, 6H), 2.29 (bs, 2H). (Spectrum No. 39)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.1, 143.6, 138.7, 133.5, 129.6, 128.9, 128.4, 127.5, 127.5, 126.6, 125.7, 125.4, 125.3, 114.4, 76.4, 56.9. (Spectrum No.40)

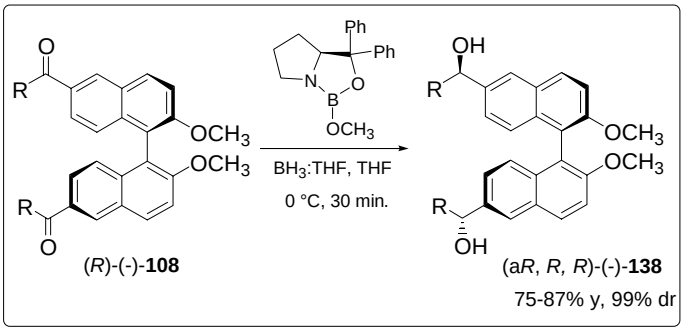
LCMS *m/z* 459 (M+1)

$[\alpha]_D^{25}$ -90.6 (*c* 0.5, $CHCl_3$)

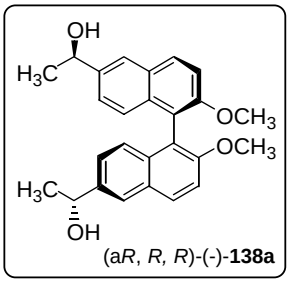
3.2.4 General procedure for the reduction of 6,6′-diacyl-1,1′-bi-2-naphthyl methyl ethers using the 30 mol% oxazaborolidine/BH_3:THF reagent system

To the solution of 6,6′-diacyl-2,2′-bis(methoxy) bi-2-naphthyl **108** (2.0 g, 5 mmol) in THF ((30 mL) at 0 ^{o}C was added 30 mol% oxazaborolidine (prepared *in situ* by the reaction of (*S*)-DPP and trimethyl borate in THF solvent at 25 ^{o}C for 2 h) followed by the addition of BH_3:THF (1 mL, 5 mmol). The mixture was stirred at 0 °C for 30 min. The reaction mixture was poured into water, and was shaken with EtOAc (25 mL). The aqueous layer was extracted in EtOAc (2 X 25 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the

residue was chromatographed on a silica gel column using 80:20 hexane/EtOAc mixture to obtain the alcohol product **138a**.



(a*R*, *R*, *R*)-(-)-**138a**:



Yield 1.74 g (87%)

Mp 184-186 °C

IR (KBr) (cm^{-1}) 3257, 2935, 2837, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.94 (d, *J* = 8.8 Hz, 2H), 7.80 (s, 2H), 7.42 (d, *J* = 9.2 Hz, 2H), 7.24-7.18 (m, 2H), 7.05 (d, *J* = 8.8 Hz, 2H), 4.95 (m, 2H), 3.72 (s, 6H), 1.98 (bs, 2H), 1.52 (d, 6H). (Spectrum No. 35)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.0, 140.7, 133.5, 129.4, 129.0, 125.6, 124.3, 124.0, 119.6, 114.5, 70.4, 24.8. (Spectrum No. 36)

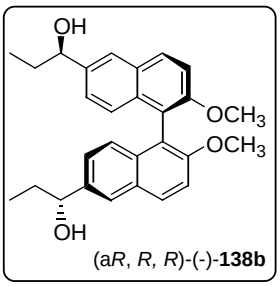
LCMS *m/z* 403 (M+1)

$[\alpha]_D^{25}$ -110.3 (*c* 1.00, $CHCl_3$) (dr was estimated by chiral HPLC analysis on Chiralcel-OD-H column, hexane/2-propanol = 80:20, flow rate: 0.5 mL/min.)

Analytical data calculated for $C_{26}H_{26}O_4$: C, 77.59; H, 6.51; O, 15.90.

Found: C, 77.46; H, 6.47; O, 16.07.

(a*R*, *R*, *R*)-(-)-**138b**:



(a*R*, *R*, *R*)-(-)-**138b**

Yield 0.67 g (78%)

Mp 156-158 °C

IR (KBr) (cm^{-1}) 3246, 2966, 2839, 1616, 1172, 1041

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.0 (d, 2H), 7.82 (s, 2H), 7.48 (d, 2H), 7.28-7.21 (m, 2H), 7.11 (d, 2H), 4.73 (m, 2H), 3.79 (s, 6H), 1.89-1.81 (m, 4H), 1.59 (bs, 2H), 0.96 (t, 6H). (Spectrum No. 37)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 157.1, 157.0, 136.3, 136.2, 132.5, 131.7, 130.7, 128.0, 125.4, 125.3, 124.6, 118.8, 118.7, 114.4, 56.5, 40.4, 26.6, 18.0. (Spectrum No. 38)

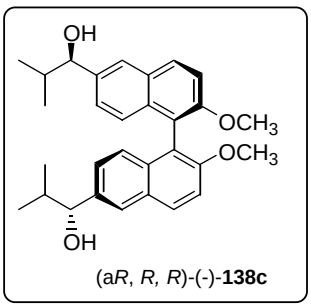
LCMS *m/z* 431 (M+1)

$[\alpha]_D^{25}$ -126.4 (*c* 0.5, $CHCl_3$) (dr was estimated by chiral HPLC analysis on Chiralcel-OD-H column, hexane/2-propanol = 80:20, flow rate: 0.5 mL/min.)

Analytical data calculated for $C_{28}H_{30}O_4$: C, 78.11; H, 7.02; O, 14.86.

Found: C, 78.32; H, 6.95; O, 14.72.

(a*R*, *R*, *R*)-(-)-**138c**:



(a*R*, *R*, *R*)-(-)-**138c**

Yield 0.68 g (75%)

Mp 126-128 °C

IR (KBr) (cm^{-1}) 3218, 2968, 2841, 1616, 1271,1062

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.53 (s, 2H), 8.14 (d, *J* = 8.2 Hz, 2H), 7.89 (dd, *J* = 8.8 Hz, 2H), 7.63 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.8 Hz, 2H), 4.42 (m, 2H), 3.80 (s, 6H), 3.73-3.67 (m, 2H), 1.51 (bs, 2H), 1.27 (d, 12H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.0, 140.7, 133.5, 129.4, 129.0, 125.6, 124.4, 124.0, 119.6, 114.5, 70.4, 56.9, 40.5, 24.8, 18.1.

LCMS *m/z* 459 (M+1)

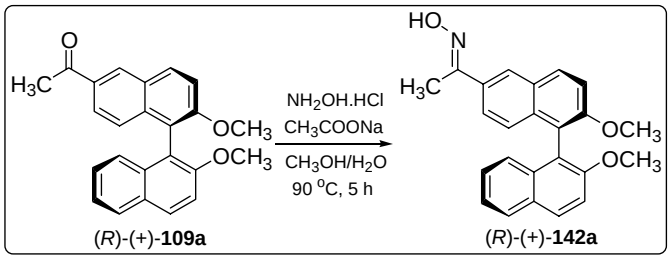
$[\alpha]_D^{25}$ -120.6 (*c* 0.5, $CHCl_3$) (dr was estimated by chiral HPLC analysis on Chiralcel-OD-H column, hexane/2-propanol = 80:20, flow rate: 0.5 mL/min.)

Analytical data calculated for $C_{30}H_{34}O_4$: C, 78.57; H, 7.47; O, 13.96.

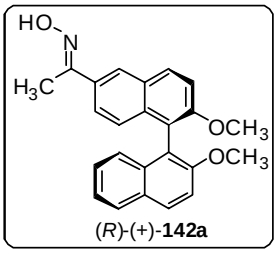
Found: C, 78.43; H, 7.51; O, 14.06.

3.3 Procedure for the preparation of ketoxime 142 of 6-acyl-1,1′-bi-2-naphthyl methyl ether derivative, 109a.

To the solution of 6-acyl-2,2′-bis(methoxy)-bi-2-naphthyl **109** (0.712 g, 2 mmol), in methanol (20 mL) was added $NH_2OH.HCl$ (0.21 g, 6 mmol), sodium acetate (0.24 g, 3 mmol) and water (5 mL). The reaction mixture was heated up to 90 ^{o}C and allowed it to stir for 5 h. The organics were removed by using reduced pressure and the residue was extracted in CH_2Cl_2 (2 X 20 mL). The combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a neutral alumina column using 80:20 hexane/EtOAc mixture to obtain the ketoxime **142** in 83% yield.



(+)-**142a**:



Yield 0.57 g (83%)

Mp 164-165 °C

IR (KBr) (cm^{-1}) 2935, 2837, 1622, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.07 (s, 1H), 7.99-7.96 (m, 2H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 1H), 7.45-7.43 (m, 2H), 7.32 (t, *J* = 8.4 Hz, 1H), 7.21 (t, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 2H), 5.87 (s, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 2.34 (s, 3H). (Spectrum No.41)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 156.0, 155.7, 155.0, 134.4, 133.9, 131.5, 130.0, 129.6, 129.2, 128.7, 128.0, 126.4, 126.0, 125.6, 125.1, 123.7, 123.6, 119.6, 119.2, 114.4, 114.2, 56.9, 56.8, 11.9. (Spectrum No.42)

LCMS *m/z* 372 (M+1)

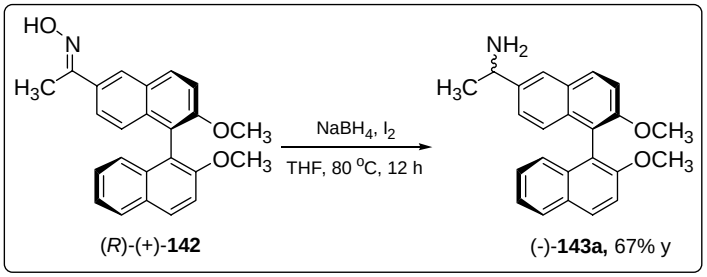
$[\alpha]_D^{25}$ +147.3 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{24}H_{21}NO_3$: C, 77.61; H, 5.70; N, 3.77; O, 12.92.

Found: C, 77.40; H, 5.82; N, 3.71; O, 13.07.

3.3.1 Procedure for the preparation of amine 143 from ketoxime 142.

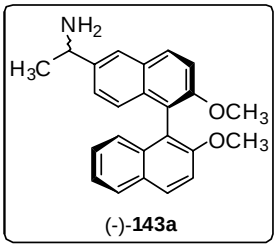
To the solution of ketoxime **142** (0.712 g, 2 mmol), in THF (20 mL) was added $NaBH_4$ (0.38 g, 10 mmol). To this, I_2 (0.13 g, 5 mmol) solution (THF, 10 mL) was added dropwise by using dropping addition funnel in 15 min. The reaction mixture was refluxed at 80 ^oC for 12 h. The reaction mixture was diluted with EtOAc (20 mL), and was shaken with sodium thiosulfate solution (3 X 20 mL) three times . The combined organics were washed with brine solution (20 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a alumina column using 80:20 hexane/EtOAc mixture to obtain the corresponding amine **143**.



(*R*)-(+)-**142** (-)-**143a,** 67% y

(-)-**143a**:

Yield 0.43 g (67%)



(-)-**143a**

Mp 164-166 °C

IR (KBr) (cm^{-1}) 3324, 2935, 2837, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.97 (t, 2H), 7.87 (d, 1H), 7.75 (s, 1H), 7.50-7.45(m, 2H), 7.37-7.21 (m, 2H), 7.13 (d, *J* = 8.8 Hz, 1H), 7.05 (d, *J* = 8.8 Hz, 2H), 4.08 (q, 1H), 3.77 (s, 6H), 1.66 (dd, 3H). (Spectrum No. 45)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.6, 154.9, 136.3, 133.9, 129.7, 129.5, 129.2, 128.9, 128.0, 126.8, 126.5, 125.5, 125.0, 123.9, 123.8, 123.6, 119.7, 119.0, 115.0, 114.1, 58.6, 56.9, 56.8, 19.3. (Spectrum No. 46)

LCMS *m/z* 358 (M+1)

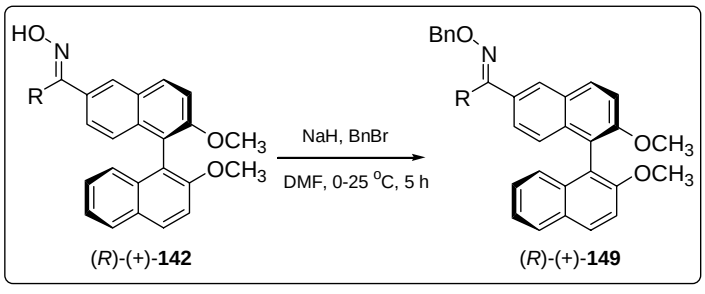
$[\alpha]_D^{25}$ -67.6 (*c* 1.0, $CHCl_3$)

Analytical data calculated for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92; O, 8.95.

Found: C, 80.51; H, 6.37; N, 4.02; O, 9.10.

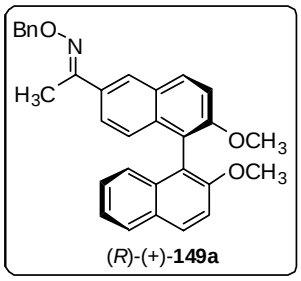
3.3.2 Procedure for the preparation of ketoxime ethers 149 from ketoxime 142

To the solution of ketoxime **142a** (0.742 g, 2 mmol), in DMF (10 mL) was added $PhCH_2Br$ (2.2 mmol) followed by the slow addition of sodium hydride (4 mmol) at 0 ^oC for 15 min. and allowed to stir for 5 h. The reaction mixture was quenched with methanol and removed the organics using rotavapour. The crude residue was diluted with EtOAc (20 mL), and washed with water for 3 times. The combined organics were washed with brine solution (20 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a neutral alumina column using 85:15 hexane/EtOAc mixture to obtain the corresponding ketoxime ether **149**.



(*R*)-(+)-**142** (*R*)-(+)-**149**

(+)-**149a**:



(*R*)-(+)-**149a**

Yield 0.84g (91%)

Mp 152-154 °C

IR (KBr) (cm^{-1}) 2935, 2837, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.05 (s, 1H), 7.99 (dd, 2H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.45-7.42 (m, 4H), 7.38-7.34 (m, 2H), 7.24 (t, *J* = 7.2 Hz, 2H), 7.20 (d, *J* = 7.2 Hz, 1H), 7.09 (d, *J* = 7.6 Hz, 2H), 5.25 (s, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 2.37 (s, 3H). (Spectrum No. 43)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.6, 154.9, 138.2, 134.3, 131.7, 130.0, 129.5, 129.2, 129.2, 128.7, 128.3, 128.2, 128.0, 127.7, 126.4, 125.9, 125.4, 125.1, 124.0, 123.5, 119.6, 114.3, 114.2, 56.9, 56.8, 12.7. (Spectrum No. 44)

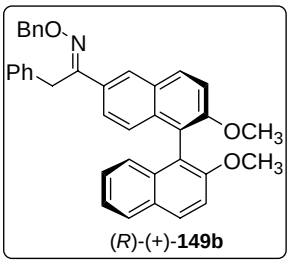
LCMS *m/z* 462 (M+1)

$[\alpha]_D^{25}$ +154.7 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{31}H_{27}NO_3$: C, 80.67; H, 5.90; N, 3.03; O, 10.40.

Found: C, 71.20; H, 4.45; N, 4.39; O, 19.96.

(+)-**149b**:



(*R*)-(+)-**149b**

Yield 0.86g (86%)

Mp 146-148 °C

IR (KBr) (cm^{-1}) 2935, 2837, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.07 (s, 1H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 7.2 Hz, 1H), 7.68 (d, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 9.2 Hz, 2H), 7.38-7.32 (m, 8H), 7.30-7.20 (m, 4H), 7.09 (t, *J* = 9.2 Hz, 2H), 5.29 (s, 2H), 4.29 (s, 2H), 3.78 (s, 3H), 3.77 (s, 3H). (Spectrum No.51)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 156.3, 155.7, 155.0, 138.0, 137.0, 134.4, 134.0, 130.8, 130.1, 129.5, 129.2, 128.7, 128.6, 128.3, 128.0, 127.7, 126.5, 126.4, 126.2, 125.5, 125.2, 124.3, 123.6, 119.5, 119.2, 114.2, 114.1, 76.4, 56.9, 56.8, 32.6. (Spectrum No. 52)

LCMS *m/z* 538 (M+1)

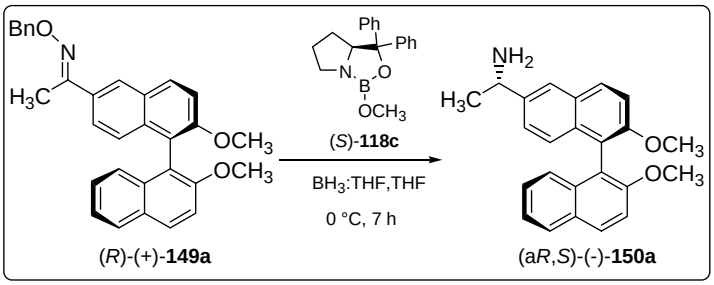
$[\alpha]_D^{25}$ +161.4 (*c* 1.0, $CHCl_3$)

Analytical data calculated for $C_{37}H_{31}NO_3$: C, 82.66; H, 5.81; N, 2.61; O, 8.93.

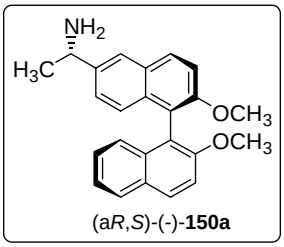
Found: C, 82.72; H, 5.93; N, 2.52; O, 8.86.

3.3.3 Procedure for the preparation of amine from ketoxime ether

To the solution of ketoxime ether **149a** (1.76 g, 2 mmol) in THF (30 mL) at 0 ^{o}C was added 30 mol% oxazaborolidine (prepared *in situ* by the reaction of (*S*)-DPP and trimethyl borate in THF solvent at 25 ^{o}C for 2 h) followed by the addition of BH_3:THF (1 mL, 5 mmol). The mixture was stirred at 0 °C for 30 min and allowed it to stir for another 7 h at 25 ^{o}C. The reaction mixture was poured into water, and was shaken with EtOAc (25 mL). The aqueous layer was extracted in EtOAc (2 X 25 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a neutral alumina column using 80:20 hexane/EtOAc mixture to obtain the amine **150a.**



(*R*,*S*)-(-)-**150a**:



Yield 0.97g (72%)

Mp 172-174 °C

IR (KBr) (cm^{-1}) 3324, 2935, 2837, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.98 (t, *J* = 9.2 Hz, 2H), 7.88 (d, *J* = 8.4 Hz, 1H), 7.82 (s, 1H), 7.47 (d, 2H), 7.30-7.14 (m, 3H), 7.10 (m, 2H), 4.70-4.60 (m, 2H), 4.30 (q, *J* = 6.4 Hz, 1H), 3.77 (s, 6H), 1.44 (d, *J* = 6.4 Hz, 3H). (Spectrum No. 47)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.7, 154.9, 136.2, 133.9, 129.6, 129.5, 129.2, 128.8, 128.5, 128.0, 127.0, 126.7, 126.4, 125.5, 125.0, 123.8, 123.6, 119.6, 119.0, 115.0, 114.1, 58.5, 56.8, 56.7, 19.3. (Spectrum No. 48)

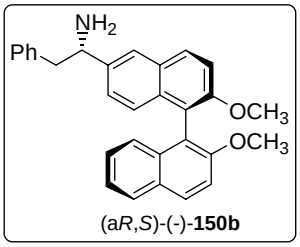
LCMS *m/z* 358 (M+1)

$[\alpha]_D^{25}$ -177.6 (*c* 1.00, $CHCl_3$) (dr was estimated by ^{1}H-NMR analysis)

Analytical data calculated for $C_{24}H_{23}NO_2$: C, 80.64; H, 6.49; N, 3.92; O, 8.95.

Found: C, 80.48; H, 6.40; N, 4.05; O, 9.07.

(-)-**150b**:



(a*R*,*S*)-(-)-**150b**

Yield 0.86g (86%)

Mp 146-148 °C

IR (KBr) (cm^{-1}) 2935, 2837, 1614, 1174, 1057

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.04-7.86 (m, 4H), 7.57-7.41 (m, 4H), 7.30-7.24 (m, 4H), 7.21-7.14 (m, 2H), 7.07 (d, *J* = 6.8 Hz, 2H), 5.63-5.55 (m, 2H), 5.24 (s, 2H), 4.58 (t, 1H), 3.77 (s, 6H). (Spectrum No. 53)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 158.5, 155.7, 154.9, 136.5, 131.4, 130.8, 130.1, 129.7, 129.2, 128.1, 126.6, 126.5, 126.4, 125.7, 125.1, 124.9, 123.6, 119.5, 118.6, 114.1, 114.0, 56.9, 56.8, 55.3, 44.6. (Spectrum No. 54)

LCMS *m/z* 538 (M+1)

$[\alpha]_D^{25}$ -161.4 (*c* 1.00, $CHCl_3$). (dr was estimated by ^{1}H-NMR analysis)

Analytical data calculated for $C_{30}H_{27}NO_2$: C, 83.11; H, 6.28; N, 3.23; O, 7.38.

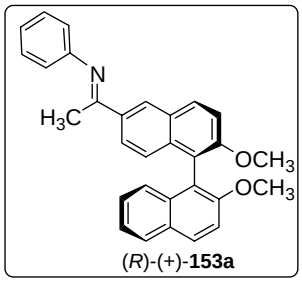
Found: C, 83.24; H, 6.35; N, 3.35; O, 7.46.

3.3.4 Procedure for the preparation of ketimine 153a from 6-acetyl-1,1′-bi-2-naphthyl methyl ether derivative 109a.

To the solution of 6-acetyl-1,1′-bi-2-naphthyl methyl ether derivative **109a** (0.712g, 2 mmol) in CH_2Cl_2 (40 mL) was added Et_3N (0.5 mL, 5 mmol) and aniline (0.2 mL, 4 mmol) under N_2 atmosphere. To this, $TiCl_4$ (2 mmol, 0.22 mL) in CH_2Cl_2 (10 mL) was added dropwise under N_2 at 0 ^oC for 15 min. The reaction mixture was stirred for 0.5 h at 0 ^oC and stirred further for 7 h at 25 ^oC. It was quenched with a saturated K_2CO_3 solution (30 mL),

and the reaction mixture was filtered through a Buchner funnel. The organic layer was separated from the filtrate and the remaining aqueous layer was extracted with CH_2Cl_2 (2 X 30 mL). The combined organics were washed with brine (20 mL) and dried over anhydrous Na_2CO_3. The solvent was and the residue was chromatographed on neutral alumina using 85:15 mixture of hexane/ethyl acetate to obtain pure product **153a.**

(+)-**153a**:



(*R*)-(+)-**153a**

Yield 0.84 g (82%)

Mp 172-174 °C

IR (KBr) (cm^{-1}) 2944, 2862, 1623, 1619, 1177, 1054

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.42 (s, 1H), 8.09 (d, *J* = 9.2 Hz, 1H), 8.01 (d, *J* = 9.2 Hz, 1H), 7.98 (d, 1H), 7.95 (d, 1H), 7.50 (t, *J* = 8.8 Hz, 2H), 7.39-7.33 (m, 3H), 7.27-7.10 (m, 4H), 6.83 (d, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 3.78 (s, 3H), 2.34 (s, 3H). (Spectrum No.55)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 165.2, 156.1, 155.0, 151.9, 135.2, 134.6, 134.0, 130.6, 129.6, 129.2, 129.0, 128.5, 128.0, 127.9, 126.4, 125.5, 125.1, 124.7, 123.6, 123.1, 119.5, 119.2, 115.1, 114.3, 114.2, 56.9, 56.7, 17.2. (Spectrum No.56)

LCMS *m/z* 432 (M+1)

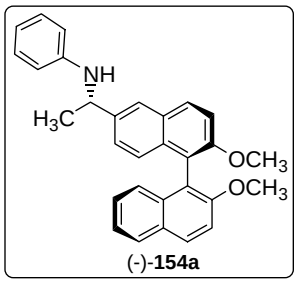
$[\alpha]_D^{25}$ +172.4 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{30}H_{25}NO_2$: C, 83.5; H, 5.84; N, 3.25; O, 7.42.

Found: C, 83.61; H, 5.95; N, 3.12; O, 7.30.

3.3.5 Procedure for the preparation of amine 154a from ketimine 153a.

The amine **154a** was prepared following the experimental procedure described in 3.3.3.



(-)-**154a**

Yield 0.59 g (60%)

Mp 172-174 °C

IR (KBr) (cm^{-1}) 3321, 2942, 2854, 1621, 1618, 1175, 1055

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.90 (d, 1H), 7.87 (d, 1H), 7.85 (d, 1H), 7.84 (s, 1H), 7.48-7.43 (m, 2H), 7.34-7.31 (m, 1H), 7.29-7.21 (m, 2H), 7.19-7.06 (m, 4H), 6.64 (t, *J* = 8.0 Hz, 1H), 6.56 (d, *J* = 8.0 Hz, 2H), 4.58 (q, *J* = 6.8 Hz, 1H), 4.07 (bs, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 1.56 (dd, 3H). (Spectrum No.57)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.0, 154.9, 147.5, 140.2, 140.1, 134.1, 133.4, 129.5, 129.4, 129.2, 128.0, 126.4, 125.9, 125.4, 125.1, 124.4, 124.3, 123.6, 119.6, 117.2, 114.4, 114.2, 113.4, 57.0, 56.9, 53.5, 24.8. (Spectrum No.58)

LCMS *m/z* 434 (M+1)

$[\alpha]_D^{25}$ +172.4 (*c* 1.00, $CHCl_3$) (dr was estimated by ^{1}H-NMR analysis)

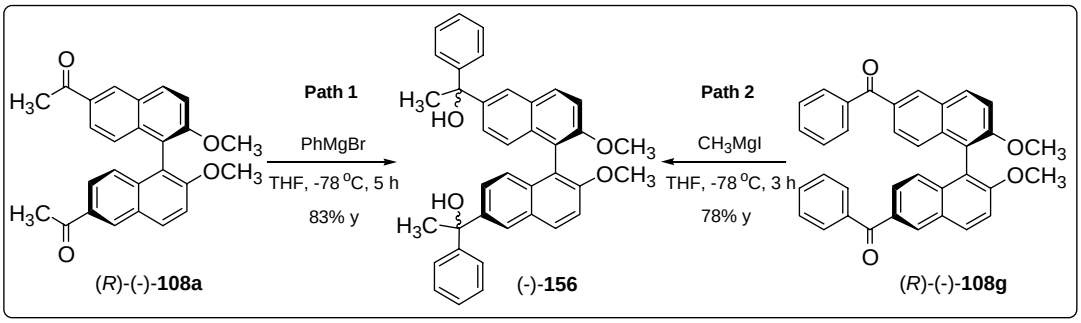
Analytical data calculated for $C_{30}H_{27}NO_2$: C, 83.11; H, 6.28; N, 3.23; O, 7.38.

Found: C, 83.32; H, 6.09; N, 3.12; O, 7.45.

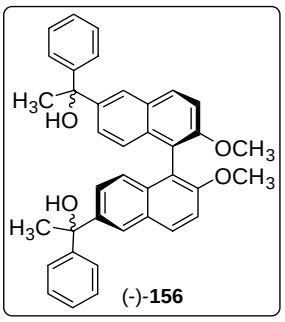
3.4 Procedure for the preparation of alcohol 156.

To the solution of diketone **108a** (0.798 g, 2 mmol), in THF (20 mL) was added PhMgBr (0.5 mL, 6 mmol) at -78 ^{o}C and allowed to stir for 5 h. The reaction mixture was diluted with EtOAc (20 mL), and was shaken with sodium thiosulfate solution three times. The combined organics were washed with brine solution (20 mL) and dried over anhydrous

Na_2SO_4. The solvent was removed and the residue was chromatographed on a alumina column using 80:20 hexane/EtOAc mixture to obtain the corresponding alcohol **156**.



(-)-**156**:



Yield 0.74g (83%)

Mp 146-148 °C

IR (KBr) (cm^{-1}) 2964, 2847, 1768, 1599, 1022

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.79 (s, 2H), 7.29-7.28 (d, 4H), 7.18-7.12 (m, 8H), 7.09-7.07 (m, 2H), 7.02-6.85 (m, 4H), 3.61 (s, 6H), 2.12 (bs, 2H), 1.86 (s, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.1, 147.9, 142.8, 133.0, 130.9, 129.7, 128.7, 128.1, 126.9, 125.9, 125.7, 125.1, 123.9, 119.4, 114.3, 68.2, 56.9, 30.8.

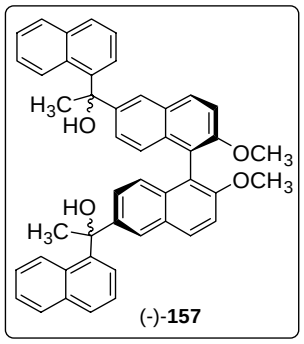
LCMS *m/z* 583 (M+1)

$[\alpha]_D^{25}$ +95.2 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{38}H_{30}O_6$: C, 78.33; H, 5.19; O, 16.48.

Found: C, 78.39; H, 5.12; O, 16.49.

(-)-**157**:



(-)-**157**

Yield 0.74g (83%)

Mp 146-148 °C

IR (KBr) (cm^{-1}) 2964, 2847, 1768, 1599, 1022

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.91-7.87 (m, 2H), 7.83-7.70 (m, 12H), 7.38-7.22 (m, 6H), 7.16-6.85 (m, 4H), 3.61 (s, 6H), 2.41 (bs, 2H), 2.01 (d, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.0, 143.4, 142.2, 134.8, 132.9, 130.9, 130.7, 129.7, 129.0, 128.8, 127.0, 125.7, 125.1, 124.7, 124.2, 123.7, 119.3, 114.3, 114.2, 68.2, 56.9, 32.6.

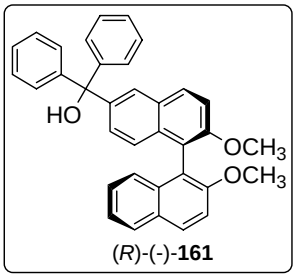
LCMS *m/z* 583 (M+1)

$[\alpha]_D^{25}$ +95.2 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{38}H_{30}O_6$: C, 78.33; H, 5.19; O, 16.48.

Found: C, 78.39; H, 5.12; O, 16.49.

(*R*)-(-)-**161**:



(*R*)-(-)-**161**

Yield 0.87g (75%)

Mp 182-184 °C

IR (KBr) (cm^{-1}) 3216, 2964, 2841, 1619, 1273, 1061

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.93-7.87 (m, 3H), 7.81-7.73 (m, 10H), 7.41-7.34 (m, 4H), 7.21-7.15 (m, 4H), 3.83(s, 6H), 2.43 (bs, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 156.4, 147.4, 143.8, 142.5, 136.2, 135.7, 135.3, 134.8, 134.1, 133.7, 132.4, 132.0, 129.8, 128.6, 127.7, 127.1, 126.9, 126.3, 125.6, 121.7, 119.6, 119.2, 116.8, 116.3, 114.3, 82.1, 56.9.

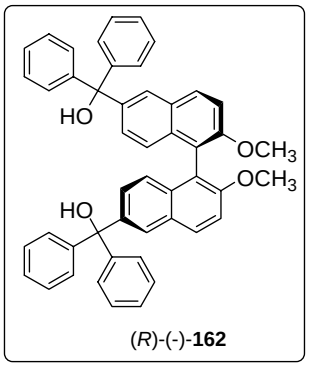
LCMS *m/z* 498 (M+1)

$[\alpha]_D^{25}$ -105.6 (*c* 0.5, $CHCl_3$)

Analytical data calculated for $C_{30}H_{30}O_4$: C, 79.27; H, 6.65; O, 14.08.

Found: C, 79.34; H, 6.77; O, 13.89.

(*R*)-(-)-**162**:



(*R*)-(-)-**162**

Yield 0.91g (82%)

Mp 138-140 °C

IR (KBr) (cm^{-1}) 3342, 2964, 2847, 1597, 1021

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.96 (s, 2H), 7.49-7.43 (m, 6H), 7.32-7.28 (m, 12H), 7.26-7.16 (m, 8H), 6.98 (d, 2H), 3.74 (s, 6H), 2.12 (bs, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 155.3, 146.8, 141.8, 133.1, 133.0, 128.4, 128.0, 127.9, 127.2, 126.8, 126.7, 125.2, 119.3, 114.3, 82.1, 56.9.

LCMS *m/z* 679 (M+1)

$[\alpha]_D^{25}$ -145.4 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{38}H_{30}O_6$: C, 78.33; H, 5.19; O, 16.48.

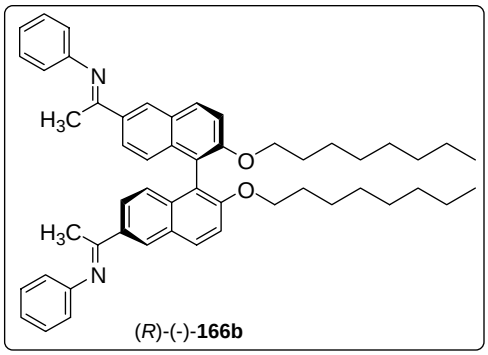
Found: C, 78.39; H, 5.12; O, 16.49.

3.5.1 Procedure for the preparation of ketimine 166b from diketone 108l.

The ketimine **166b** was prepared following the experimental procedure described in 3.3.4.

Yield 1.10 g (74%)

IR (Neat) (cm^{-1}) 2949, 2872, 1621, 1617, 1172, 1058



(*R*)-(-)-**166b**

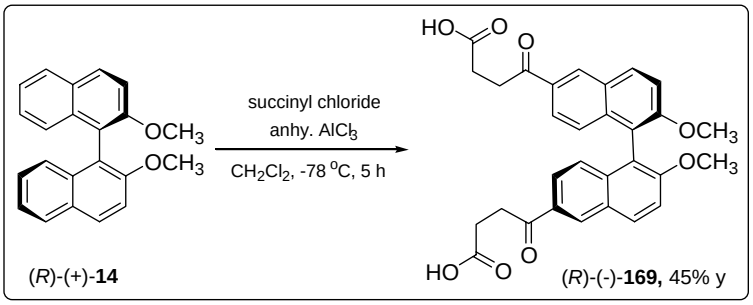
^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.42 (s, 2H), 8.05 (d, *J* = 8.8 Hz, 2H), 7.95 (d, *J* = 7.2 Hz, 2H), 7.46 (d, *J* = 9.2 Hz, 2H), 7.36 (t, *J* = 8.0 Hz, 4H), 7.20 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 7.2 Hz, 2H), 6.81 (d, *J* = 8.0 Hz, 4H), 4.03-3.95 (m, 4H), 2.34 (s, 6H), 1.45-1.26 (m, 4H), 1.25-1.22 (m, 4H), 1.08-0.98 (m, 13H), 0.89-0.85 (m, 9H). (Spectrum No.59)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 165.1, 155.8, 152.0, 135.3, 134.4, 130.3, 128.9, 128.5, 127.8, 125.5, 124.4, 123.0, 119.5, 115.8, 69.5, 31.7, 29.4, 29.2, 29.1, 25.7, 22.6, 17.2, 14.1. (Spectrum No.60)

LCMS *m/z* 746 (M+1)

3.5.2 Procedure for the acylation of 1,1′-bi-2-naphthyl methyl ether using succinyl chloride and $AlCl_3$.

Anhydrous $AlCl_3$ (0.67 g, 5 mmol) and succinyl chloride (2 mmol) were added to CH_2Cl_2 (30 mL) at 0°C. To this mixture, 2,2′-bis(methoxy)-bi-2-naphthyl (0.628 g, 2 mmol) **14** was added, and the mixture was stirred at -78 °C for 5 h. The reaction mixture was poured into ice cold water, and was shaken with CH_2Cl_2 (25 mL). The aqueous layer was extracted in CH_2Cl_2 (2 X 25 mL), and the combined organic phases were washed with brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the residue was chromatographed on a silica gel column using 80:20 hexane/EtOAc mixture to obtain the diketoacid **169** in 45% yield.



(*R*)-(-)-**162**:

Yield 0.51 g (45%)

Mp 158-160 °C

IR (KBr) (cm^{-1}) 3468, 2962, 2839, 1716, 1674, 1614, 1481, 1261

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.64 (s, 2H), 8.22 (d, *J* = 8.8 Hz, 2H), 7.72 (d, *J* = 8.8 Hz 2H), 7.61 (d, *J* = 8.8 Hz, 2H), 7.04 (d, *J* = 9.2 Hz, 2H), 3.78 (s, 6H), 3.37 (t, *J* = 6.4 Hz, 4H), 2.69 (t, *J* = 6.4 Hz, 4H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 196.5, 172.9, 155.7, 134.6, 130.5, 129.0, 126.5, 123.7, 122.9, 117.0, 113.3, 55.4, 31.8, 26.9.

LCMS *m/z* 513 (M-1)

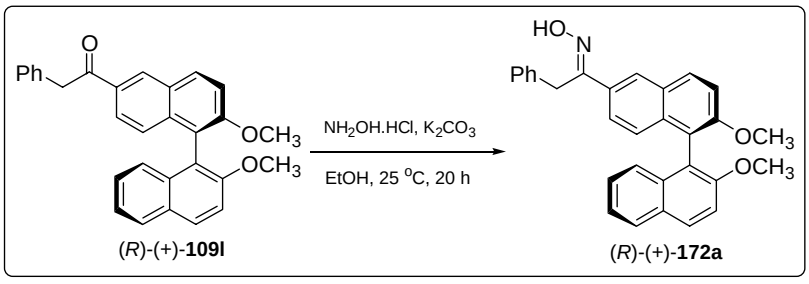
$[\alpha]_D^{25}$ -127.2 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{38}H_{30}O_6$: C, 78.33; H, 5.19; O, 16.48.

Found: C, 78.39; H, 5.12; O, 16.49.

3.6 Procedure for the preparation of ketoxime 172 of 6-acyl-1,1′-bi-2-naphthyl methyl ether derivative, 109.

To the solution of 6-phenylacyl-2,2′-bis(methoxy) bi-2-naphthyl **109l** (0.62 g, 2 mmol), in ethanol (20 mL) was added $NH_2OH.HCl$ (0.14 g, 4 mmol) and potassium carbonate (0.5 g, 5 mmol). The reaction mixture was allowed to stir for 20 h. The organics were removed by using reduced pressure and the residue was extracted in CH_2Cl_2 (2 X 20 mL), and the combined organic phases were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the product, ketoxime **172a** obtained was used in the next step without further purification.



(*R*)-(+)-**109l** (*R*)-(+)-**172a**

(*R*)-(+)-**172a**:

Yield 0.87 g (97%)

Mp 156-158 °C

IR (KBr) (cm^{-1}) 3267, 2939, 2839, 1619, 1606, 1514, 1344

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.56 (s, 1H), 8.08-7.88 (m, 3H), 7.32-7.09 (m, 12 H), 4.31 (s, 2H), 3.78 (s, 6H), 1.66 (bs, 1H). (Spectrum No.49)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 157.3, 155.8, 154.9, 136.8, 134.4, 133.9, 130.5, 129.2, 125.7, 125.1, 124.0, 119.6, 119.1, 114.4, 114.1, 56.9, 31.0. (Spectrum No.50)

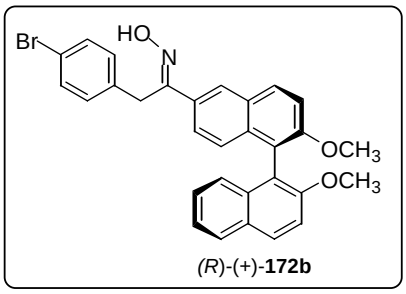
LCMS *m/z* 448 (M+1)

$[\alpha]_D^{25}$ -123.2 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{30}H_{25}NO_3$: C, 68.45; H, 4.60; Br, 15.18; N, 2.66; O, 9.12.

Found: C, 68.39; H, 4.65; Br, 15.21; N, 2.62; O, 9.14.

(*R*)-(+)-**172b**:



(R)-(+)-**172b**

Yield 0.72 g (70%)

Mp 148-150 °C

IR (KBr) (cm^{-1}) 2964, 2847, 1621, 1599, 1022

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.64 (s, 1H), 8.12-7.85 (m, 3H), 7.43-7.18 (m, 11H), 4.39 (s, 2H), 3.82 (s, 6H), 1.69 (bs, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 163.5, 157.8, 135.4, 134.3, 133.5, 131.8, 131.3, 130.6, 127.8, 126.5, 125.2, 118.1, 114.6, 113.2, 112.7, 56.8, 31.2.

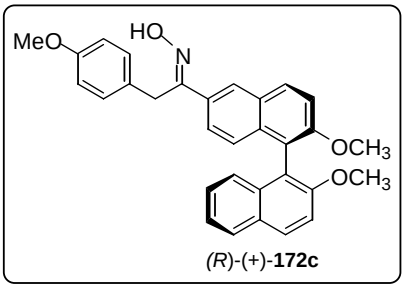
LCMS *m/z* 528 (M+2)

$[\alpha]_D^{25}$ +95.2 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{30}H_{24}BrNO_3$: C, 68.48; H, 4.57; Br, 15.22; N, 2.64; O, 9.18.

Found: C, 68.36; H, 4.61; Br, 15.23; N, 2.68; O, 9.11.

(*R*)-(+)-**172c**:



(*R*)-(+)-**172c**

Yield 0.71 g (74%)

Mp 132-134 °C

IR (KBr) (cm^{-1}) 2964, 2847, 1618, 1593, 1020

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.39 (s, 1H), 7.98-7.09 (m, 14H), 4.28 (s, 2H), 3.84 (s, 3H), 3.77 (s, 6H), 1.65 (bs, 1H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 163.4, 156.4, 155.2, 146.1, 138.2, 134.2, 132.6, 130.7, 129.9, 128.2, 126.7, 125.4, 124.7, 123.6, 119.1, 114.4, 56.8, 56.6, 56.5.

LCMS *m/z* 478 (M+1)

$[\alpha]_D^{25}$ +105.2 (*c* 1.00, $CHCl_3$)

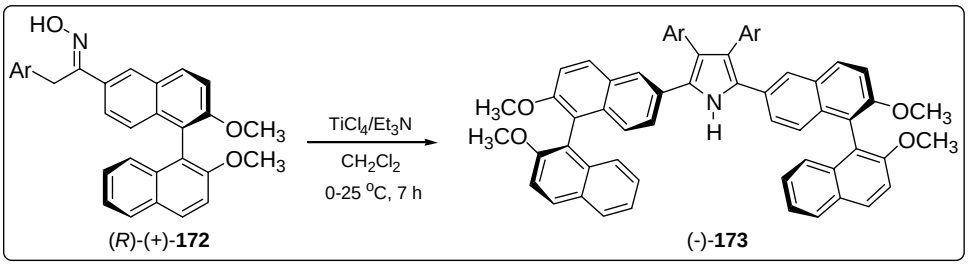
Analytical data calculated for $C_{31}H_{27}NO_4$: C, 77.97; H, 5.70; N, 2.93; O, 13.40.

Found: C, 77.94; H, 5.73; N, 2.96; O, 13.37.

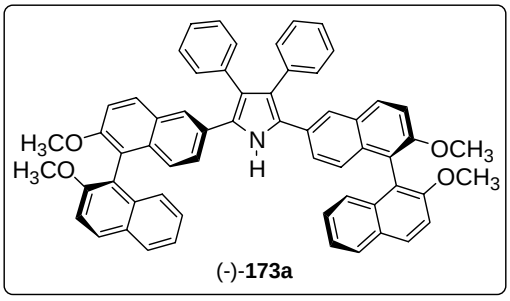
3.6.1 Procedure for the synthesis of chiral pyrrole 173a from ketoxime 172a.

Dichloromethane (25 mL), Et_3N (0.42 mL, 3 mmol) and ketoxime **172a** (0.45 g, 1 mmol) were taken under an N_2 atmosphere. $TiCl_4$ (0.26 mL, 2.5 mmol) in CH_2Cl_2 was added drop wise under N_2 at 0 ^oC for 15 min. The reaction mixture was stirred for 0.5 h at 0 ^oC and stirred further for 7 h at 0 to 25 ^oC. It was quenched with a saturated K_2CO_3 solution (10

mL) and the reaction mixture was filtered through a Buchner funnel. The precipitate was washed with CH_2Cl_2 (2 X 10 mL) and the combined organics were evaporated using rotary evaporator to obtain the chiral pyrrole **173a**.



(-)-**173a:**



Yield 0.36 g (85%)

Mp 134-136 °C

IR (KBr) (cm^{-1}) 3267, 2939, 1619, 1606, 1514, 1344

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.99-7.96 (m, 3H), 7.89-7.80 (m, 7H), 7.70 (s, 1H), 7.48-7.10 (m, 17H), 6.98-6.94 (m, 4H), 3.77-3.74 (m, 12H). (Spectrum No. 61)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 157.3,154.9, 136.6, 135.7, 133.8, 132.2, 132.0, 131.6, 131.3, 131.1, 130.4, 129.7, 129.1, 128.0, 126.5, 125.7, 125.4, 124.9, 123.6, 121.5, 119.5, 114.4, 114.1, 114.0, 56.8, 56.6. (Spectrum No. 62)

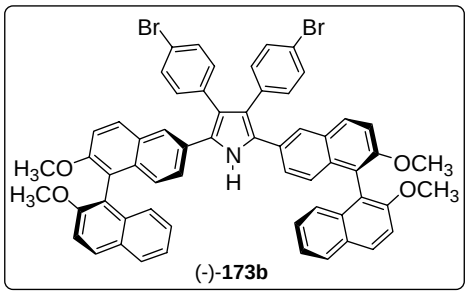
LCMS *m/z* 842 (M+1)

$[\alpha]_D^{25}$ -178.2 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{60}H_{45}NO_4$: C, 85.38; H, 5.37; N, 1.66; O, 7.58.

Found: C, 85.36; H, 5.39; N, 1.70; O, 7.52.

(-)-**173b:**



(-)-**173b**

Yield 0.48 g (78%)

Mp 142-144 °C

IR (KBr) (cm^{-1}) 3279, 2942, 2835, 1618 , 1604, 1348

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.04-7.87 (m, 8H), 7.85 (d, 2H), 7.50-7.42(m, 12H), 7.36-6.99 (m, 8H), 3.82-3.73 (m, 12H).

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 157.3, 154.9, 136.6, 135.7, 133.8, 132.5, 132.0, 131.6, 131.3, 131.1, 130.5, 129.8, 129.2, 129.1, 128.1, 126.5, 125.9, 125.6, 124.9, 123.6, 121.6, 119.6, 118.7, 114.5, 57.6, 56.8.

LCMS *m/z* 1003 (M+2)

$[\alpha]_D^{25}$ -172.5 (*c* 1.00, $CHCl_3$)

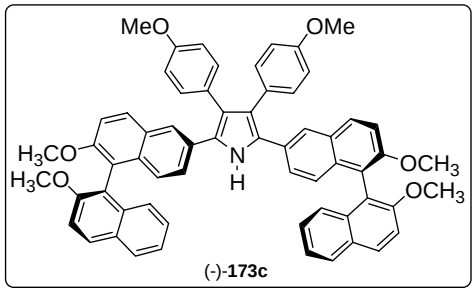
Analytical data calculated for $C_{60}H_{43}Br_2NO_4$: C, 71.94; H, 4.33; Br, 15.95; N, 1.40; O, 6.39.

Found: C, 71.98; H, 4.35; Br, 15.89, N, 1.37; O, 6.41.

(-)-**173c:**

Yield 0.44 g (82%)

Mp 138-140 °C



(-)-**173c**

IR (KBr) (cm^{-1}) 3267, 2937, 1619, 1608, 1514, 1343

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 7.85-7.46 (m, 8 H), 7.45-7.41 (m, 5 H), 7.32-7.29 (m, 3 H), 7.23-7.0 (m, 14H), 3.82-3.69 (m, 18H). (Spectrum No. 63)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 157.3, 154.9, 136.6, 135.7, 133.8, 132.5, 132.0, 131.6, 131.3, 131.1, 130.5, 129.8, 129.2, 128.1, 126.5, 125.9, 125.6, 124.9, 123.6, 121.5, 119.6, 118.7, 114.5, 114.1, 57.6, 56.8, 56.6. (Spectrum No. 64)

LCMS *m/z* 905 (M+1)

$[\alpha]_D^{25}$ -168.7 (*c* 1.00, $CHCl_3$)

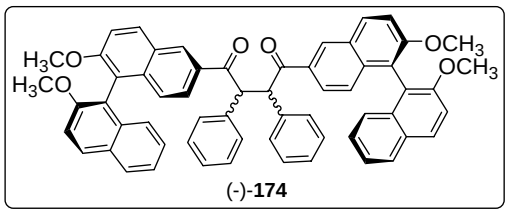
Analytical data calculated for $C_{62}H_{49}NO_6$: C, 82.37; H, 5.46; N, 1.55; O, 10.62.

Found: C, 82.41; H, 5.42; N, 1.49; O, 10.68.

3.6.2 Procedure for the preparation of diketone 174:

To the solution of 6-phenylacyl-2,2′-bis(methoxy) bi-2-naphthyl **109l** (0.62 g, 2 mmol), in THF (20 mL) was added potassium tert-butoxide (0.45 g, 4 mmol) in small portions over a period of 20 min at 0 °C. The transparent solution was allowed to stir for another 20 min. followed by the dropwise addition of iodine (0.508 g, 2 mmol) in 20 mL of anhydrous THF. The reaction mixture was allowed to stir for 5 h at 0 to 25 °C. Aqueous sodium bisulfate was added to remove excess iodine. The mixed solution was extracted with EtOAc (2 X 20 mL). The combined organics were washed with water (10 mL), brine solution (10 mL) and dried over anhydrous Na_2SO_4. The solvent was removed and the

residue was chromatographed on a silica gel column using 70:30 hexane/EtOAc mixture to obtain the diketone **174** in 83% yield.



(-)-**174**

Yield 0.56 g (83%)

Mp 146-148 °C

IR (KBr) (cm^{-1}) 2984, 2968, 1643, 1596, 1023

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm): 8.61 (s, 2H), 8.03 (d, *J* = 8.6 Hz, 2H), 7.96 (d, *J* = 8.8 Hz, 2H), 7.85 (d, *J* = 8.6 Hz, 2H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.63 (t, *J* = 9.6 Hz, 1H), 7.44 (t, *J* = 8.8 Hz, 4H), 7.41-7.30 (m, 5H), 7.26-7.19 (m, 6H), 7.04-6.99 (m, 6H), 5.55 (d, 2H), 3.77 (s, 6H), 3.72 (s, 6H). (Spectrum No. 65)

^{13}C-NMR (100 MHz, $CDCl_3$, δ ppm): 195.6, 157.5, 155.0, 147.1, 142.4, 136.7, 133.8, 131.5, 131.4, 130.8, 130.6, 129.9, 129.2, 128.1, 127.9, 126.5, 126.1, 124.8, 124.4, 123.8, 123.7, 119.8, 118.5, 114.8, 114.0, 56.8, 56.6, 44.9. (Spectrum No. 66)

LCMS *m/z* 864 (M+1)

$[\alpha]_D^{25}$ +119.6 (*c* 1.00, $CHCl_3$)

Analytical data calculated for $C_{60}H_{46}O_6$: C, 83.50; H, 5.37; O, 11.12.

Found: C, 83.46; H, 5.39; O, 11.15.

3.6.3 Procedure for the synthesis of chiral pyrrole 173a from diketone 174

To the solution of diketone **174** (1 mmol, 0.87 g) in acetic acid (5 mL) was added ammonium acetate (1.7 g, 22 mmol) and the reaction mixture was allowed to reflux for 36 h. The reaction was poured into ice water and extracted with ethyl acetate (2 X 20 mL). The

combined organics were washed with 1M sodium bicarbonate (2 X 30 mL), water and brine solution. The organics were dried over anhydrous Na_2SO_4 and the solvents were evaporated using rotary evaporator to obtain the chiral pyrrole **173a**.

Yield 0.74 g (88%)

The IR, ^{1}H-NMR and ^{13C}-NMR data show 1:1 correspondence with the data of the compound previously obtained in reaction using the $TiCl_4/Et_3N$ reagent system (In section 3.6.1, compound **173a**).

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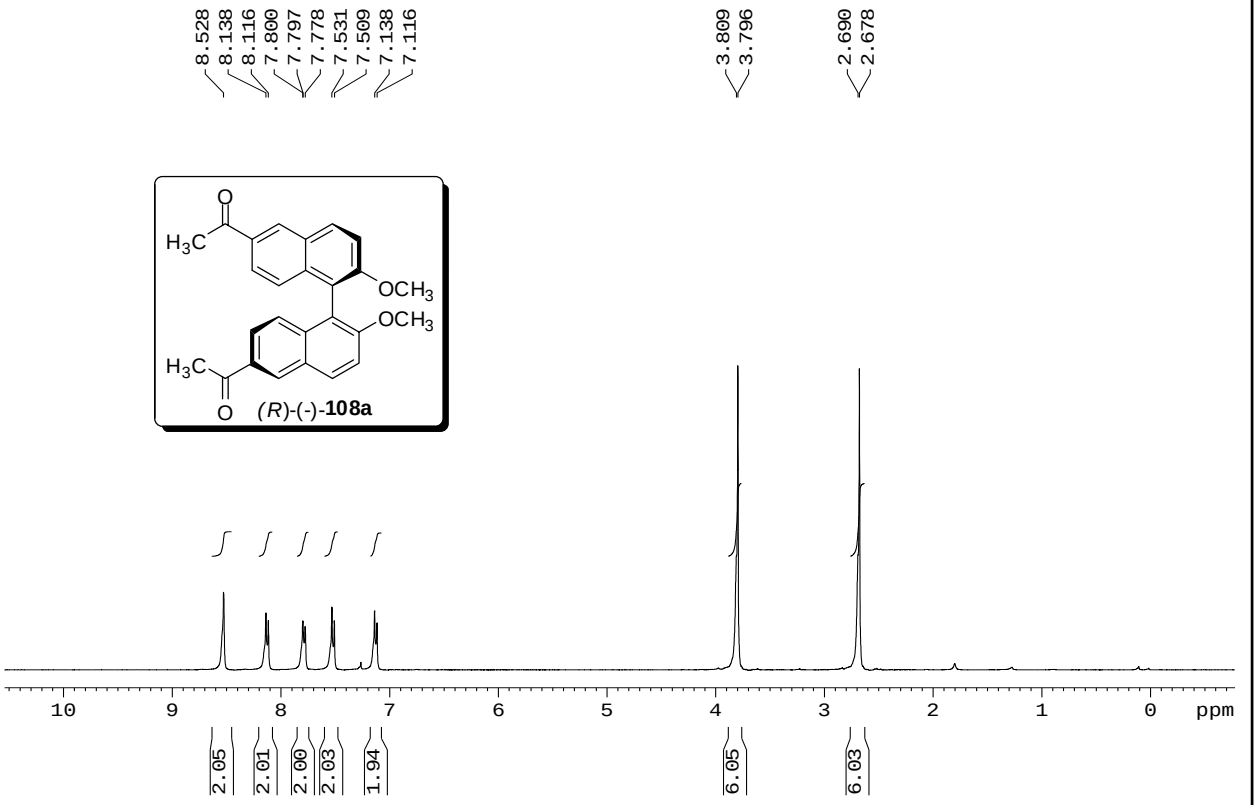
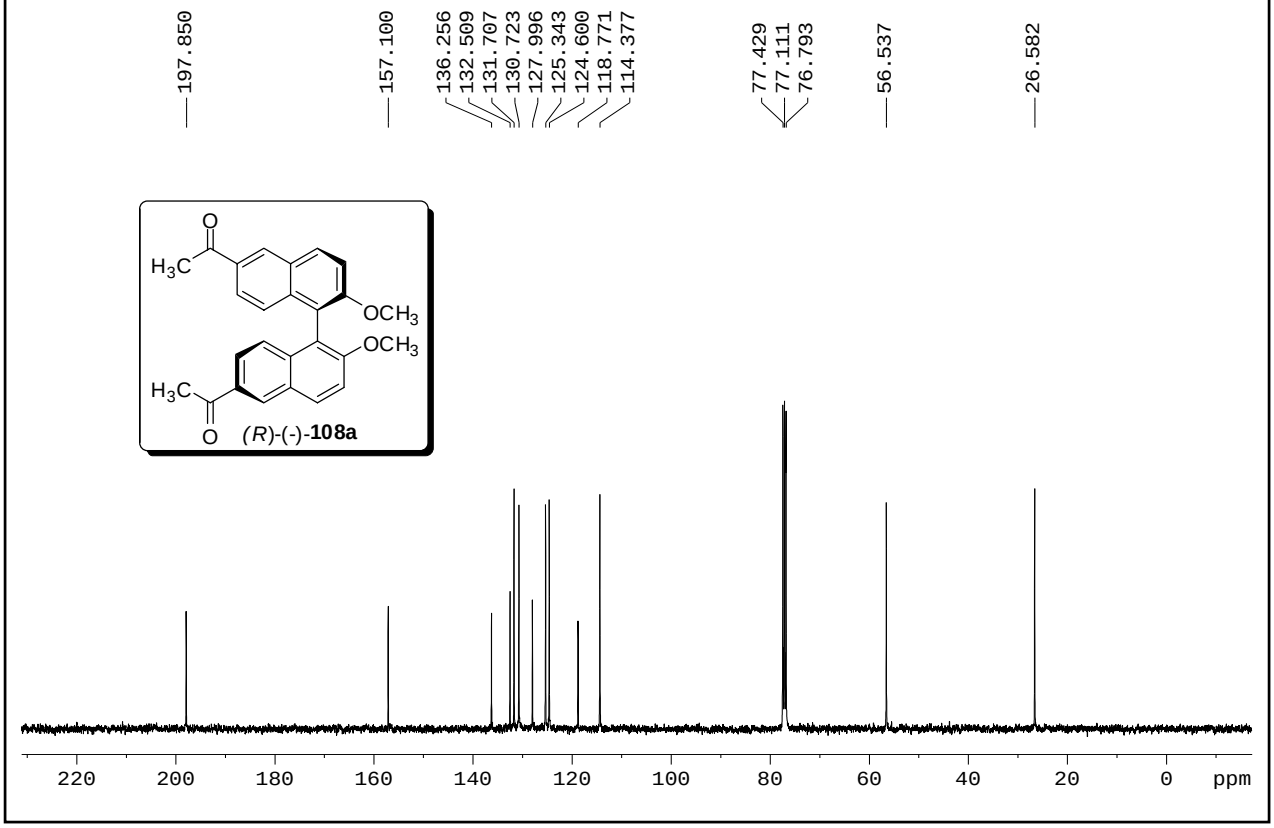
Appendix I

(Representative Spectra)

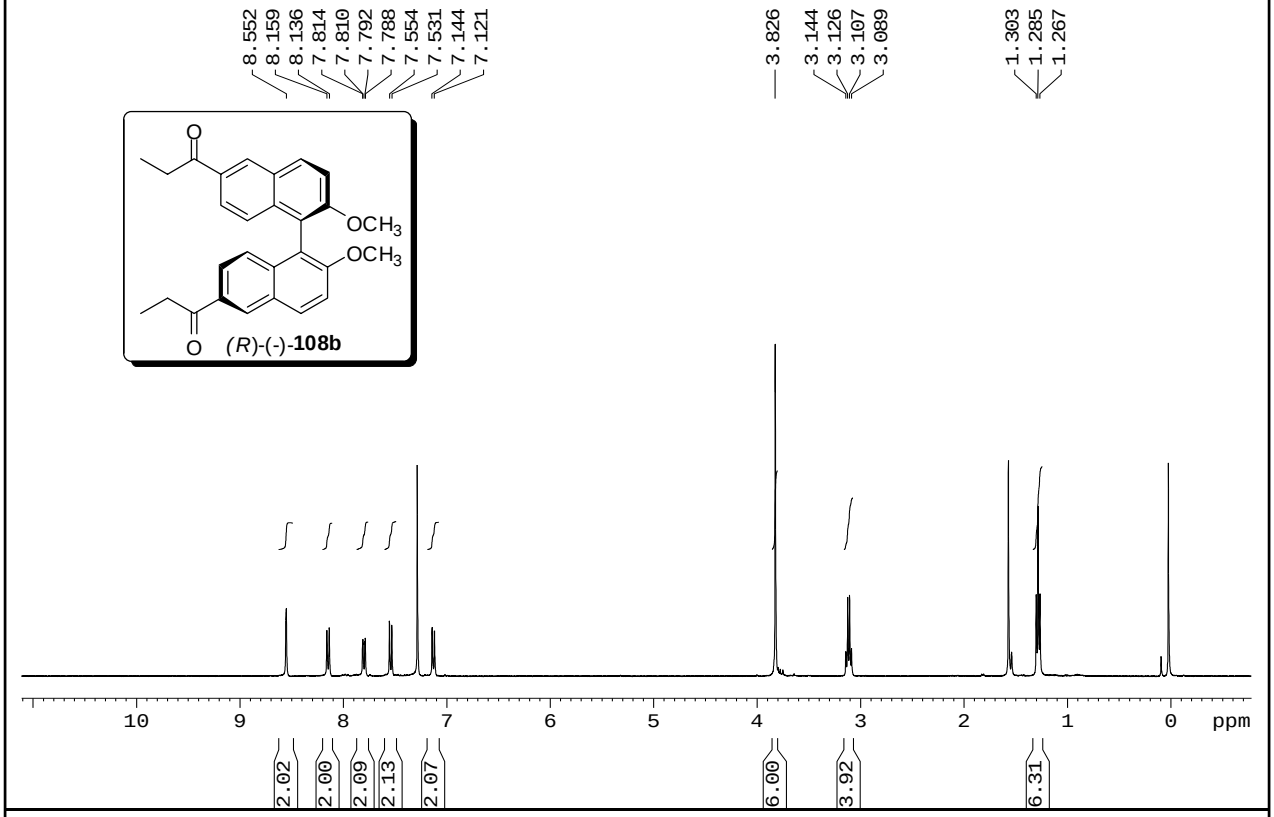
Spectrum No. 1 (Chapter 2, Section 2.1.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



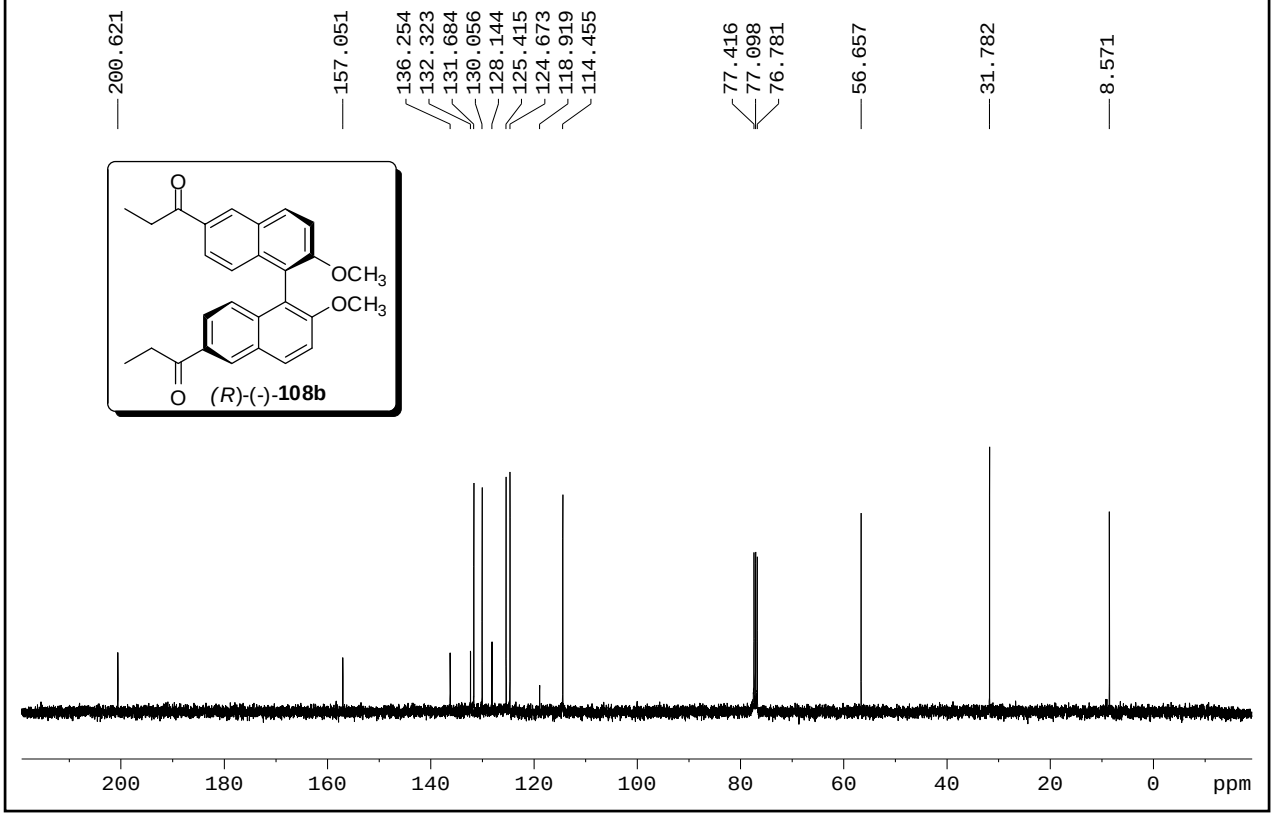
Spectrum No. 2 (Chapter 2, Section 2.1.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



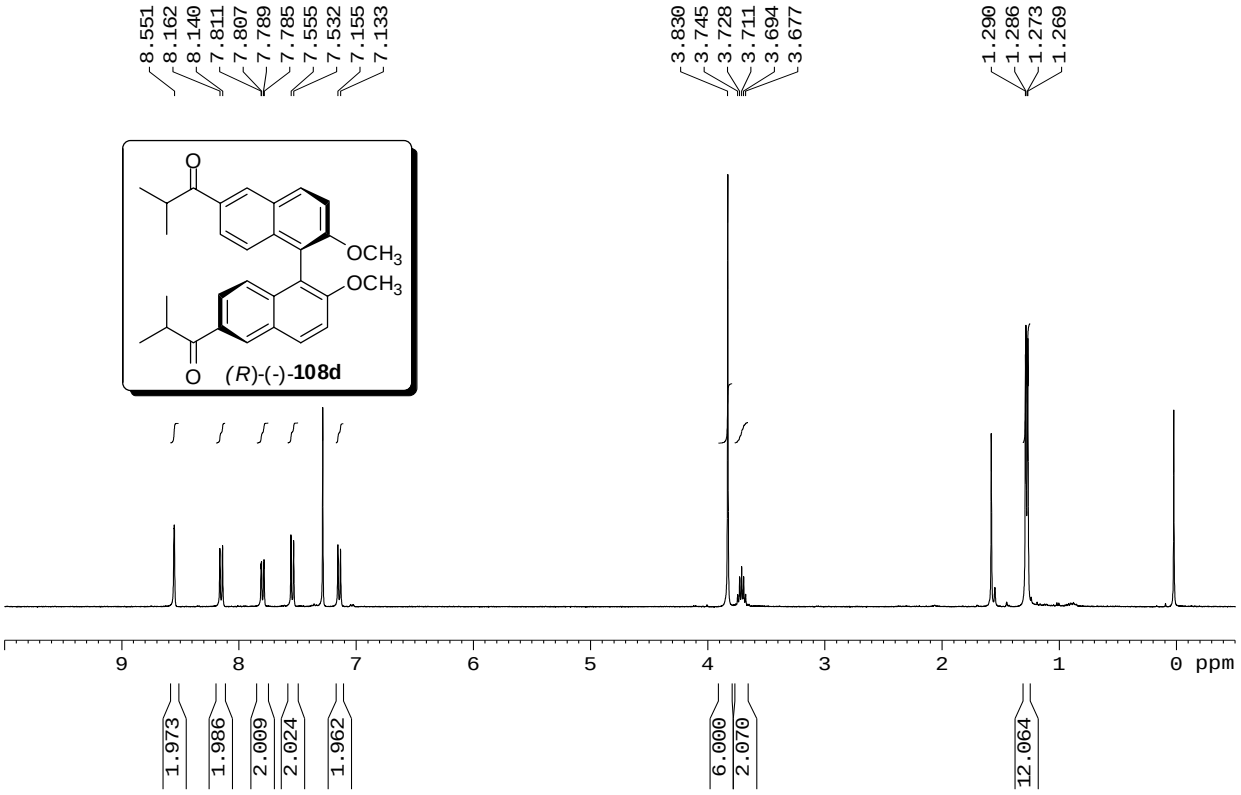
Spectrum No. 3 (Chapter 2, Section 2.1.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



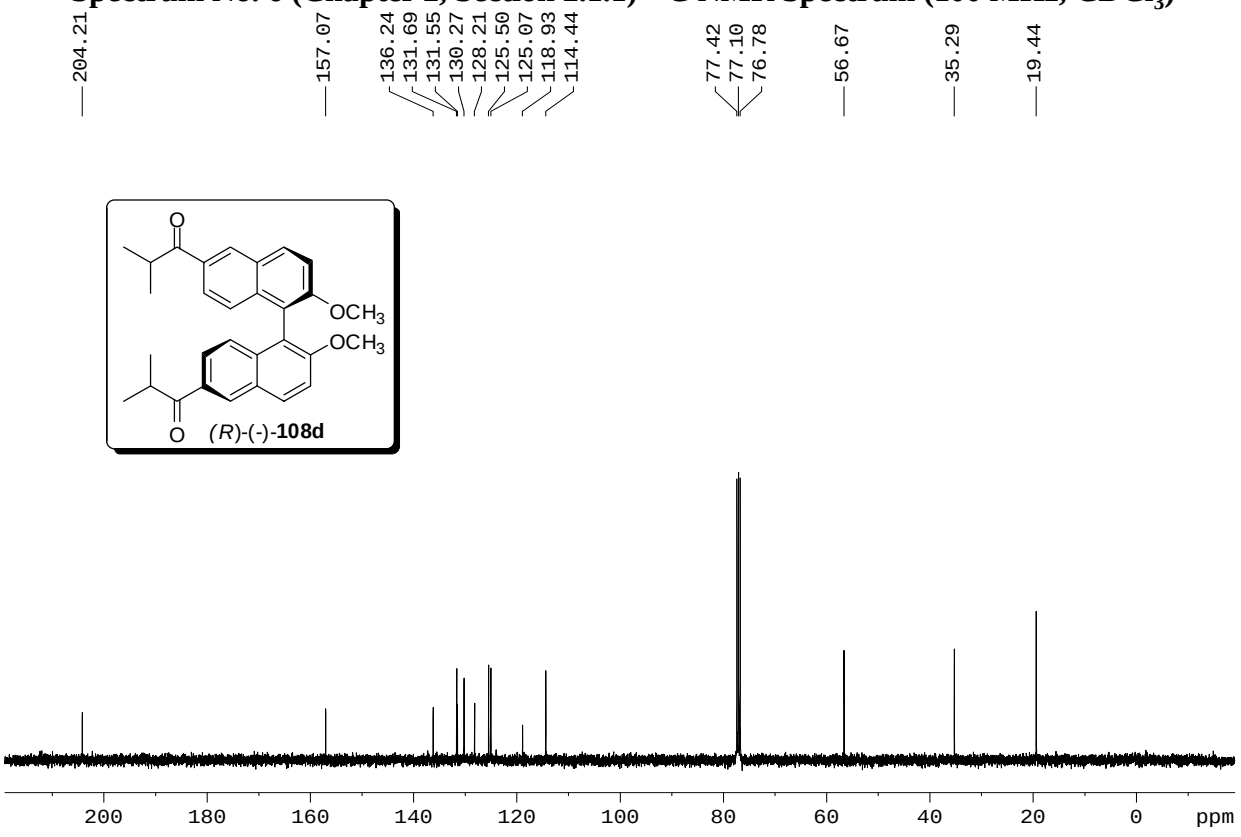
Spectrum No. 4 (Chapter 2, Section 2.1.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



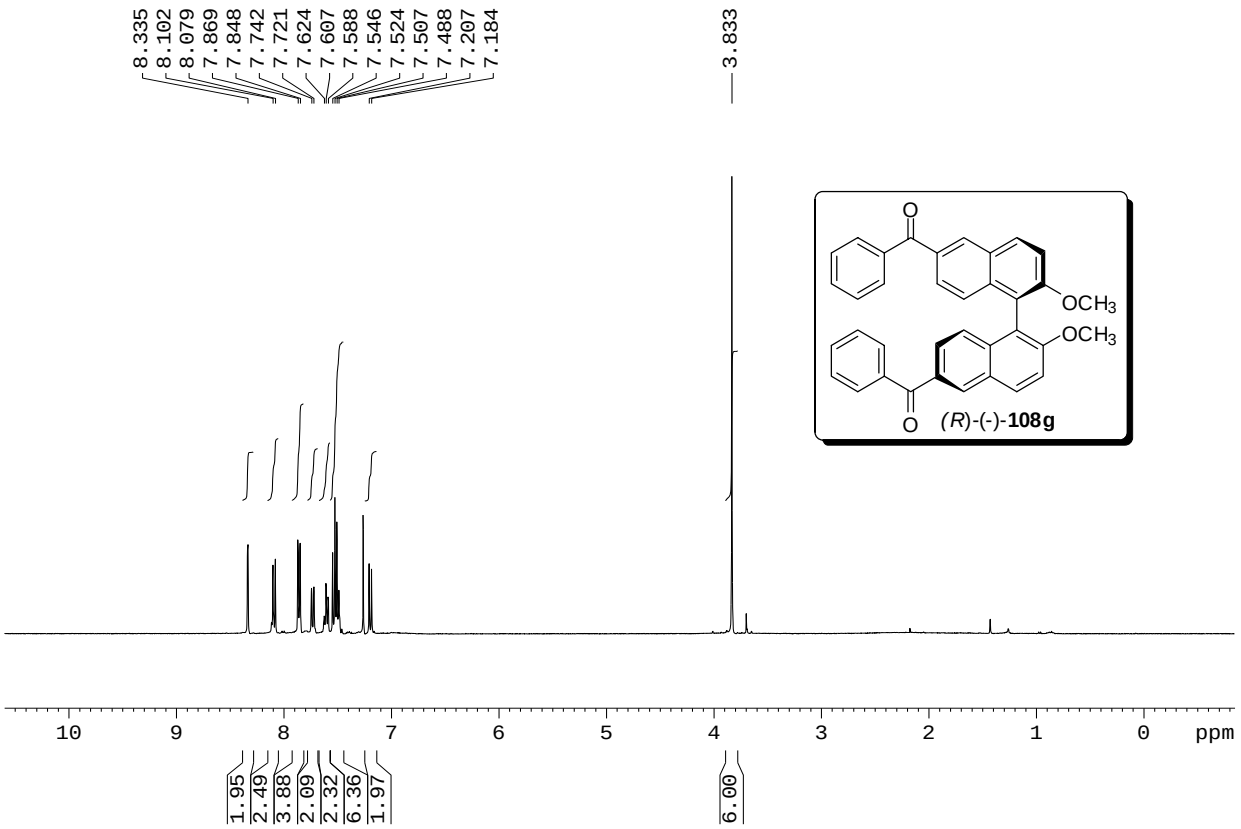
Spectrum No. 5 (Chapter 2, Section 2.1.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



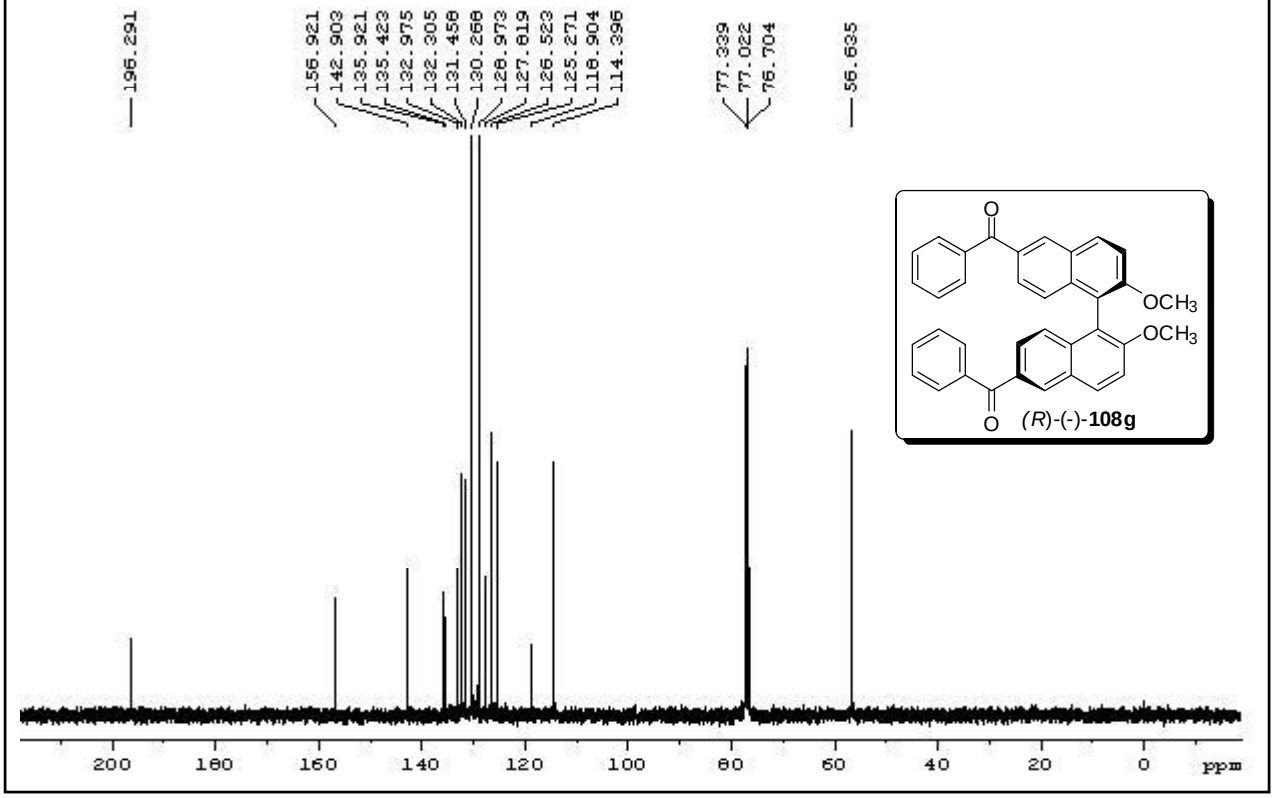
Spectrum No. 6 (Chapter 2, Section 2.1.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



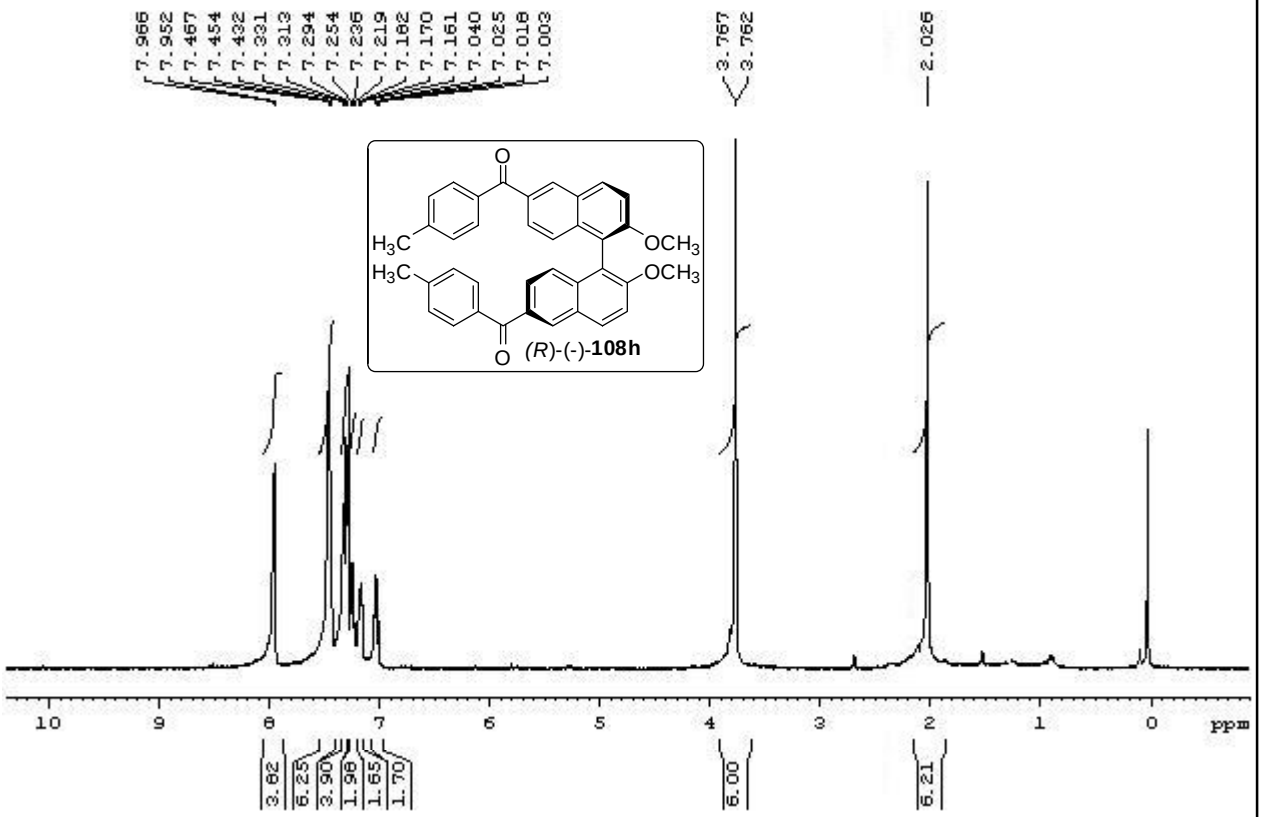
Spectrum No. 7 (Chapter 2, Section 2.1.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



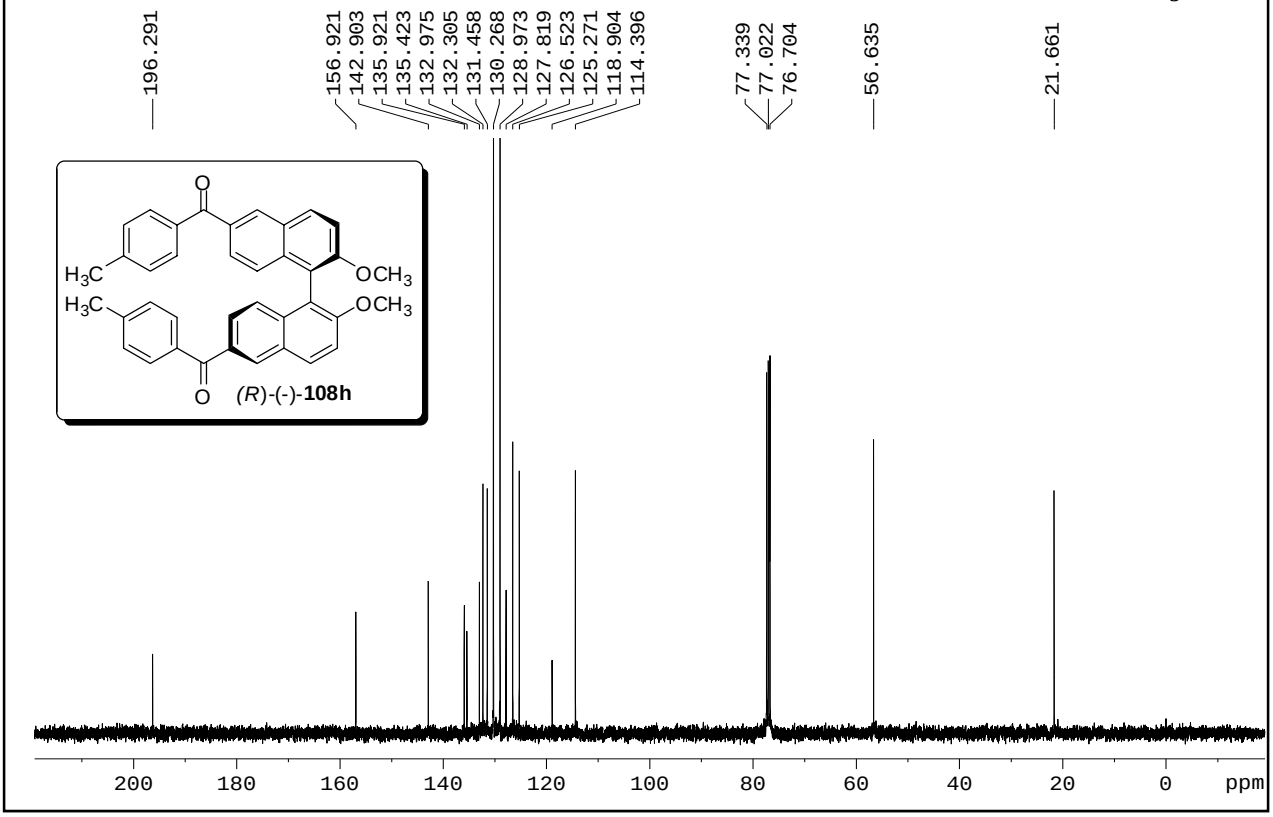
Spectrum No. 8 (Chapter 2, Section 2.1.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



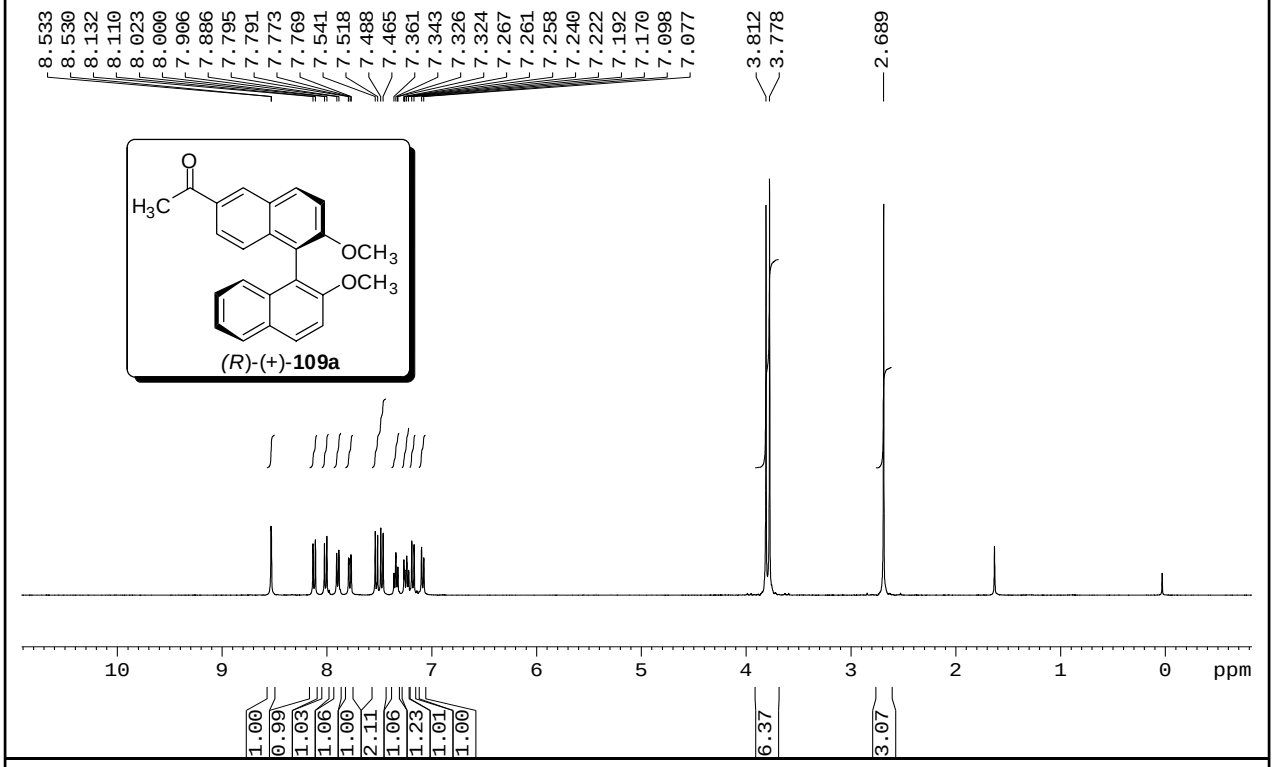
Spectrum No. 9 (Chapter 2, Section 2.1.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



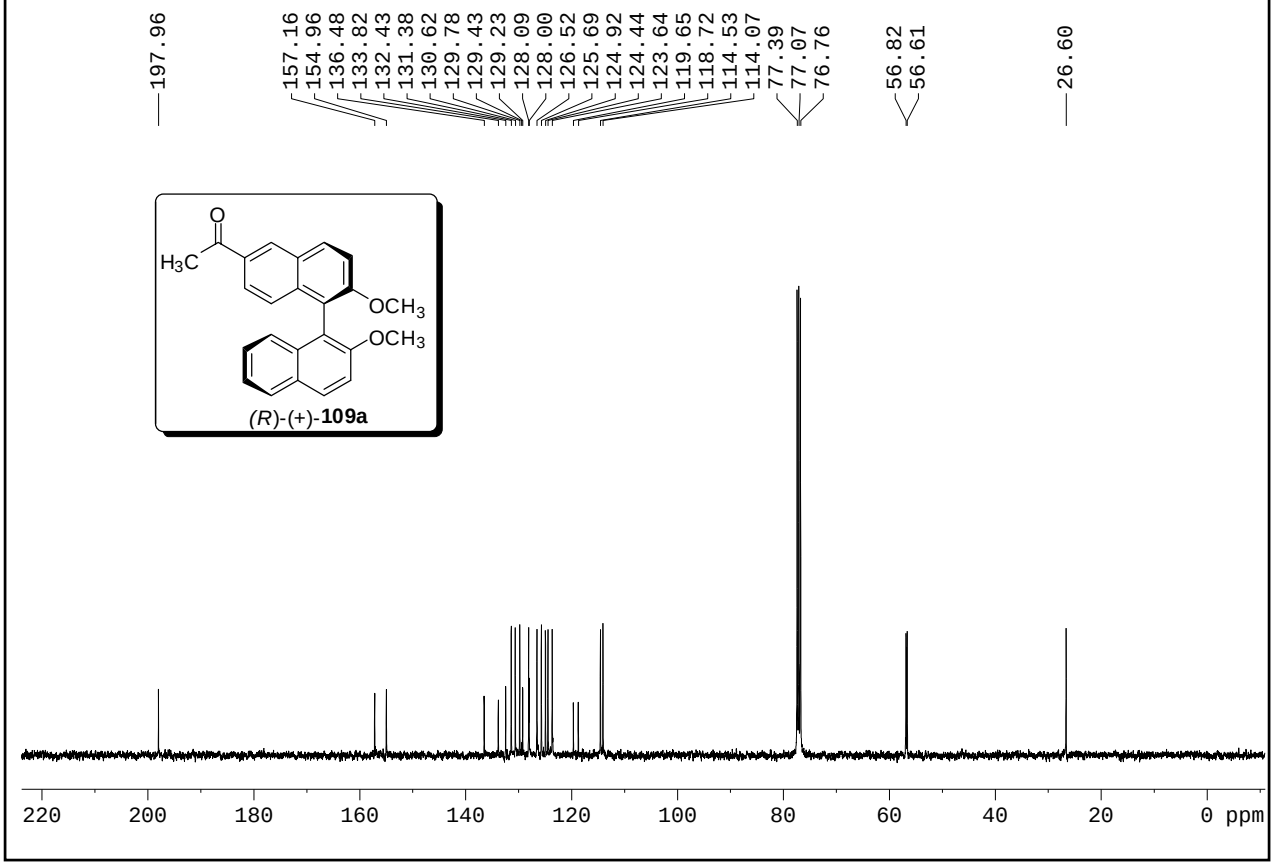
Spectrum No. 10 (Chapter 2, Section 2.1.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



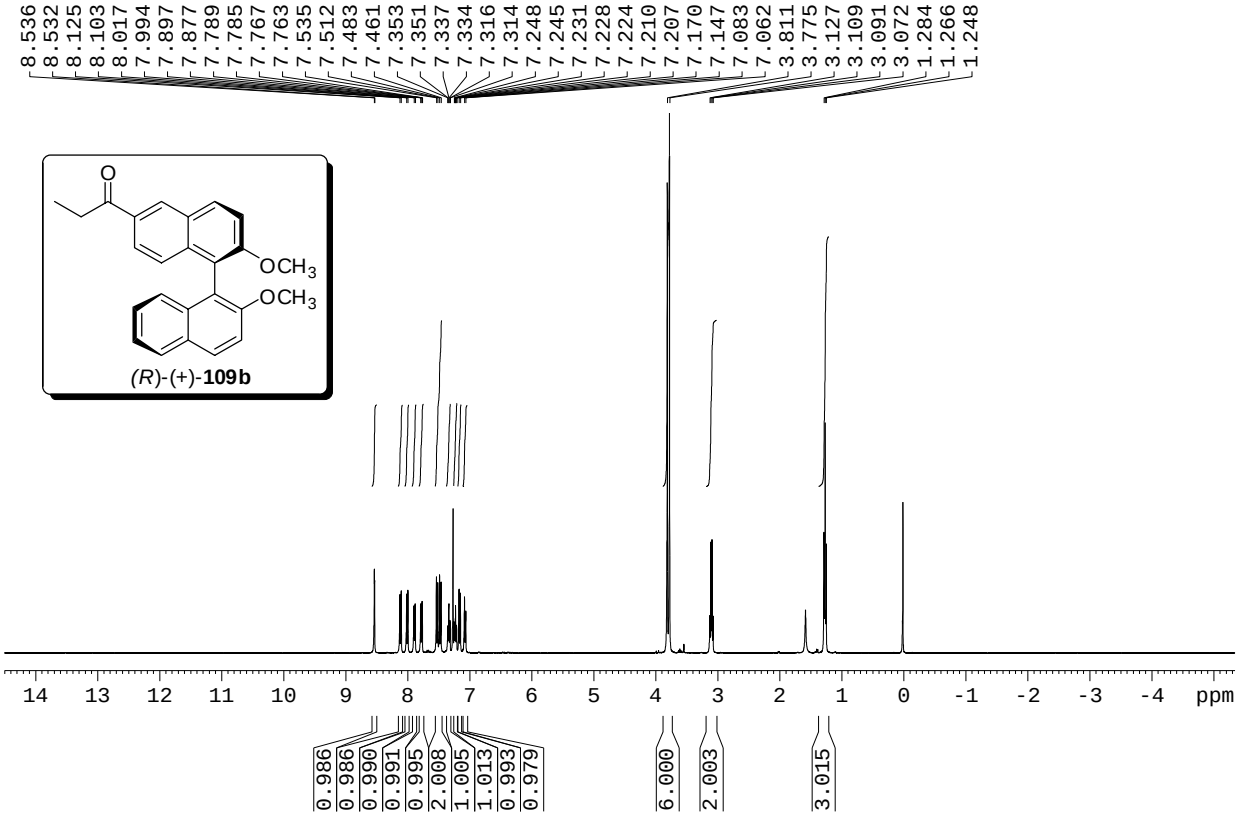
Spectrum No. 11 (Chapter 2, Section 2.1.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



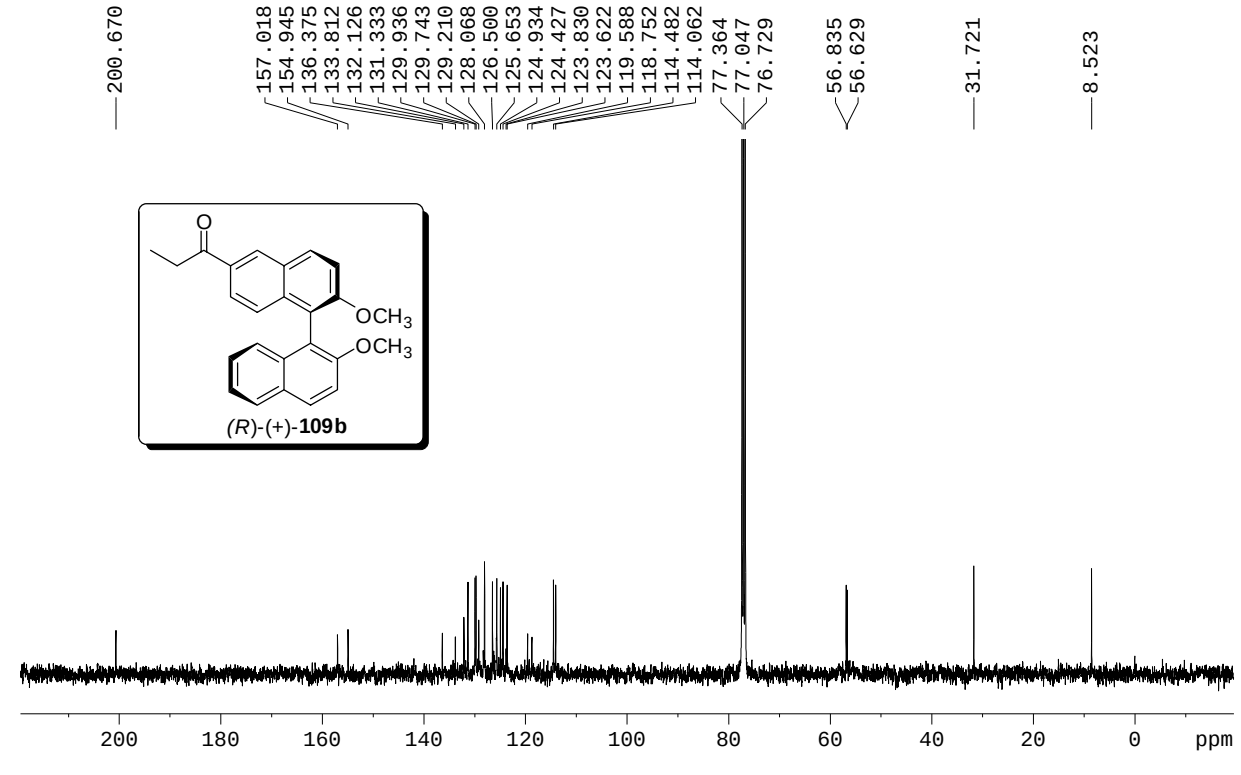
Spectrum No. 12 (Chapter 2, Section 2.1.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



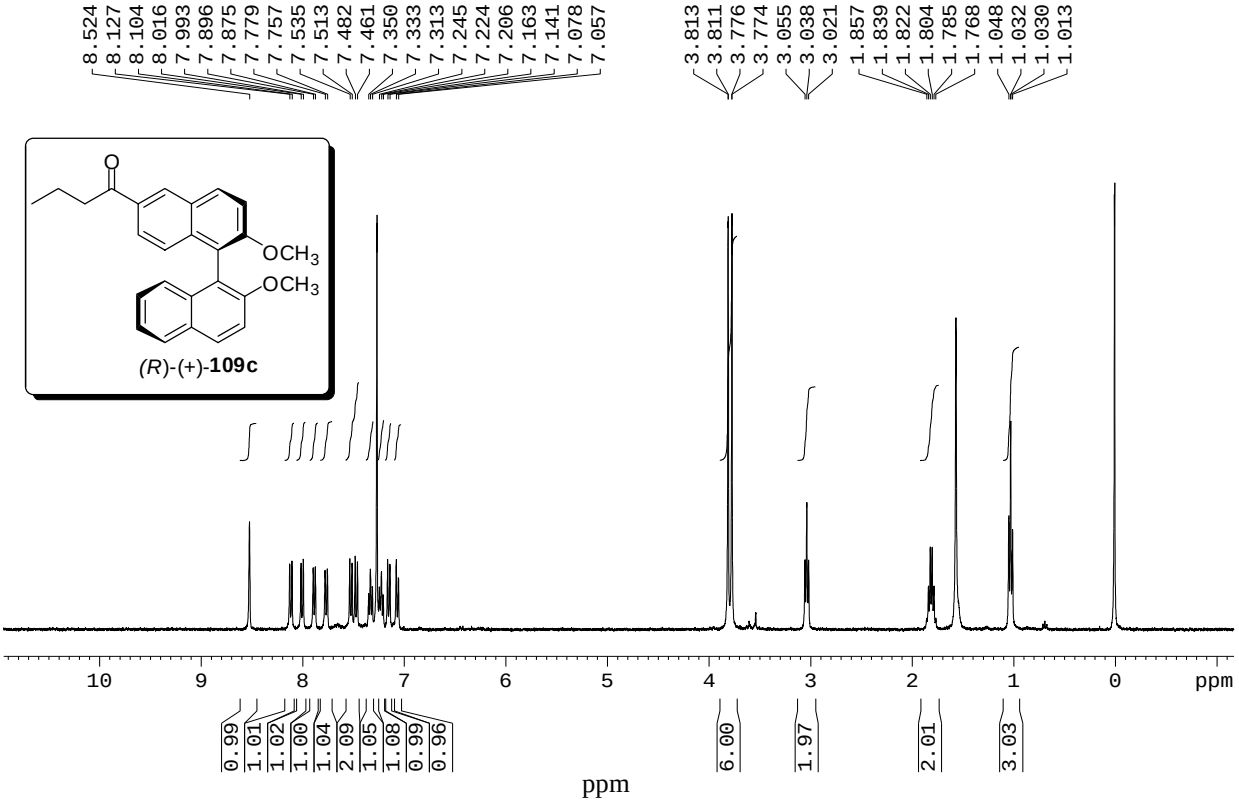
Spectrum No. 13 (Chapter 2, Section 2.1.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



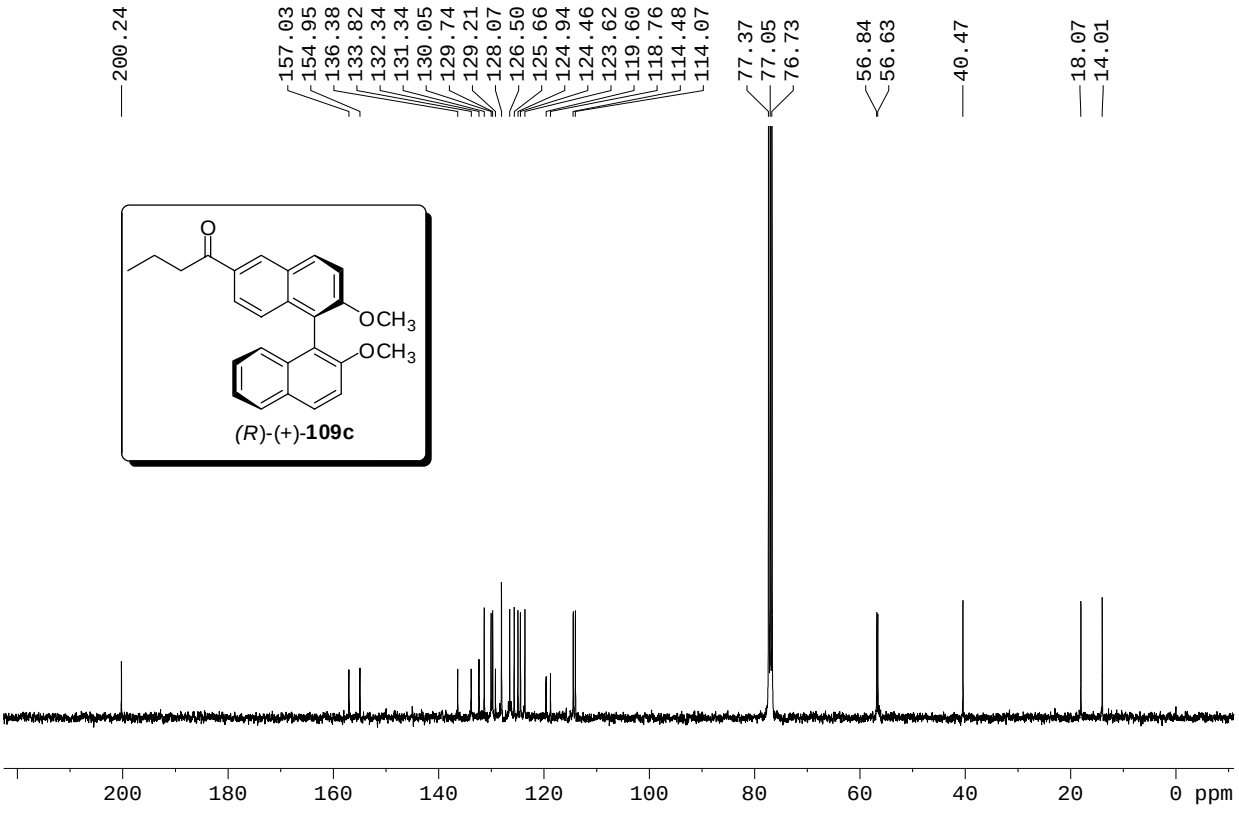
Spectrum No. 14 (Chapter 2, Section 2.1.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



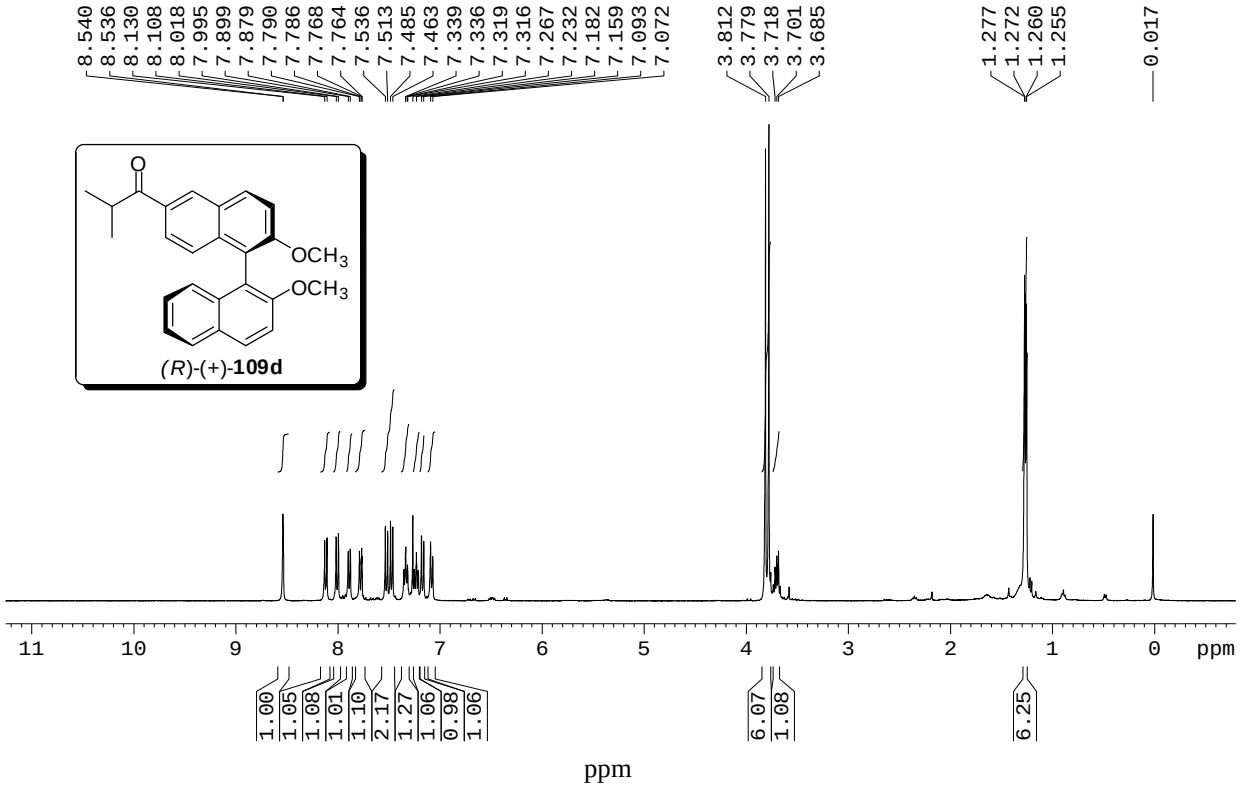
Spectrum No. 15 (Chapter 2, Section 2.1.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



Spectrum No. 16 (Chapter 2, Section 2.1.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)

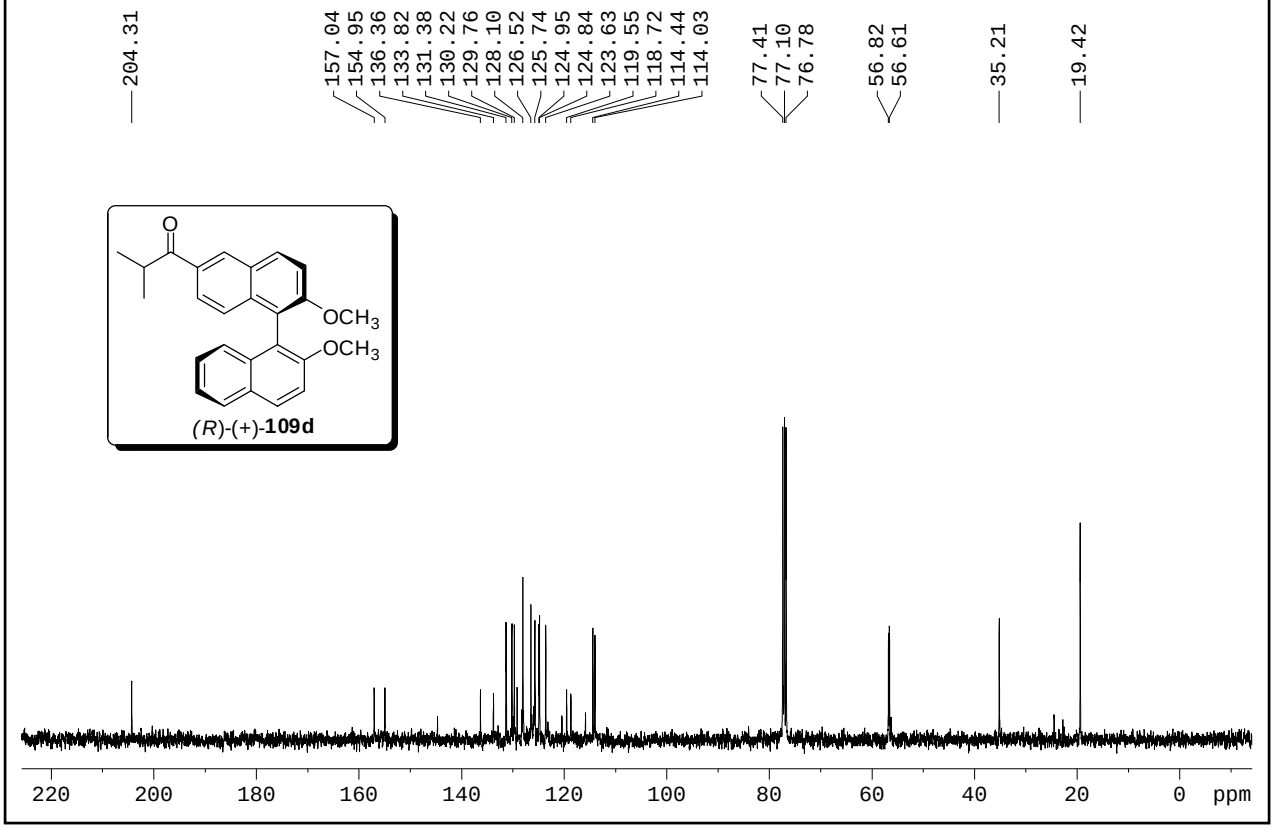


Spectrum No. 17 (Chapter 2, Section 2.1.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)

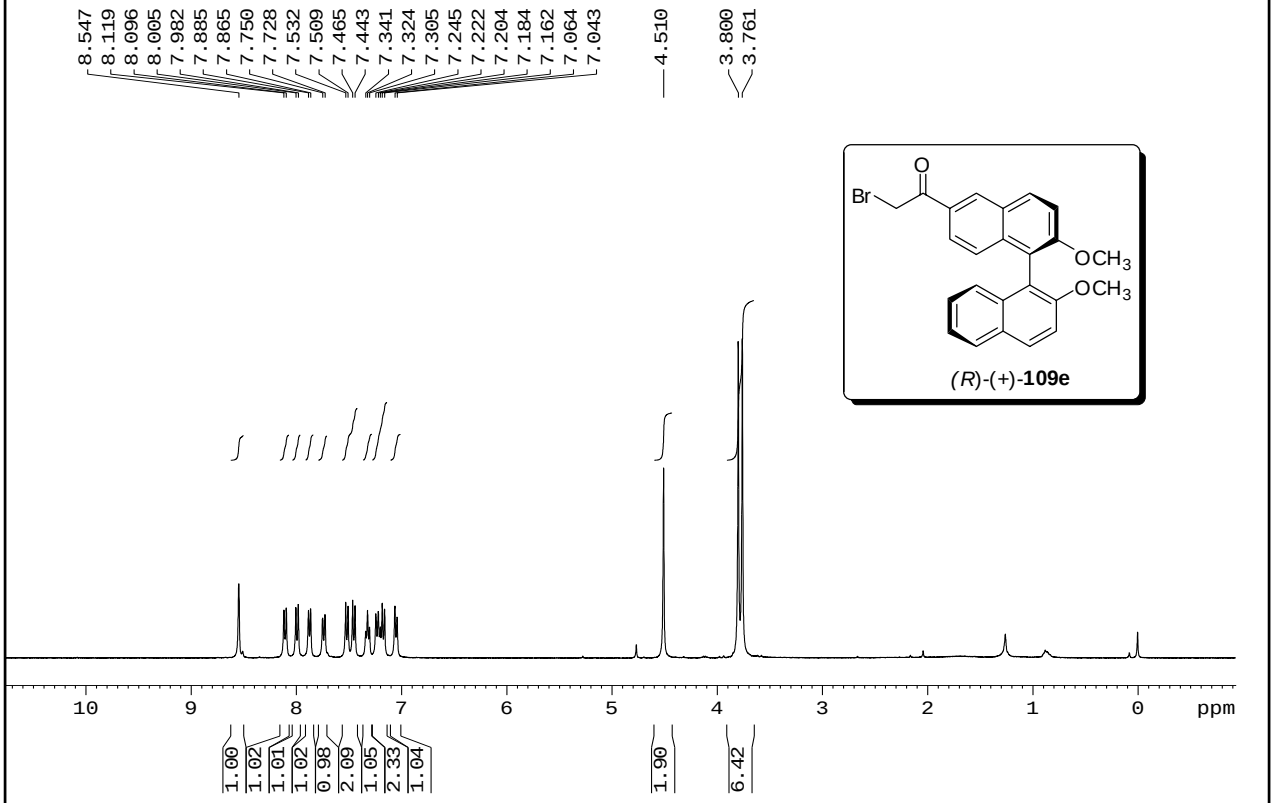


ppm

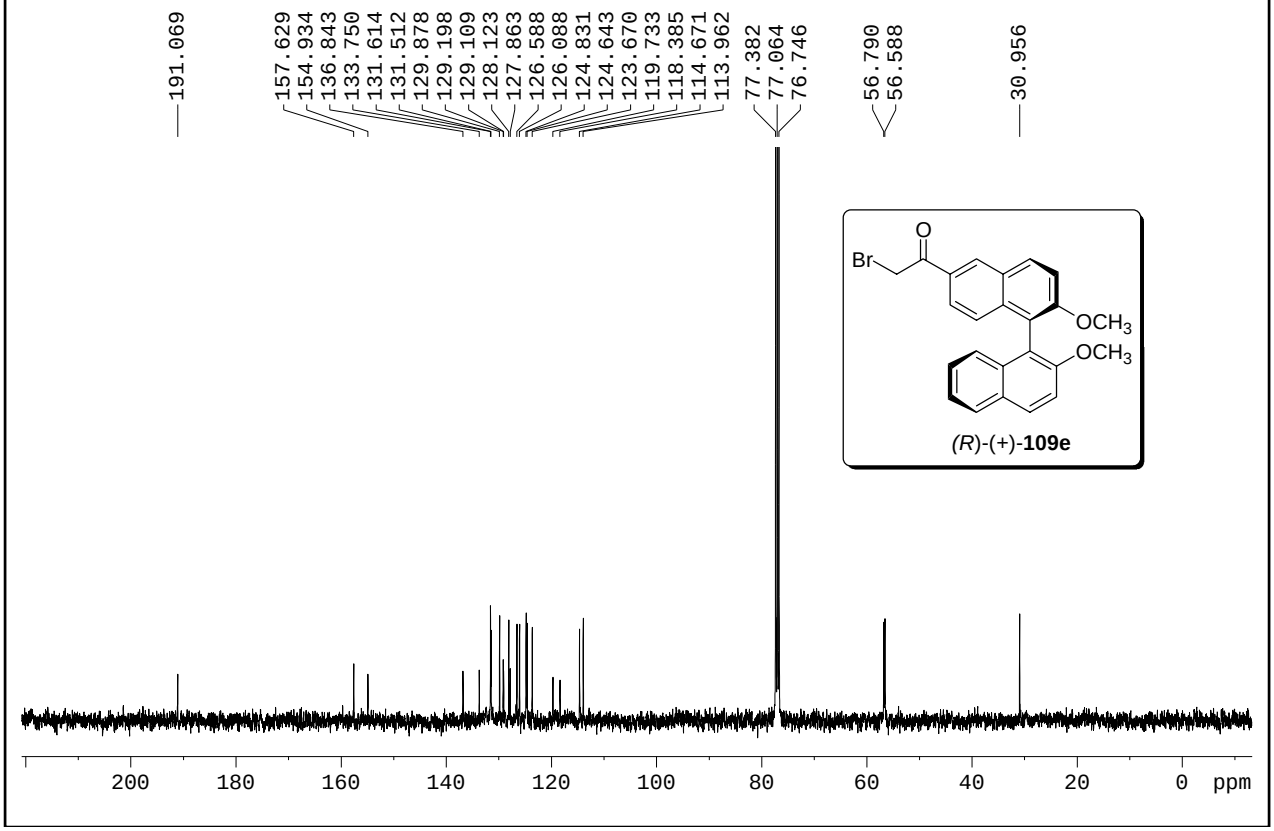
Spectrum No. 18 (Chapter 2, Section 2.1.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



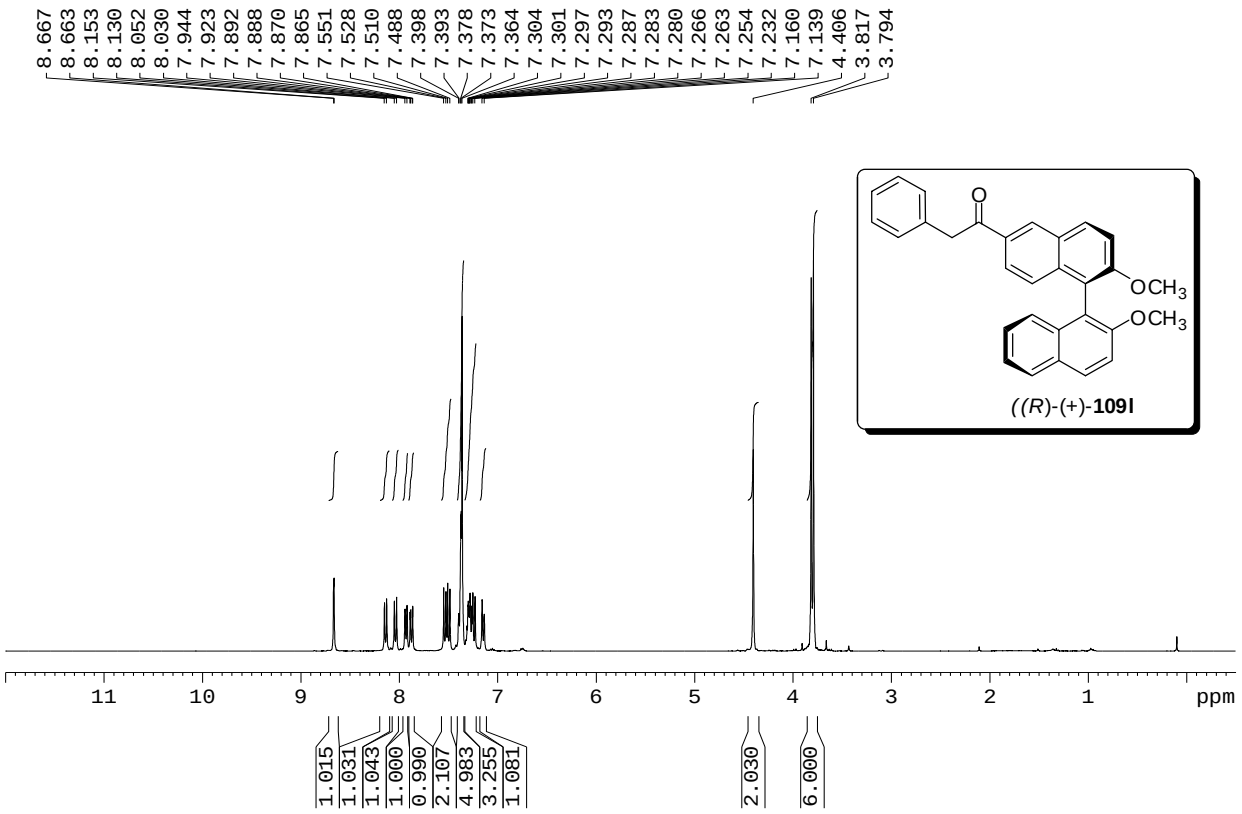
Spectrum No. 19 (Chapter 2, Section 2.1.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



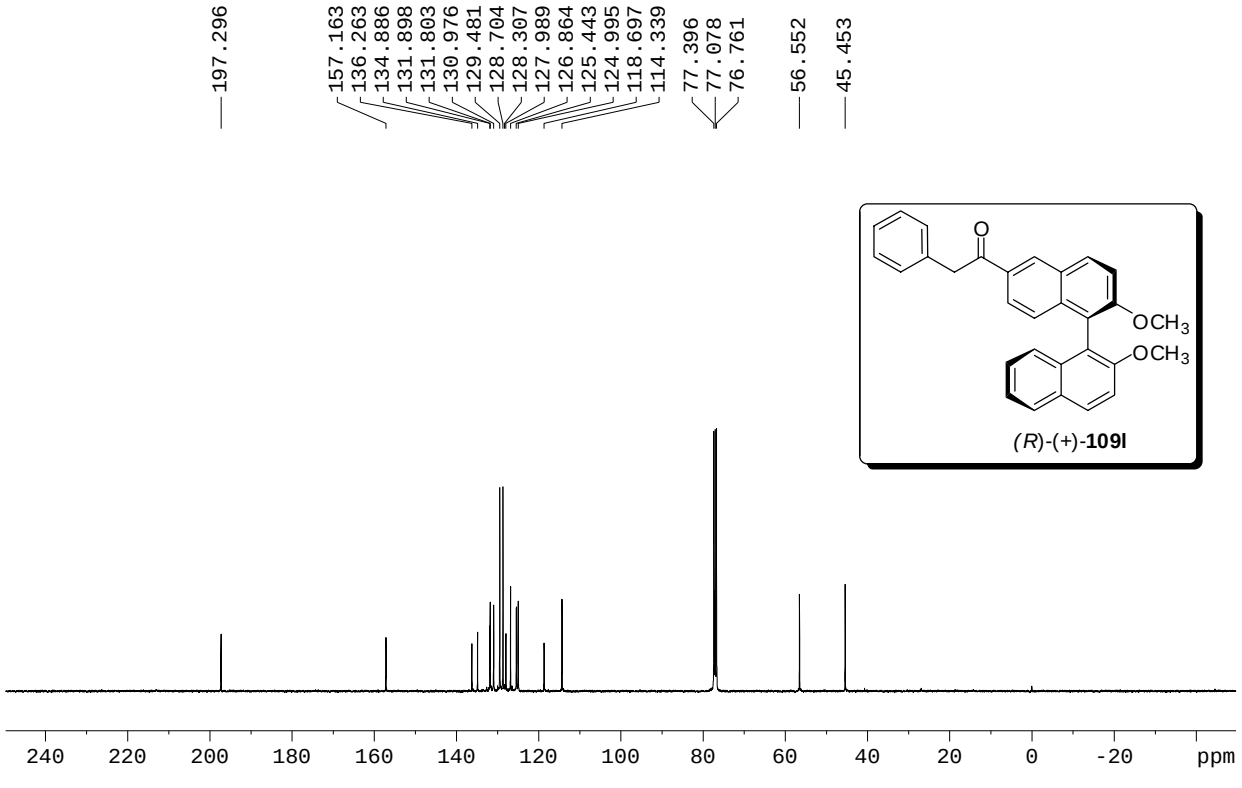
Spectrum No. 20 (Chapter 2, Section 2.1.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



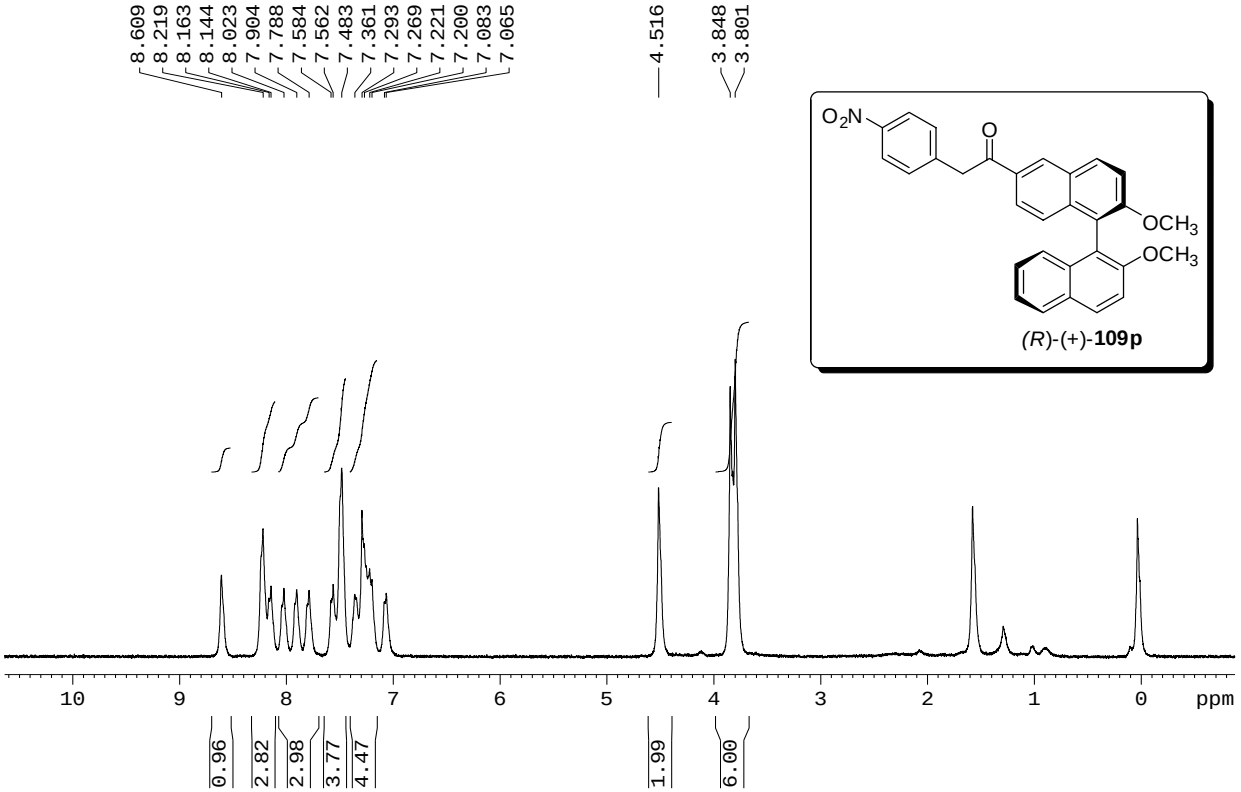
Spectrum No. 21 (Chapter 2, Section 2.1.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



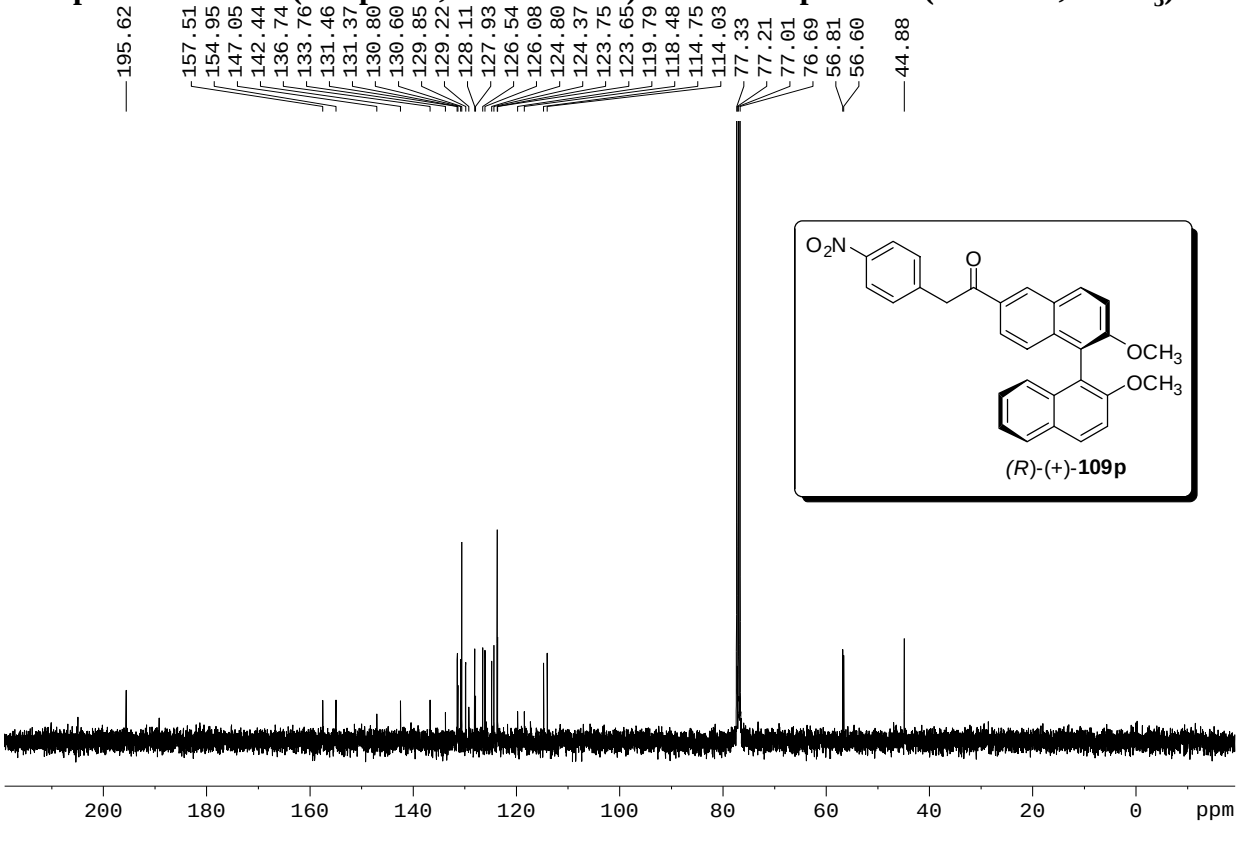
Spectrum No. 22 (Chapter 2, Section 2.1.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



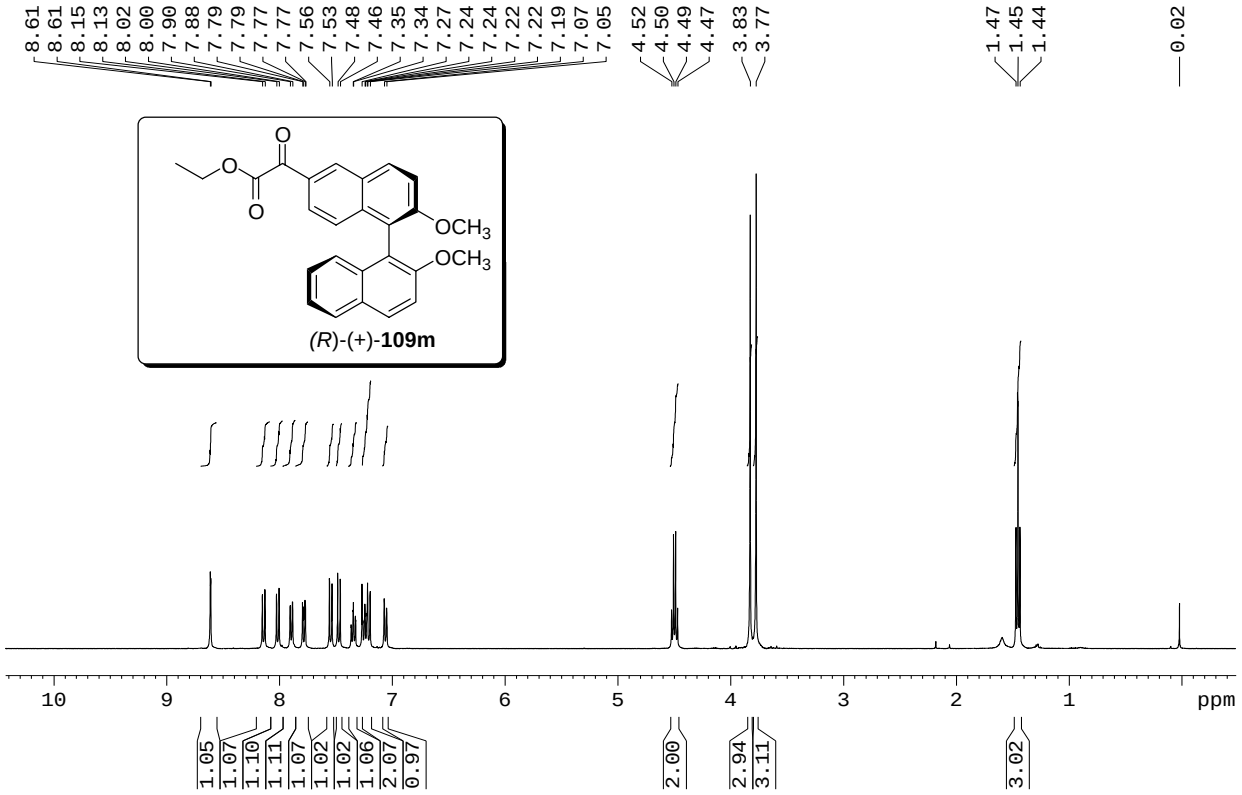
Spectrum No. 23 (Chapter 2, Section 2.1.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



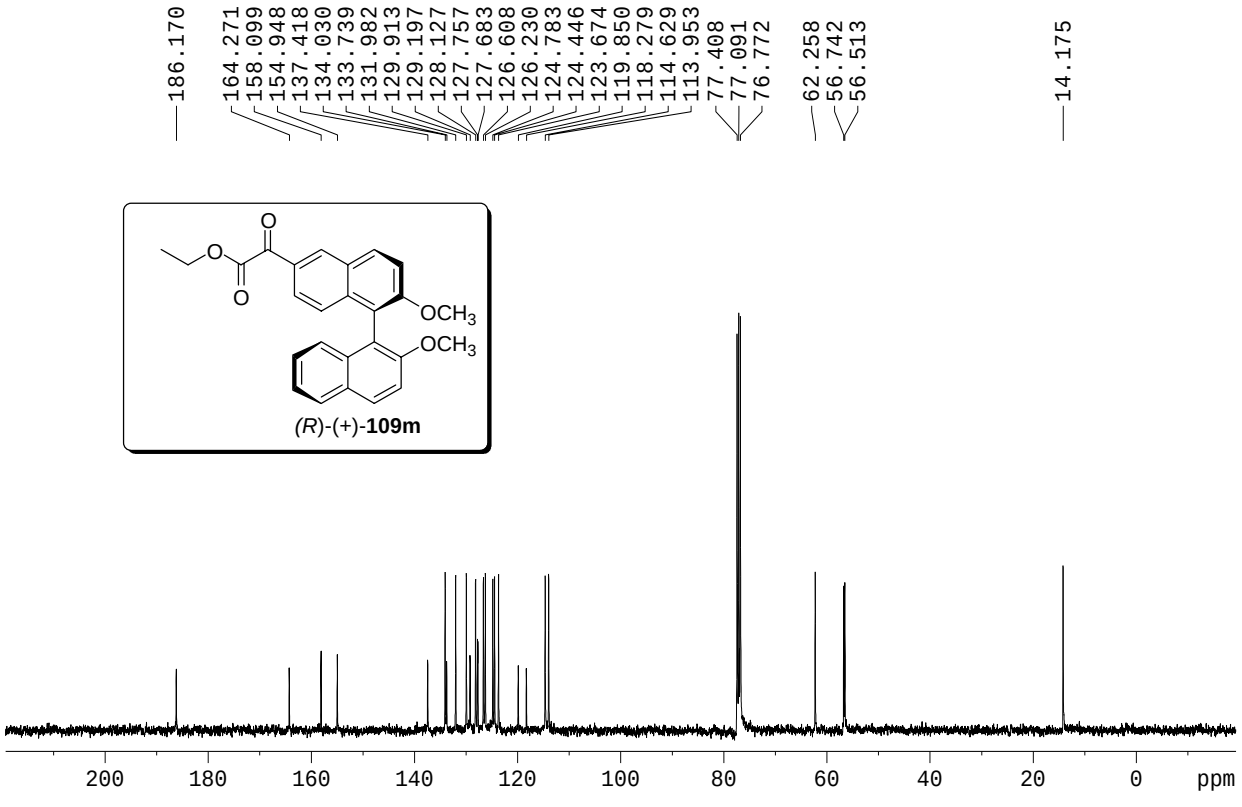
Spectrum No. 24 (Chapter 2, Section 2.1.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



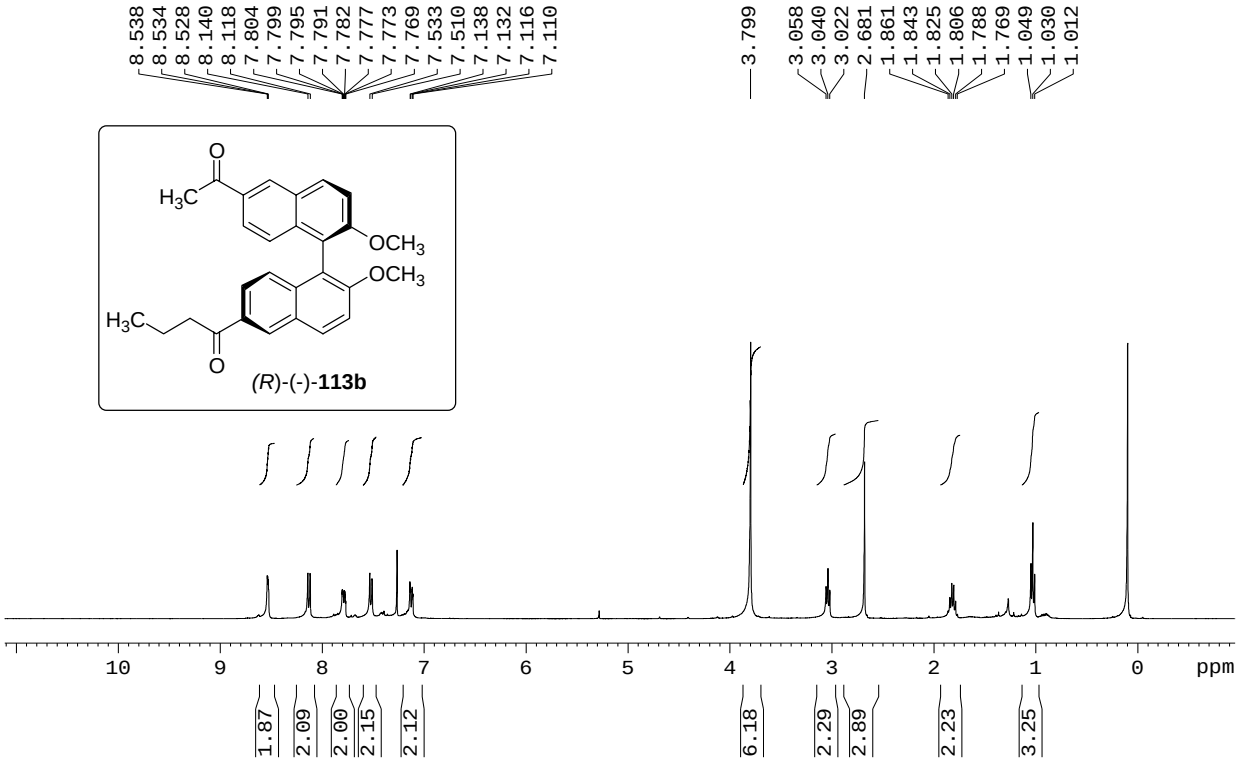
Spectrum No. 25 (Chapter 2, Section 2.1.2) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



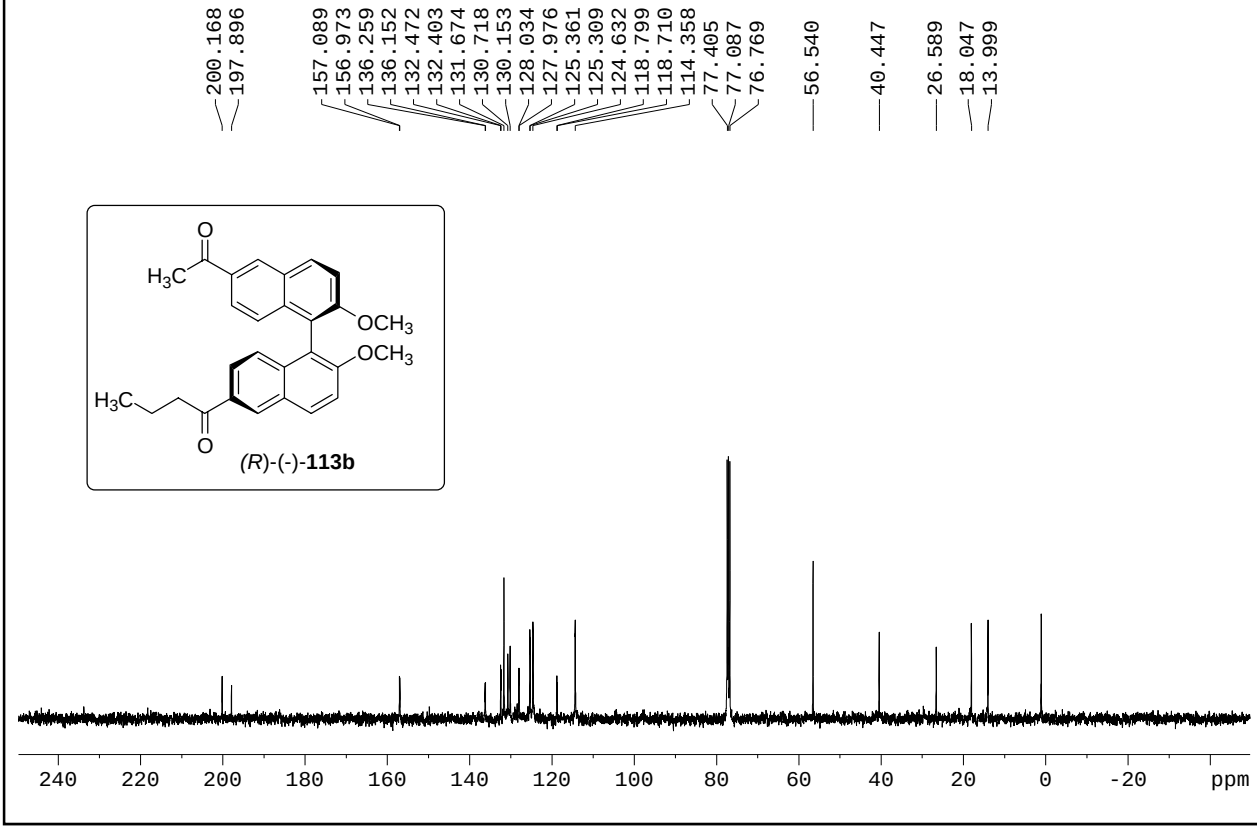
Spectrum No. 26 (Chapter 2, Section 2.1.2) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



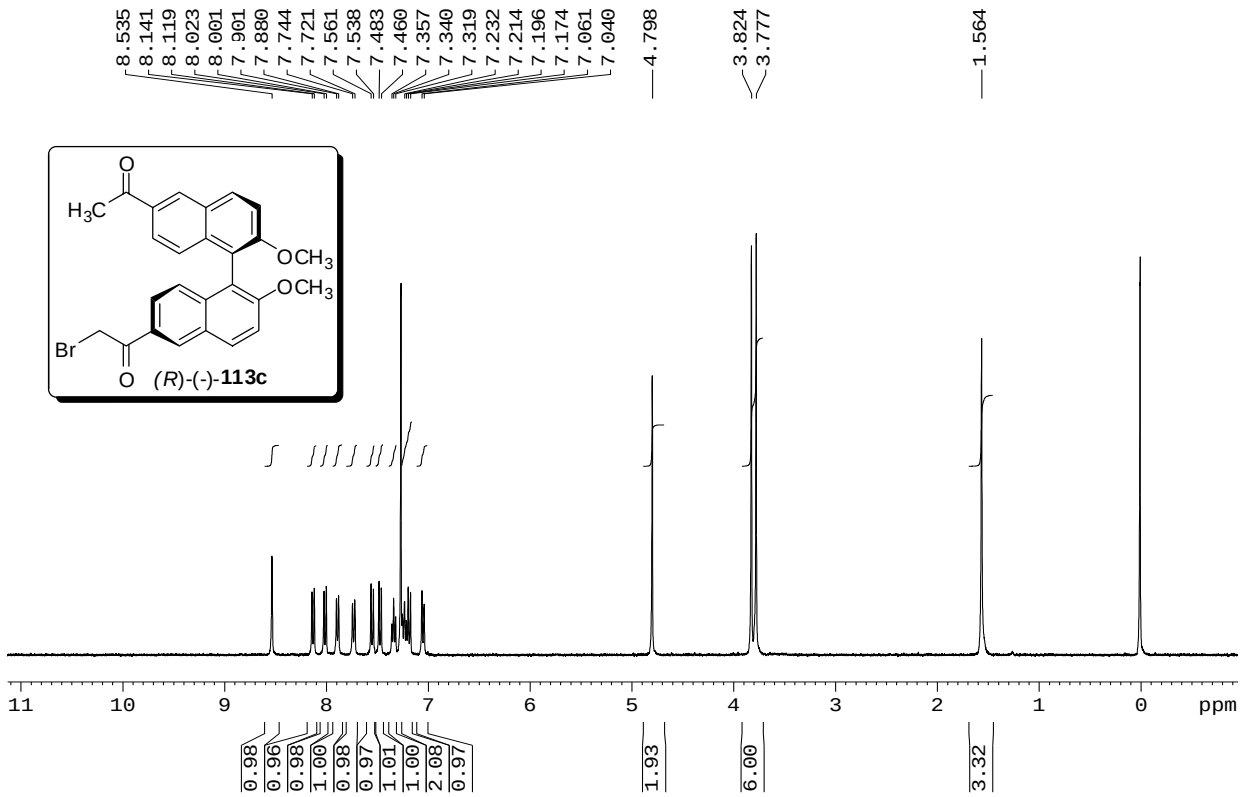
Spectrum No. 27 (Chapter 2, Section 2.1.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



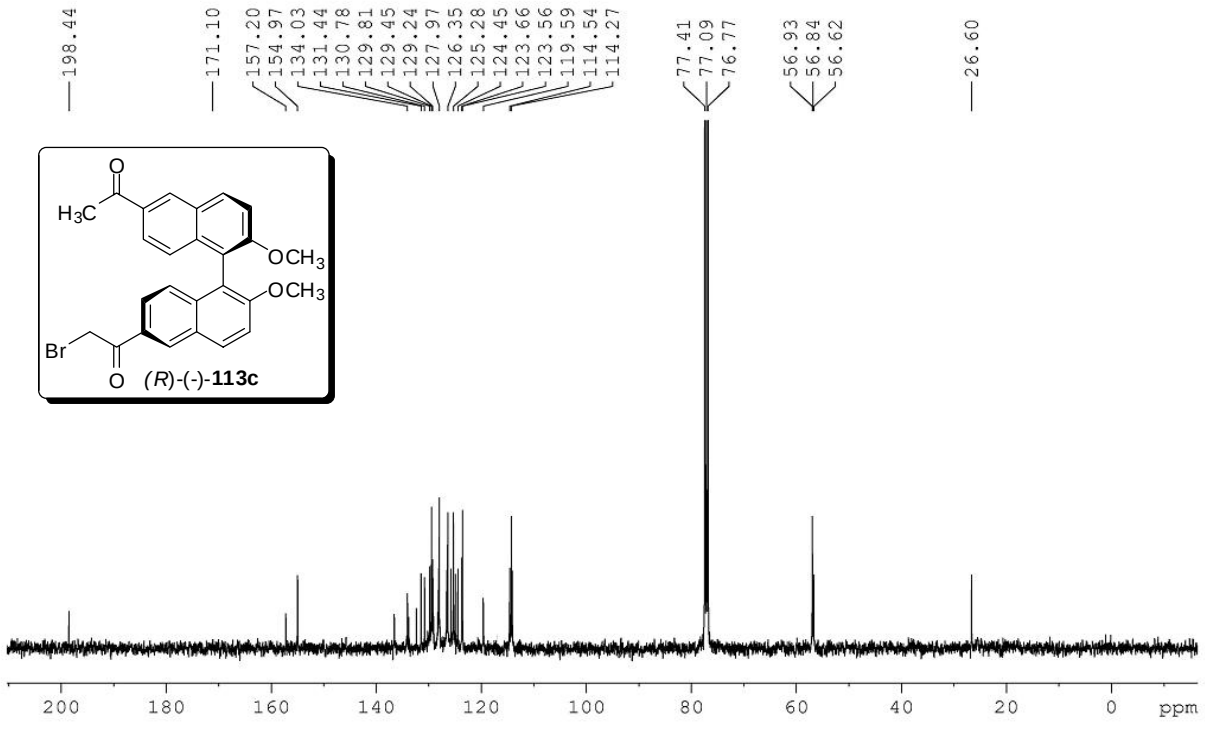
Spectrum No. 28 (Chapter 2, Section 2.1.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



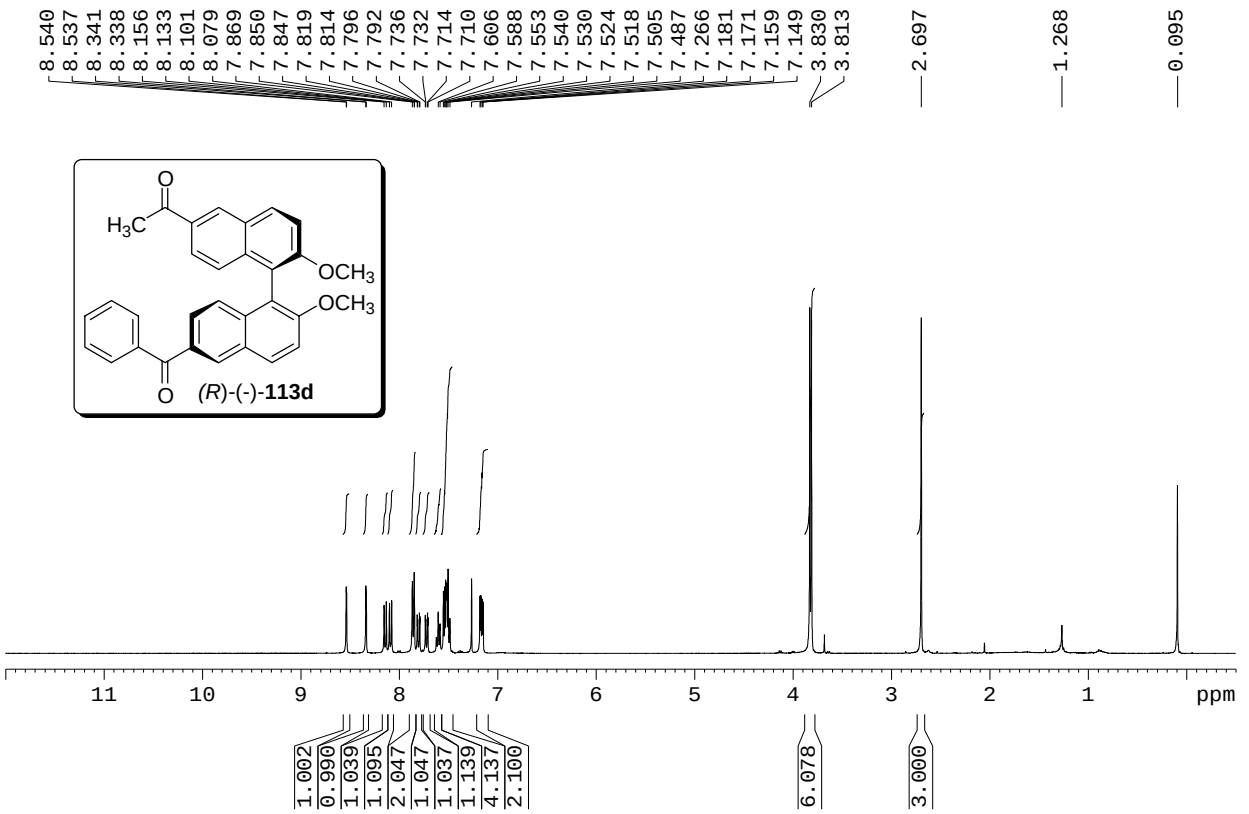
Spectrum No. 29 (Chapter 2, Section 2.1.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



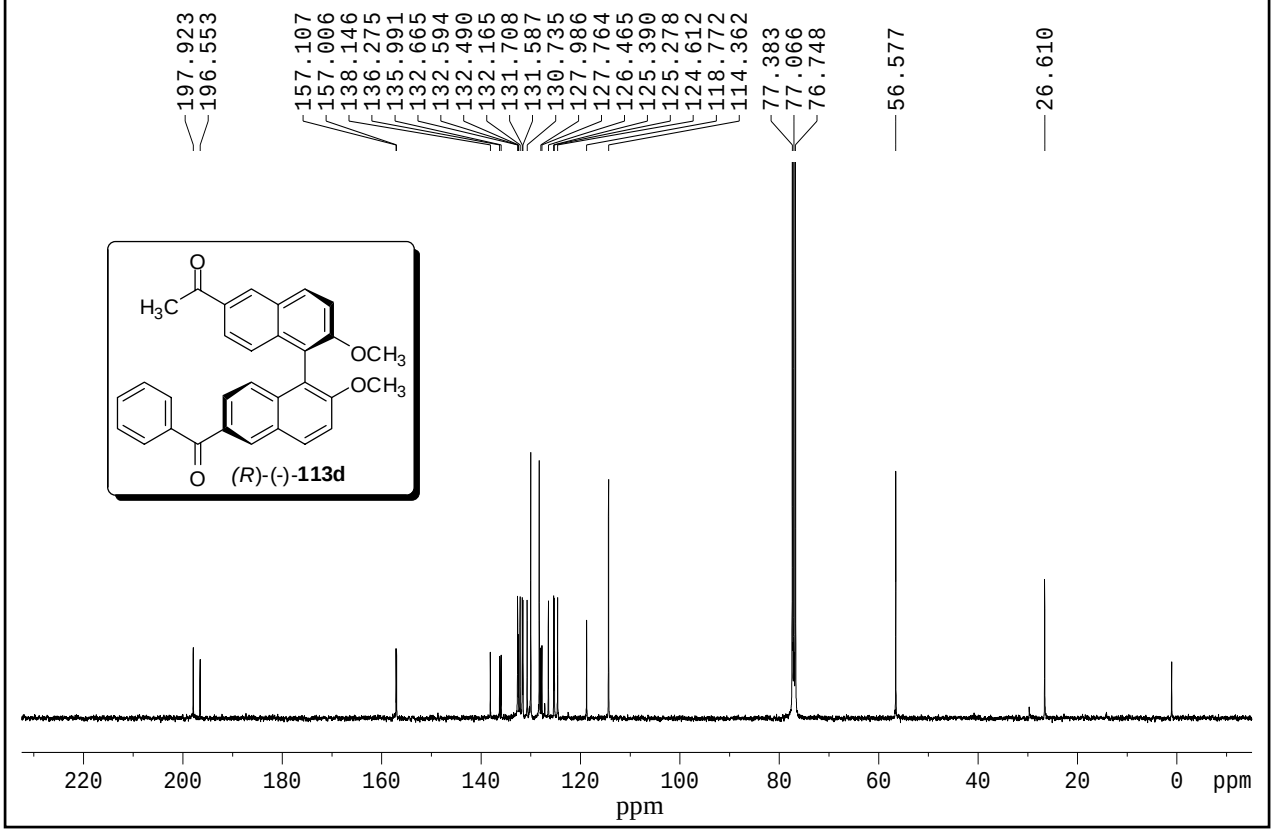
Spectrum No. 30 (Chapter 2, Section 2.1.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



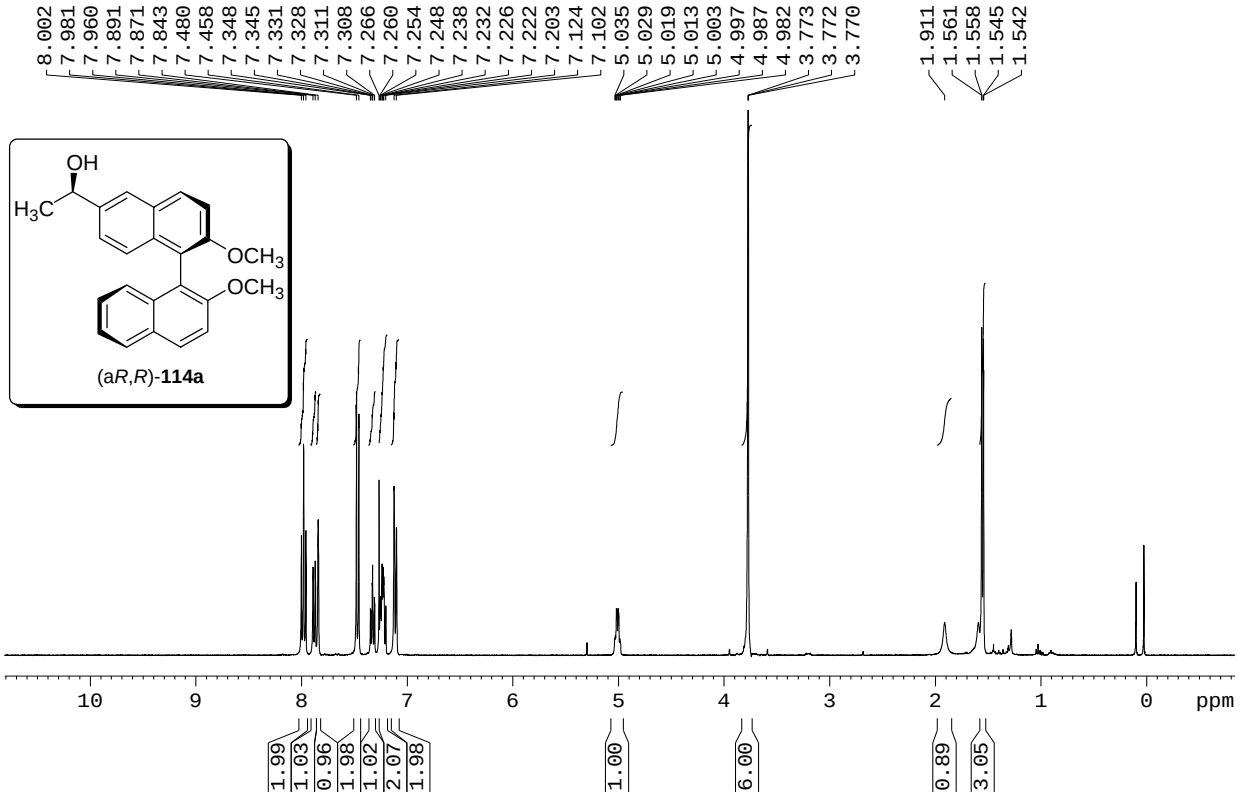
Spectrum No. 31 (Chapter 2, Section 2.1.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



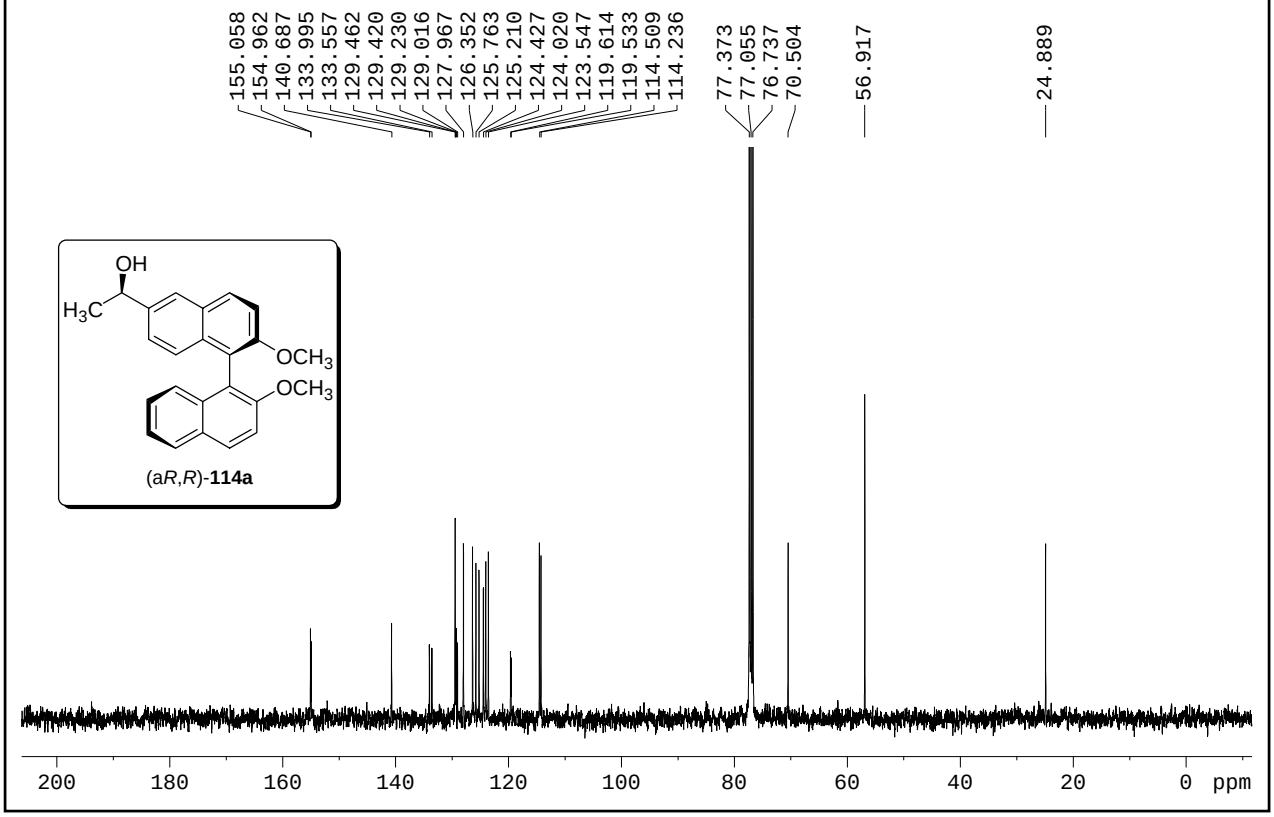
Spectrum No. 32 (Chapter 2, Section 2.1.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



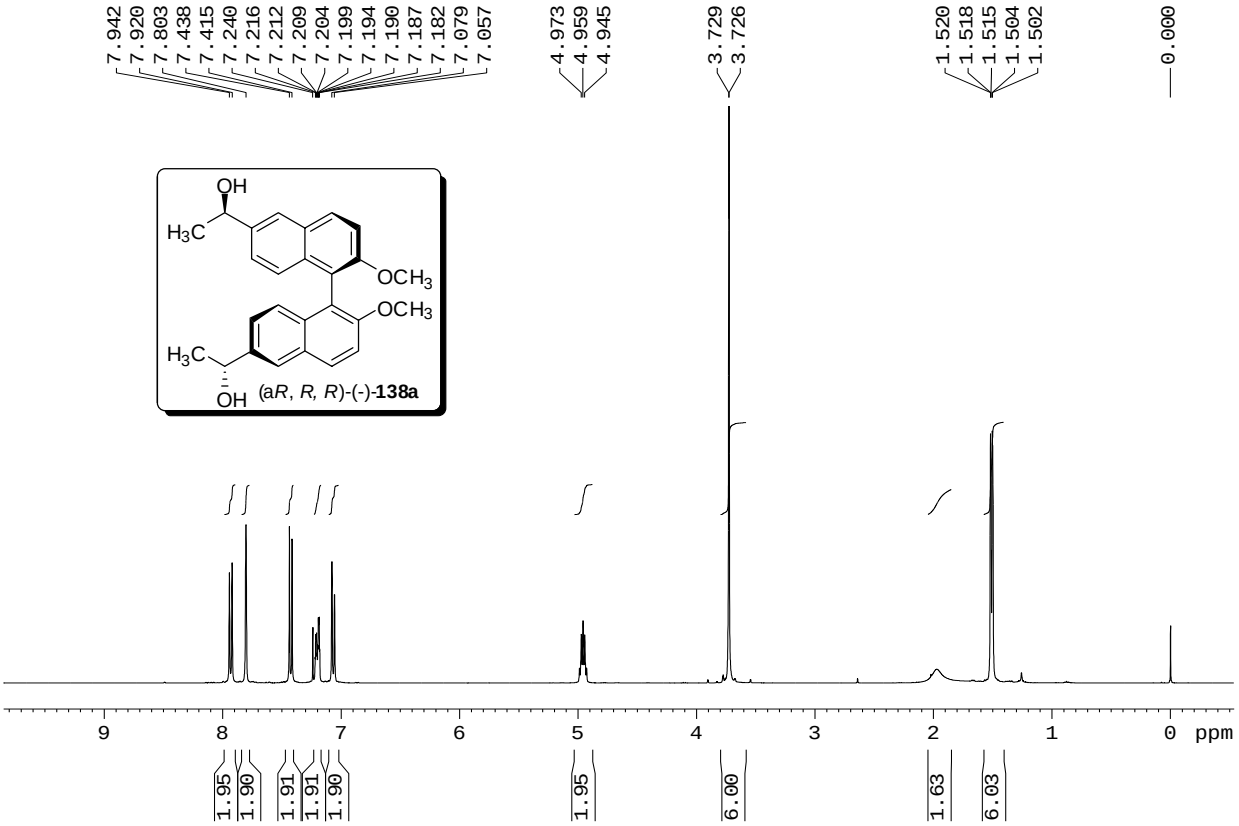
Spectrum No. 33 (Chapter 2, Section 2.2.1) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



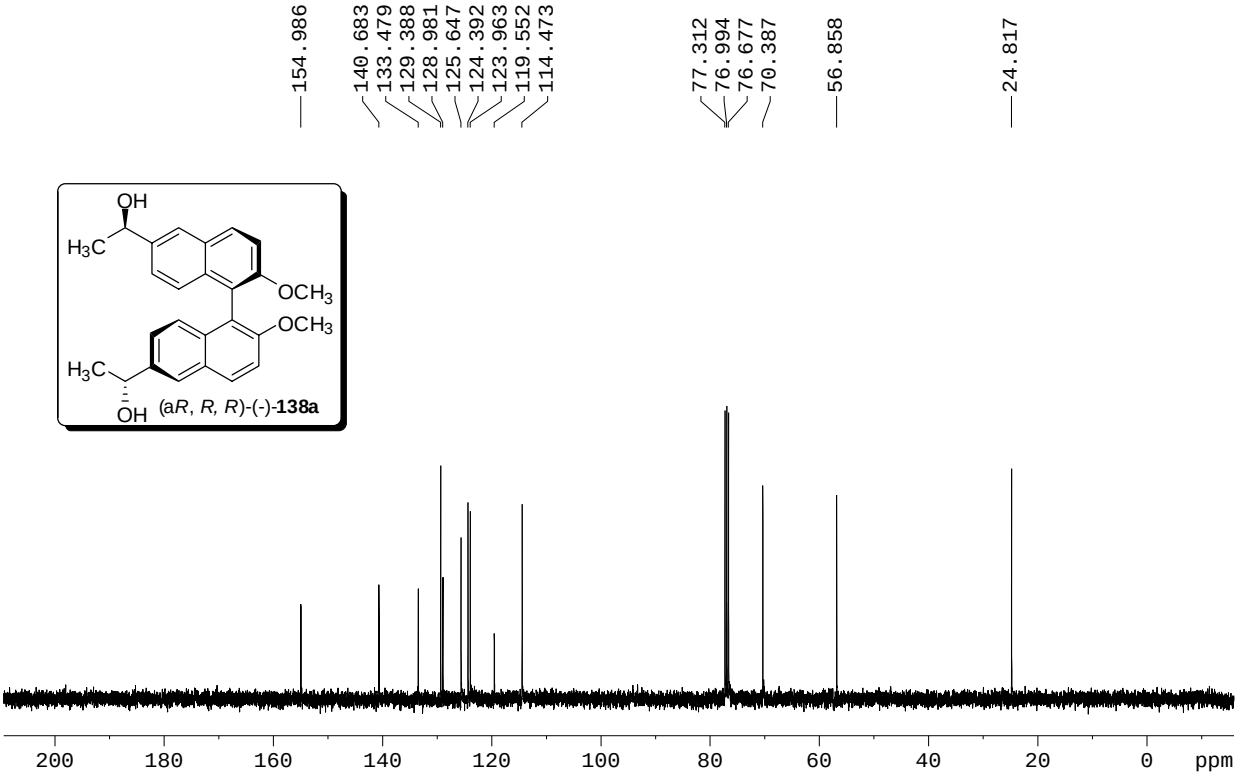
Spectrum No. 34 (Chapter 2, Section 2.2.1) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



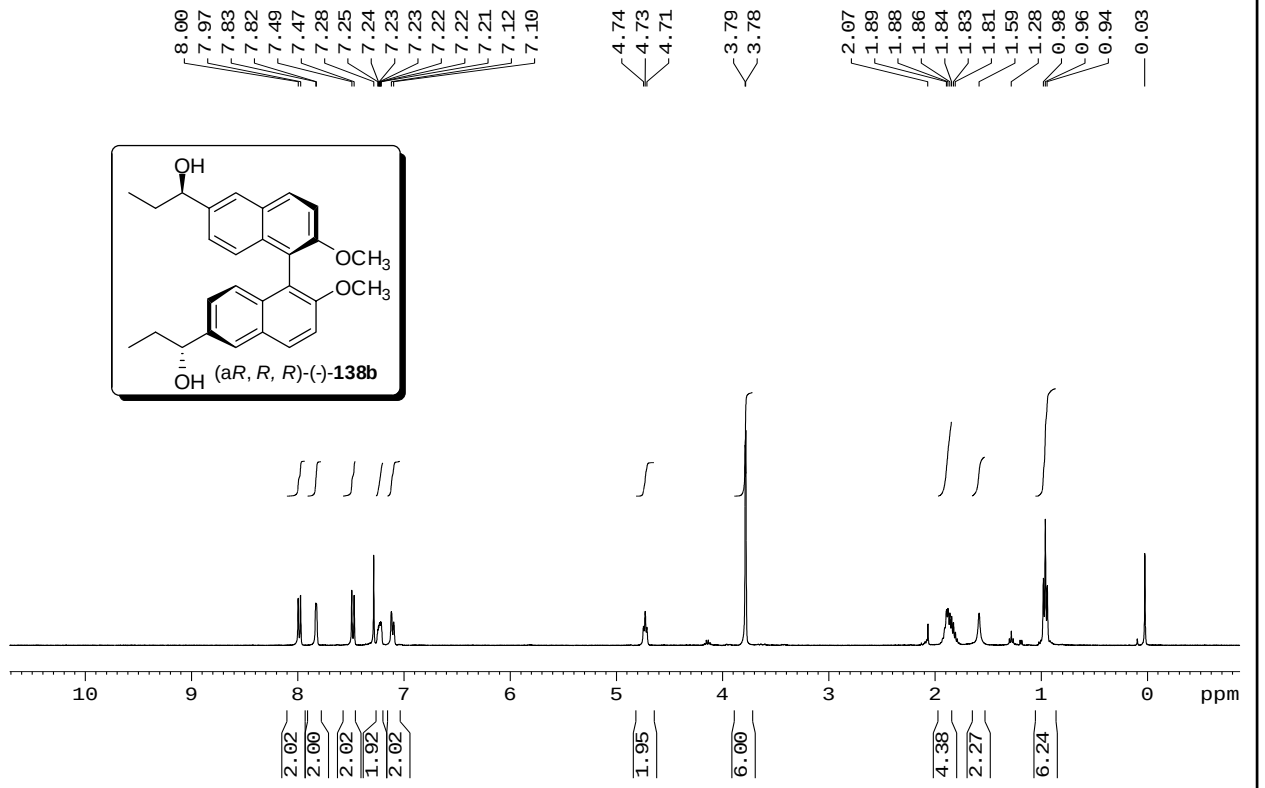
Spectrum No. 35 (Chapter 2, Section 2.2.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



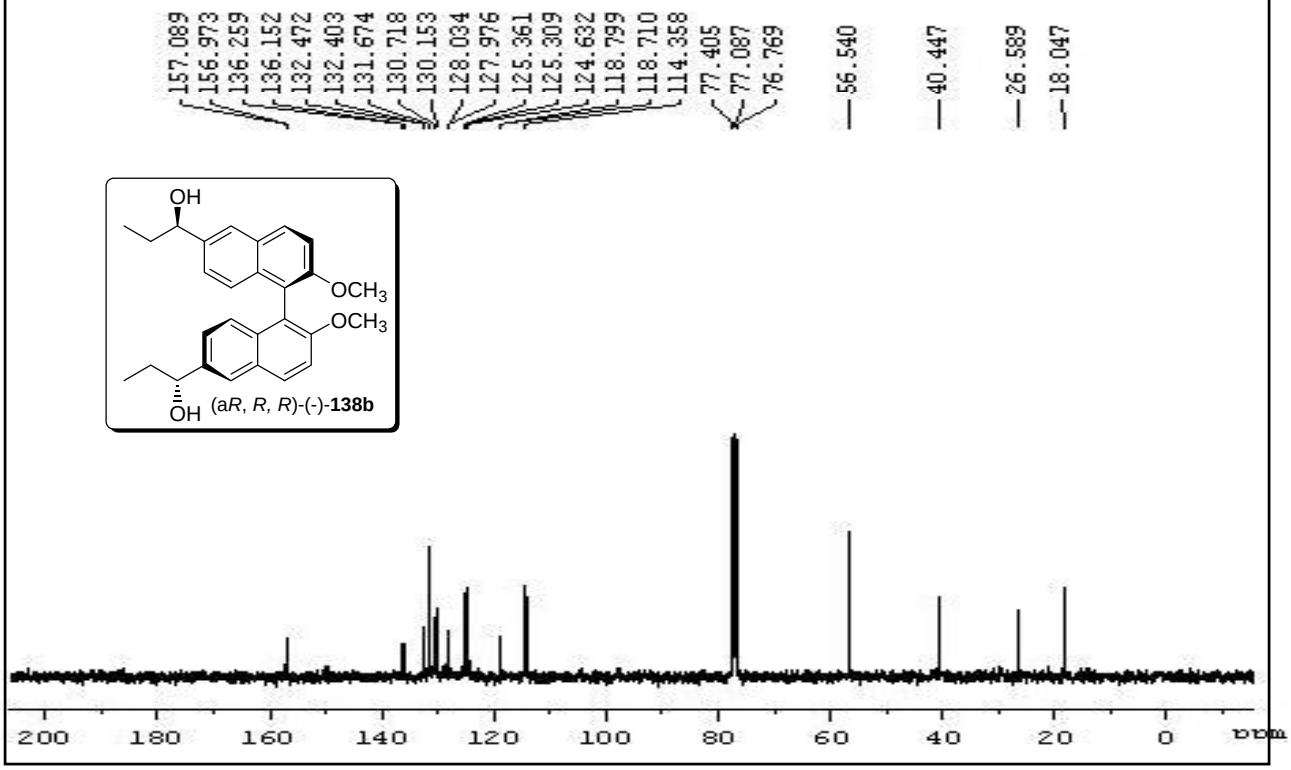
Spectrum No. 36 (Chapter 2, Section 2.2.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



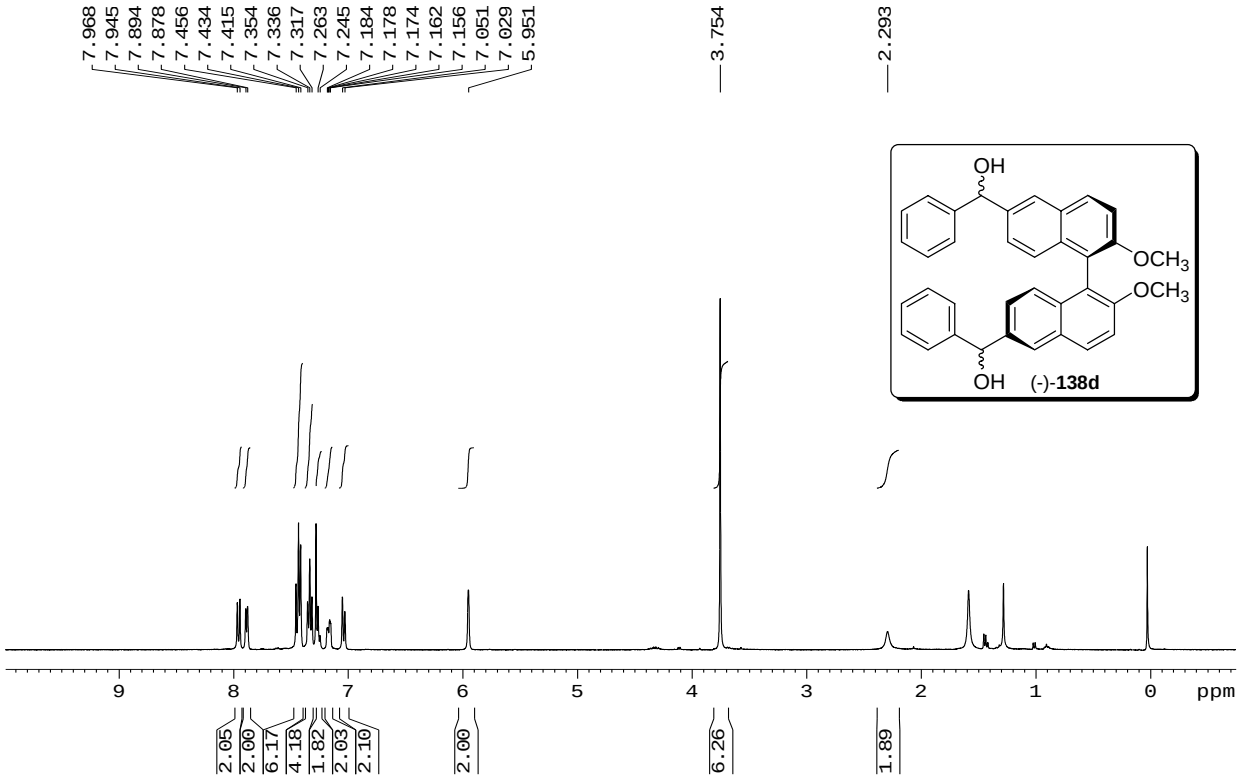
Spectrum No. 37 (Chapter 2, Section 2.2.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



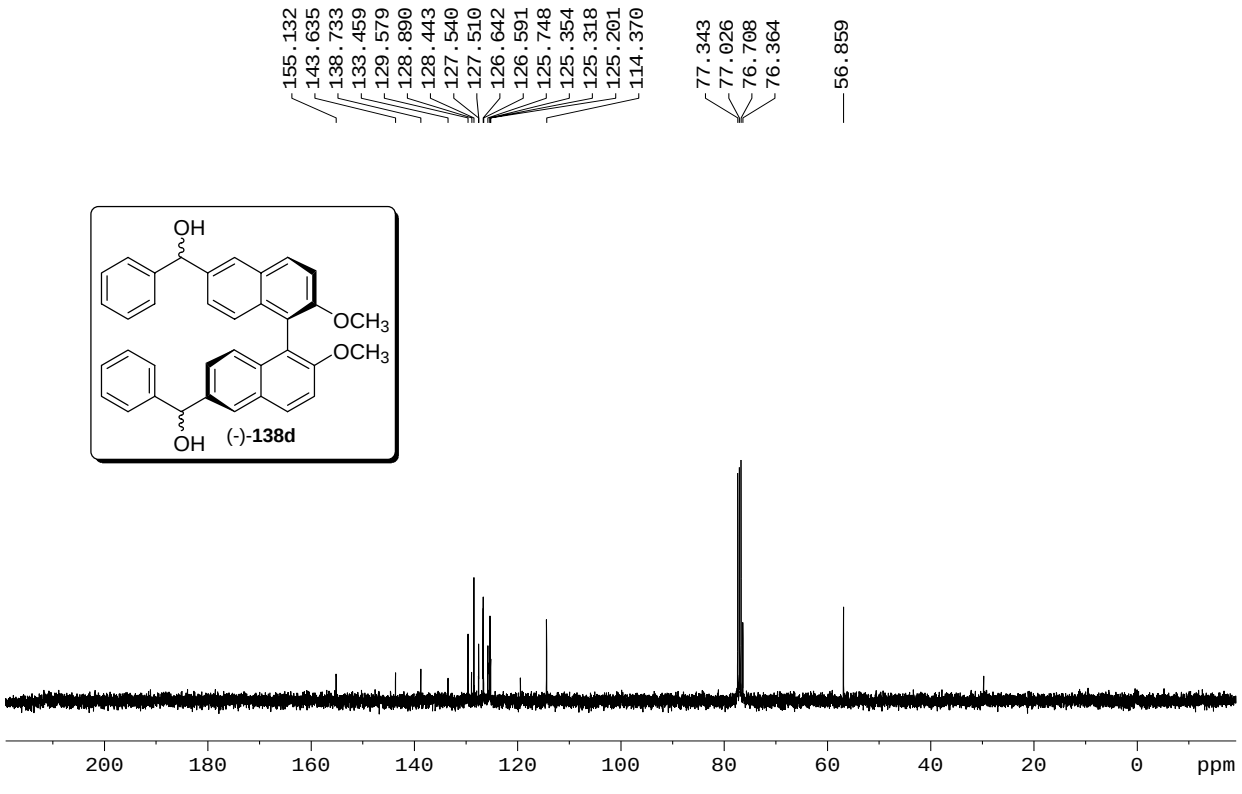
Spectrum No. 38 (Chapter 2, Section 2.2.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



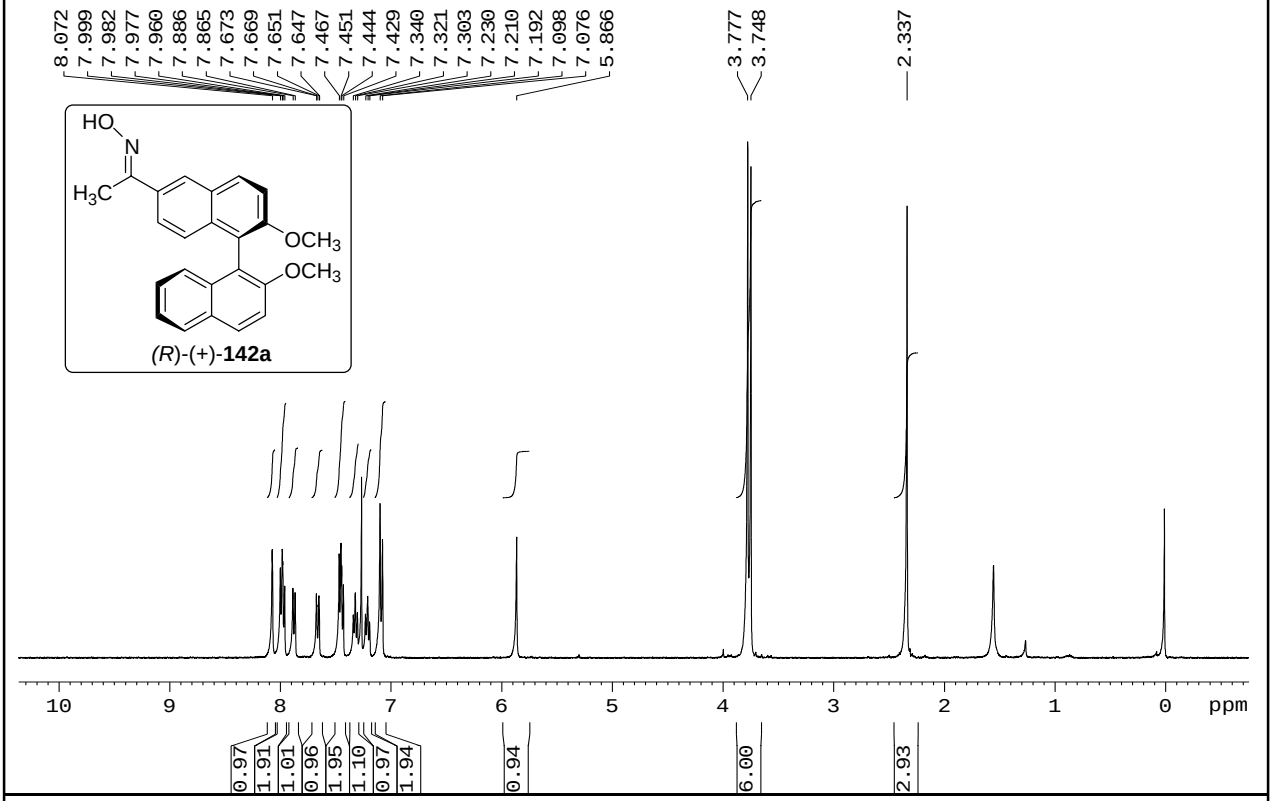
Spectrum No. 39 (Chapter 2, Section 2.2.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



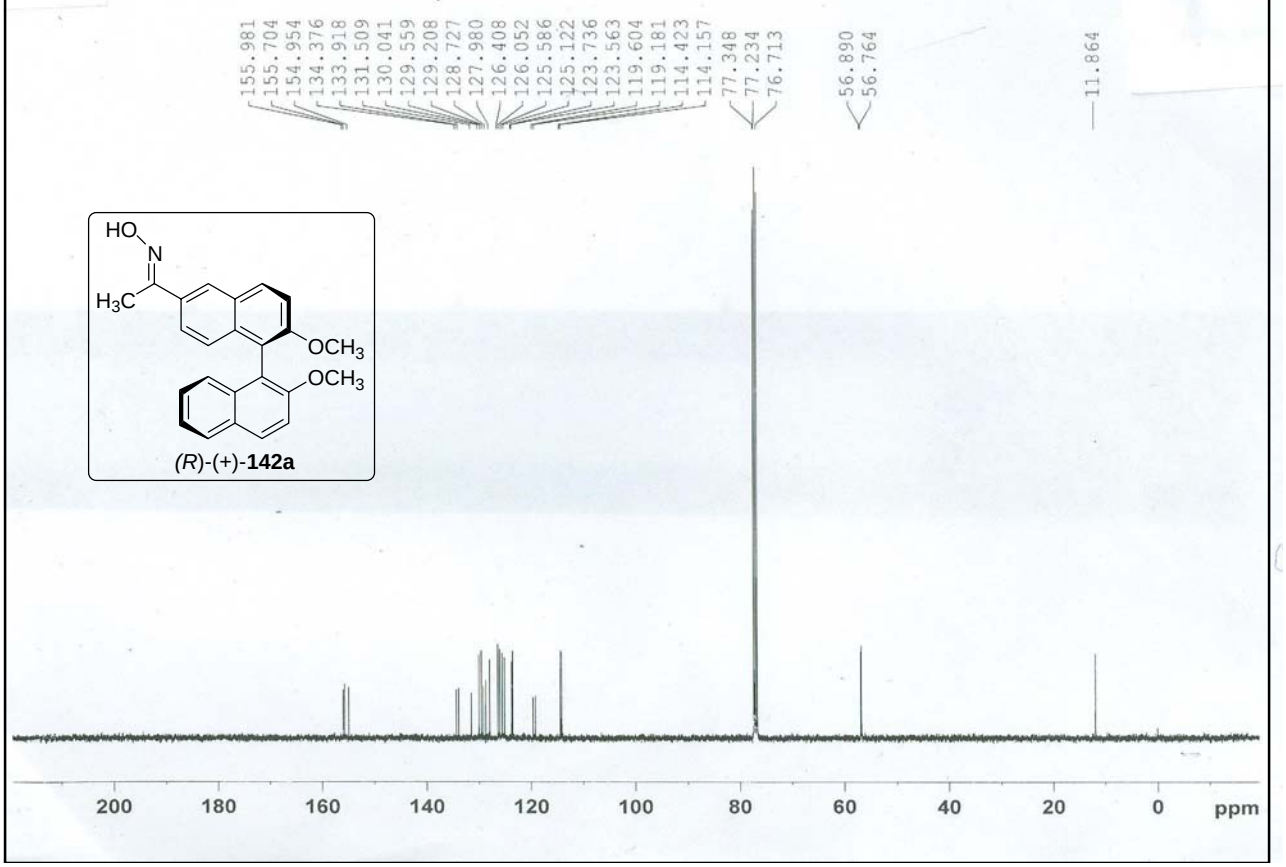
Spectrum No. 40 (Chapter 2, Section 2.2.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



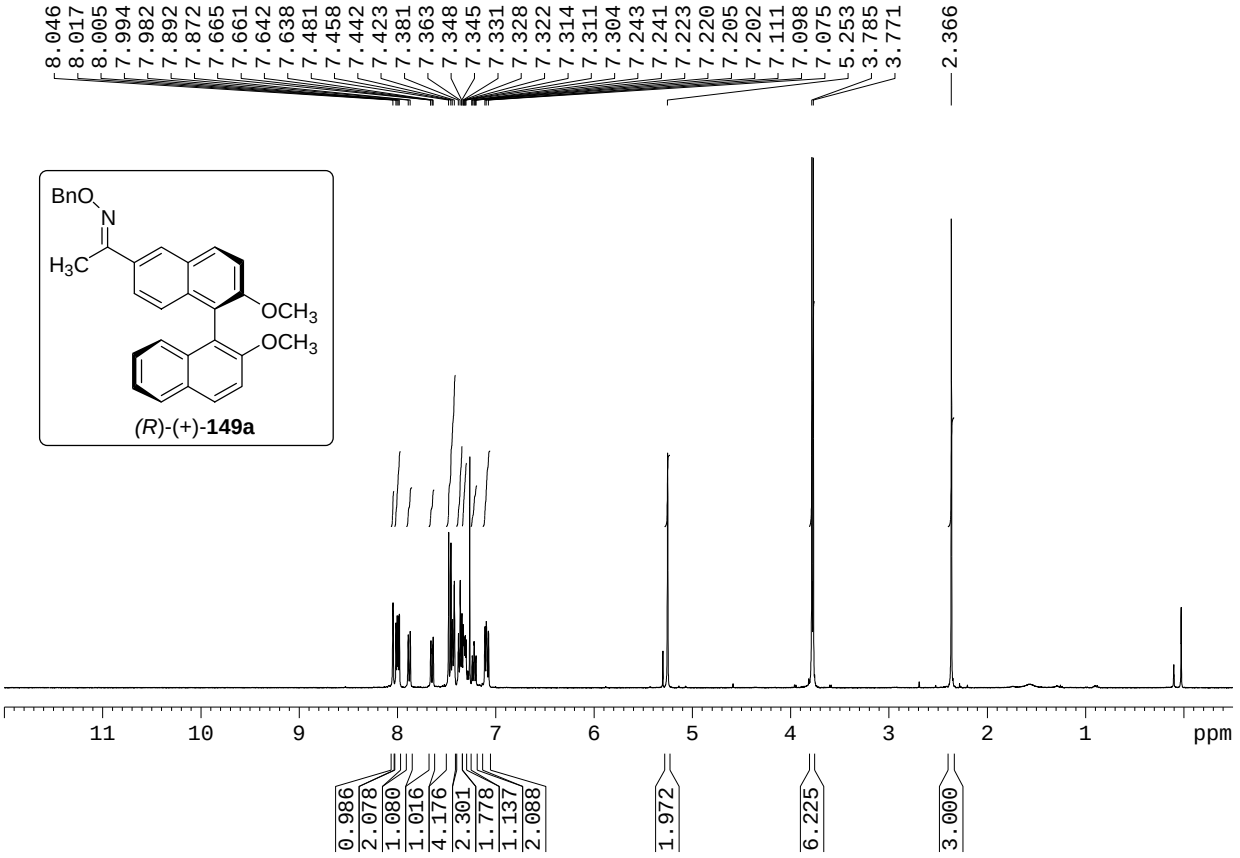
Spectrum No. 41 (Chapter 2, Section 2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



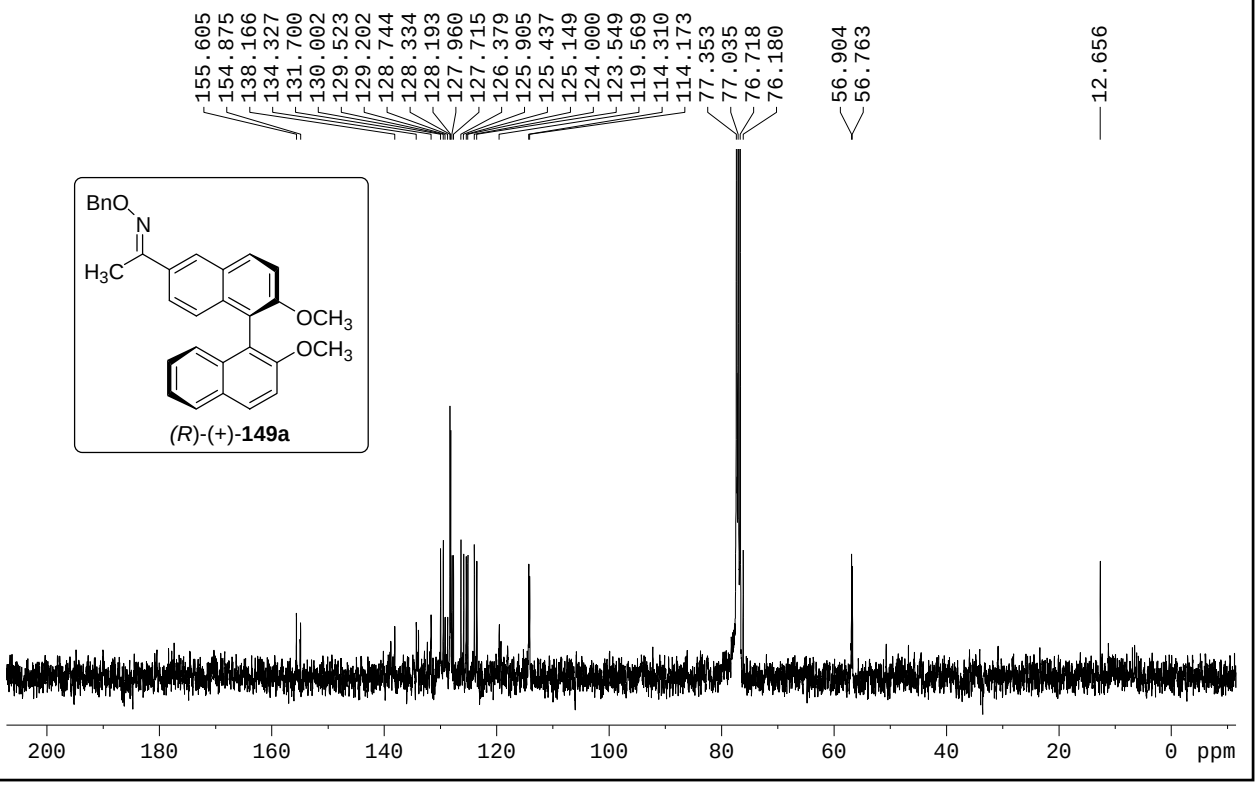
Spectrum No. 42 (Chapter 2, Section 2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



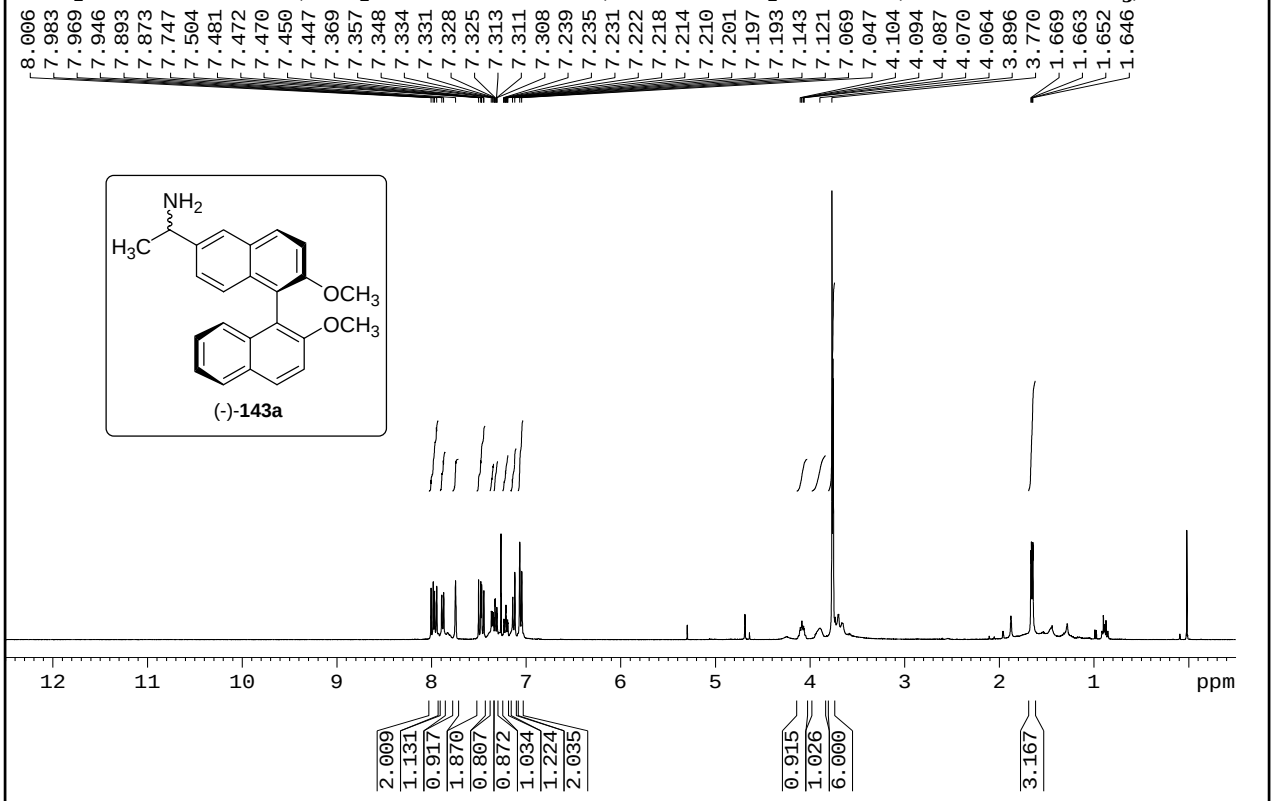
Spectrum No. 43 (Chapter 2, Section 2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



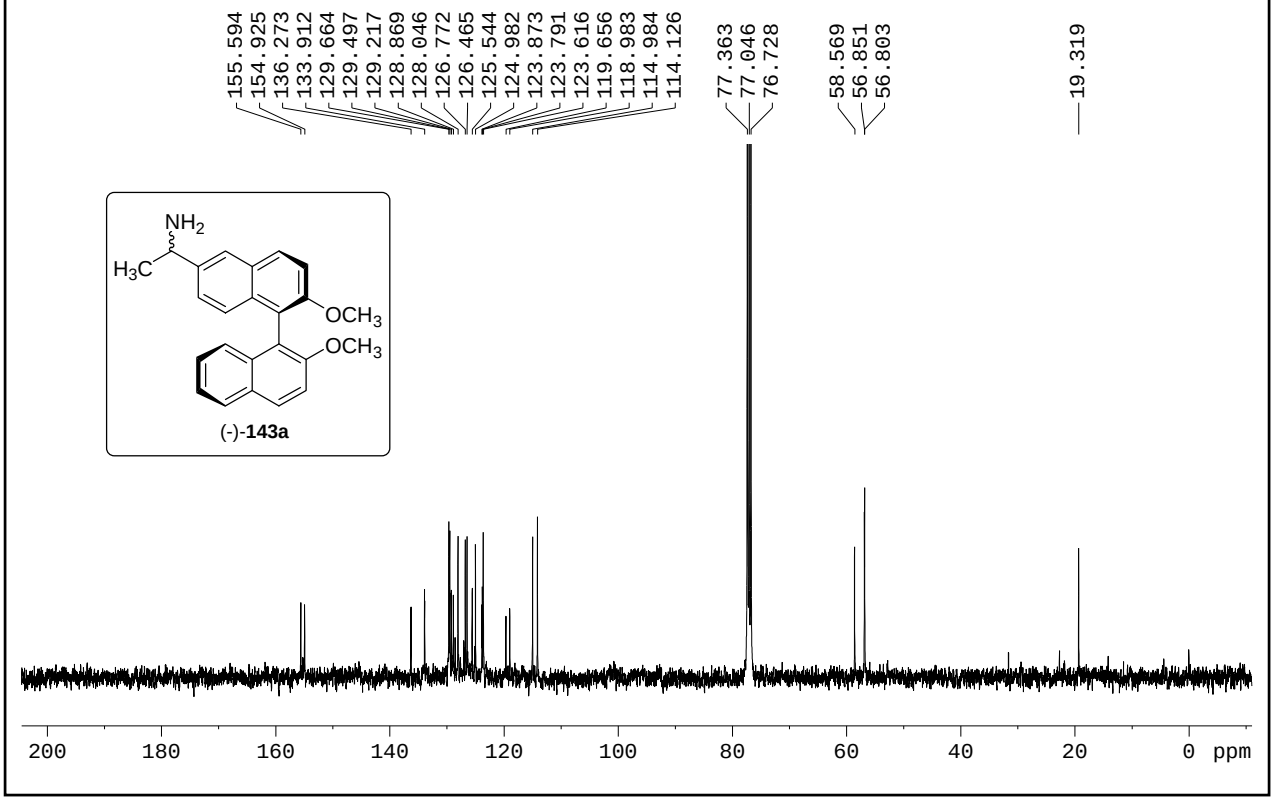
Spectrum No. 44 (Chapter 2, Section 2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



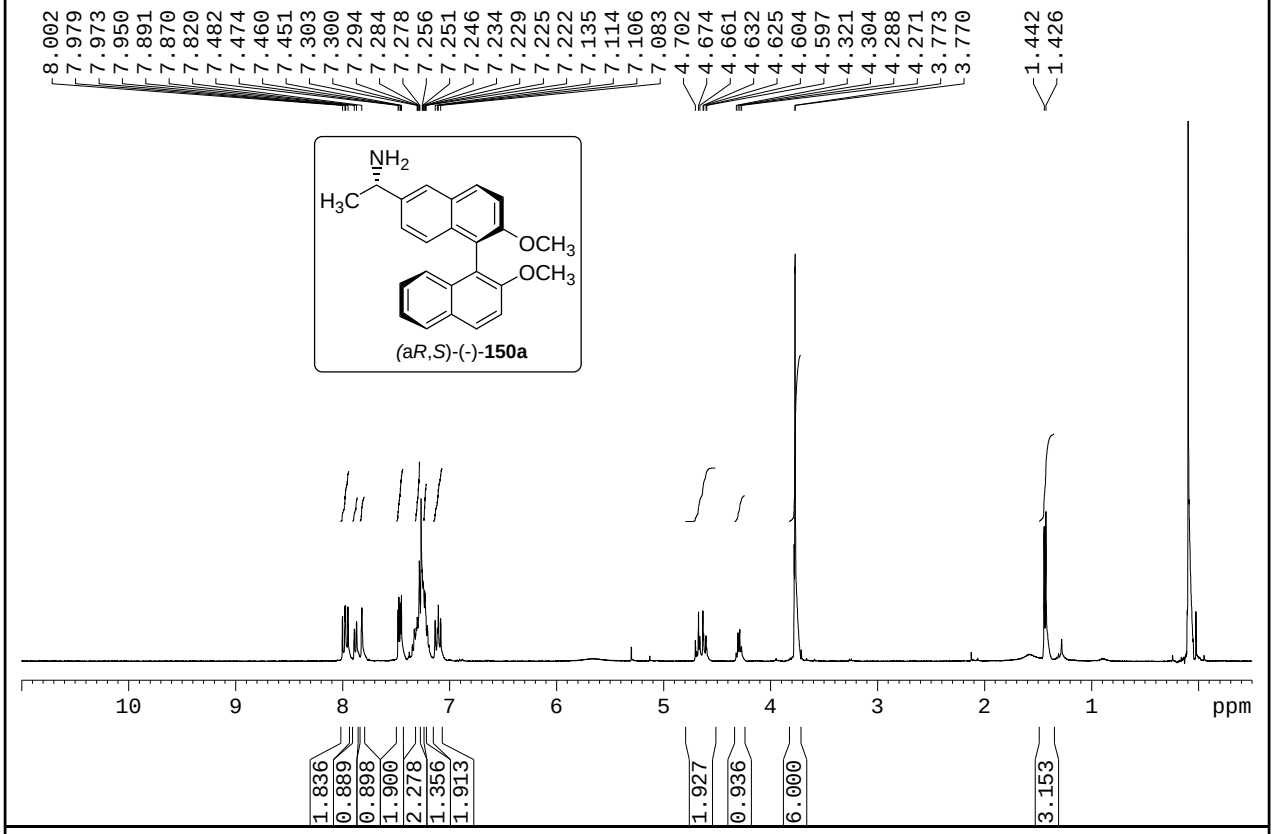
Spectrum No. 45 (Chapter 2, Section 2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



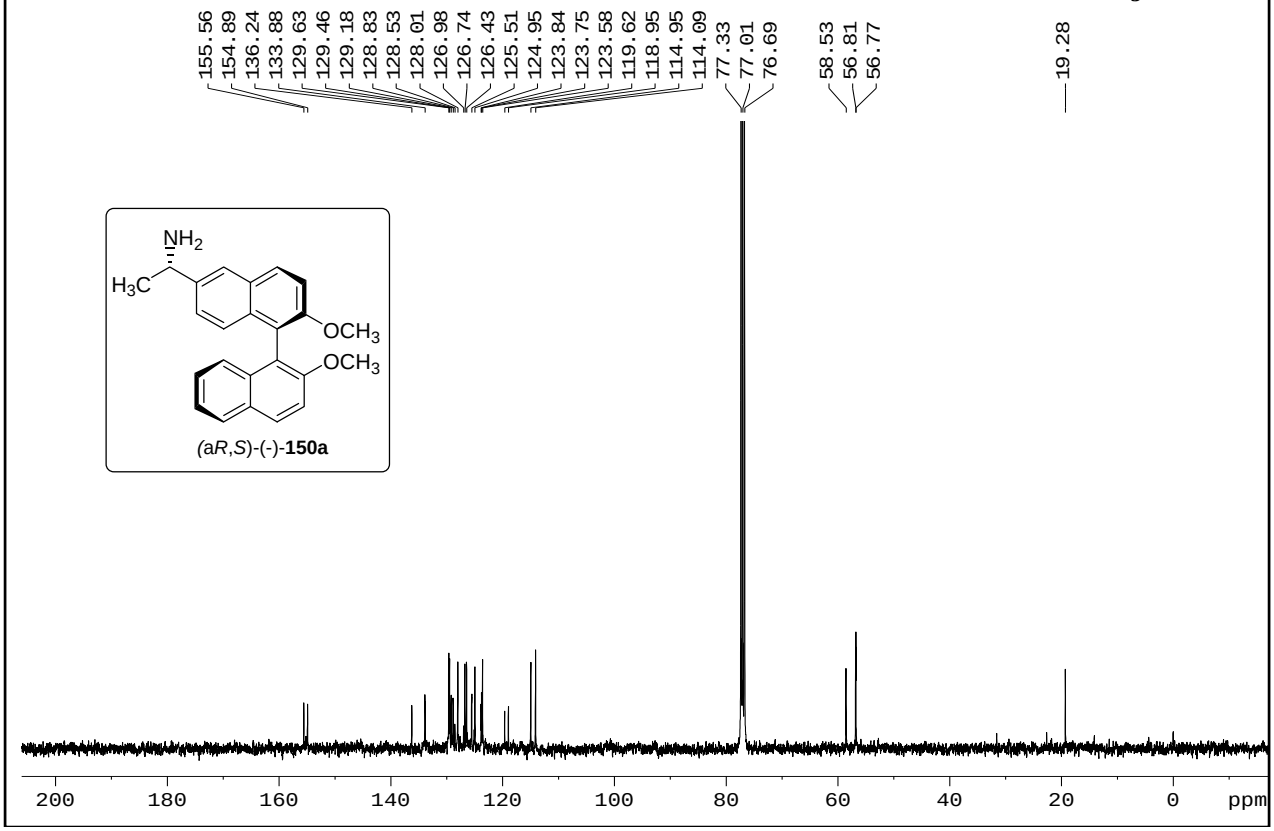
Spectrum No. 46 (Chapter 2, Section 2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



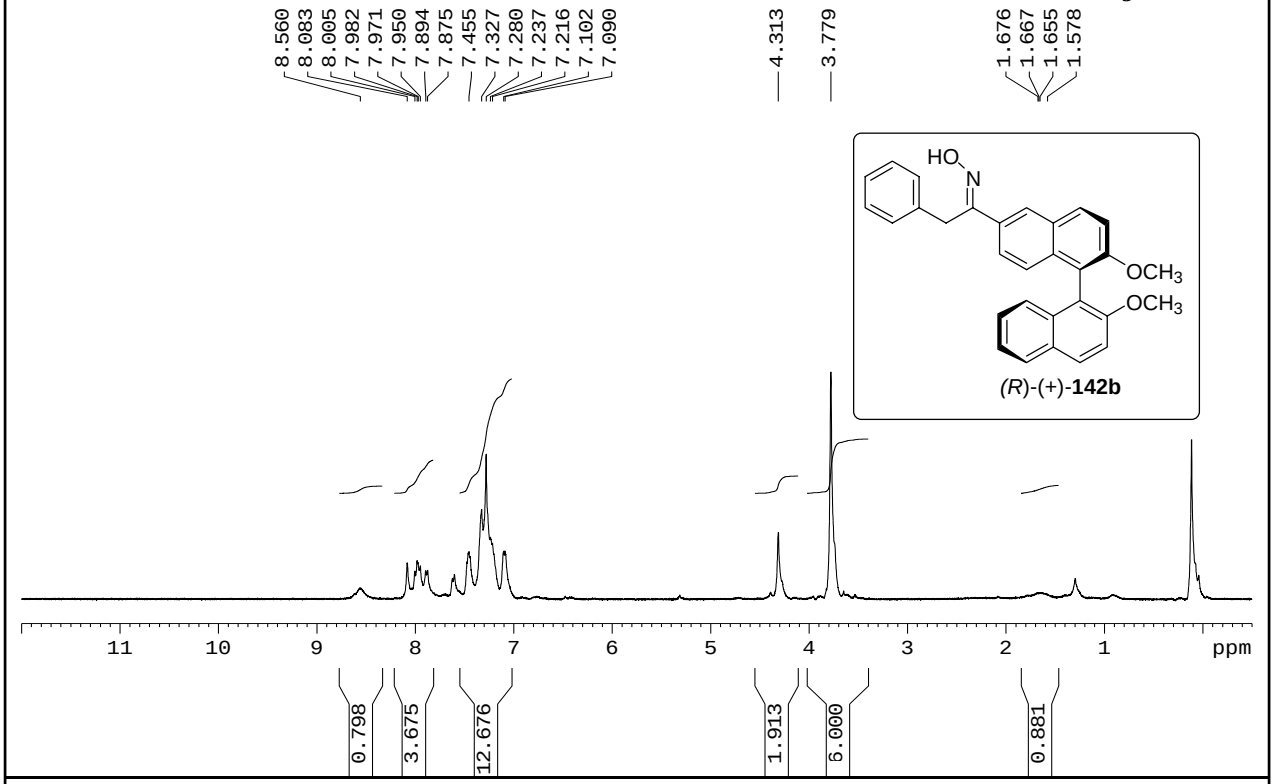
Spectrum No. 47 (Chapter 2, Section 2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



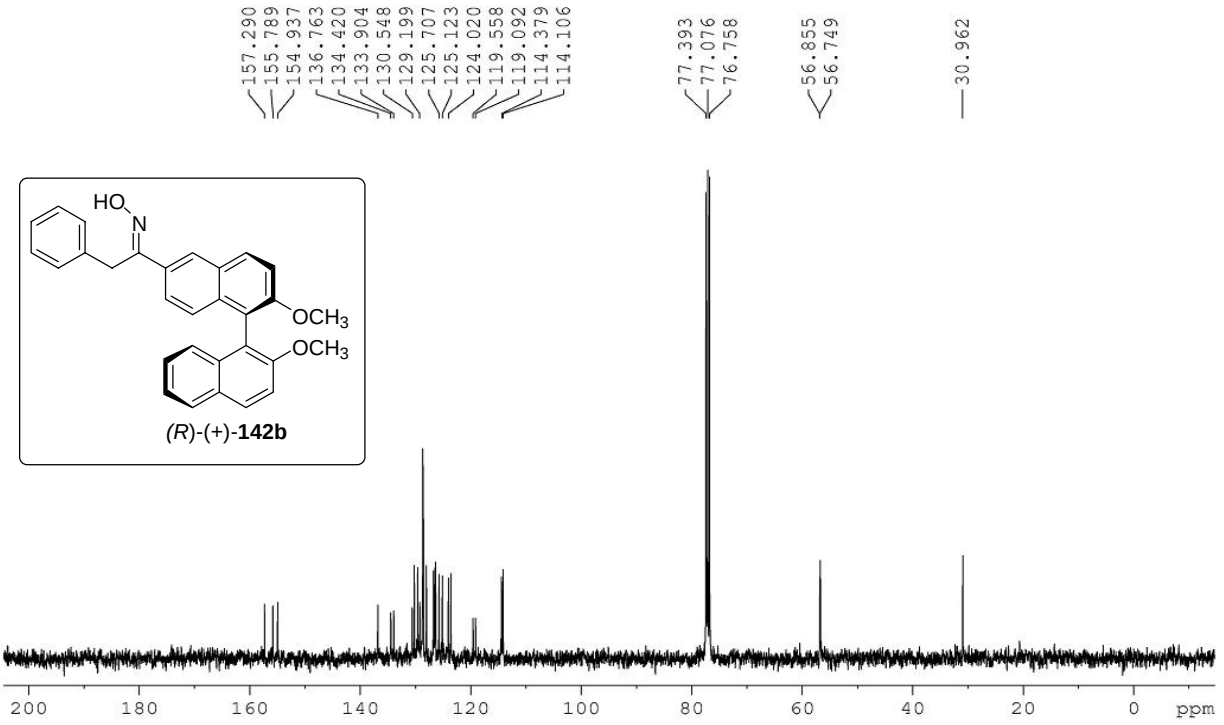
Spectrum No. 48 (Chapter 2, Section 2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



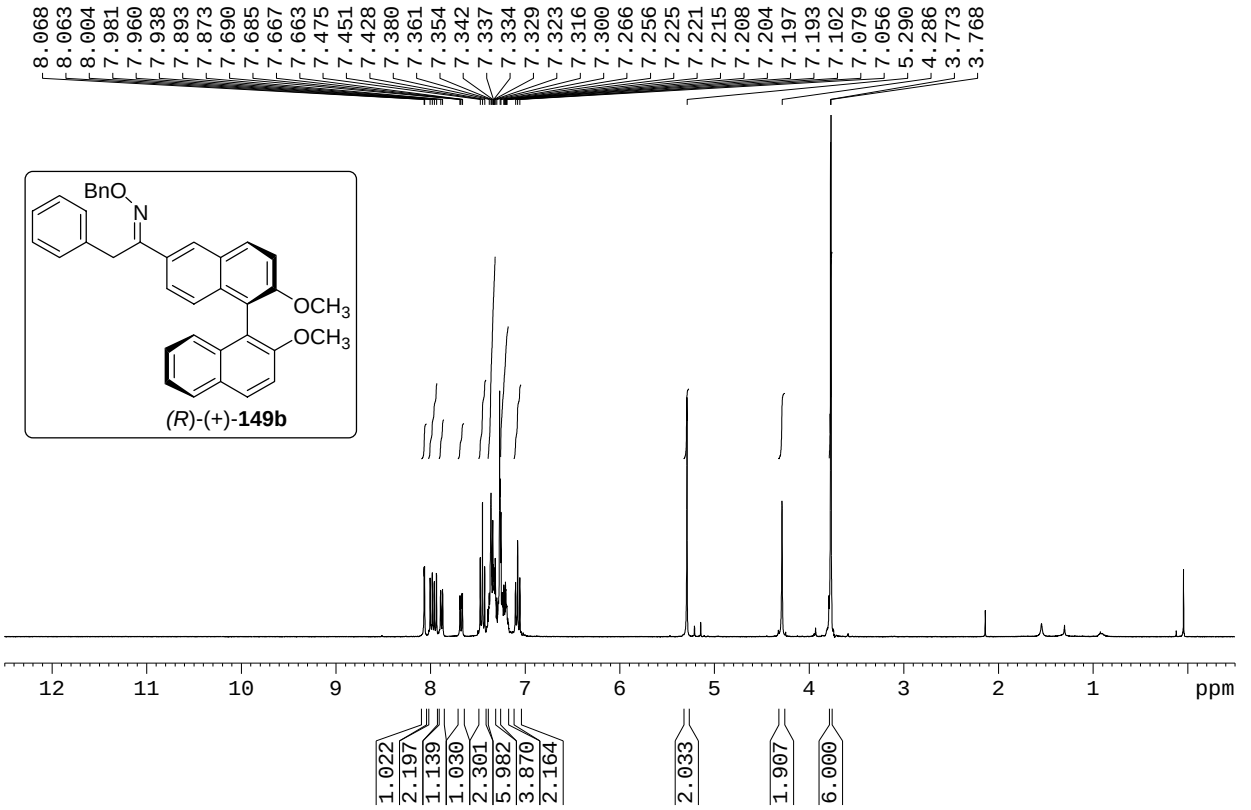
Spectrum No. 49 (Chapter 2, Section 2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



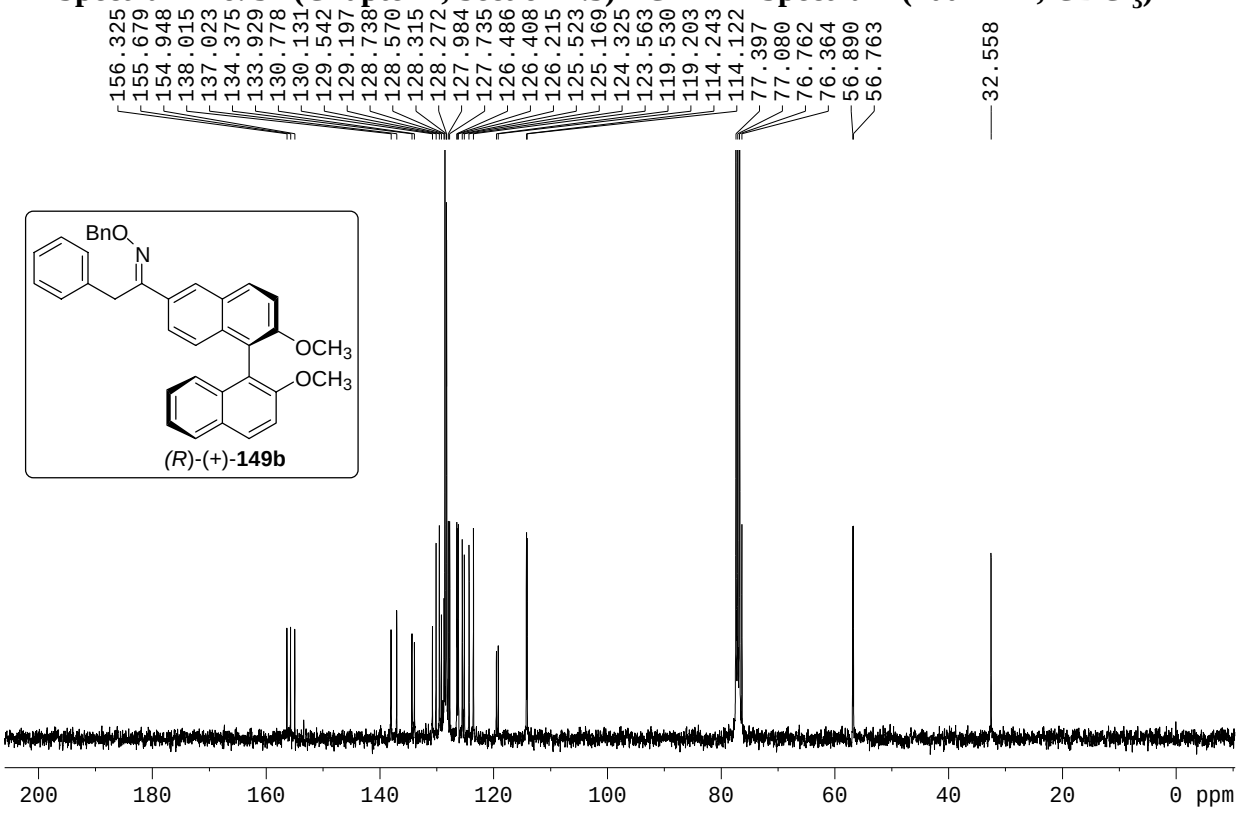
Spectrum No. 50 (Chapter 2, Section 2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



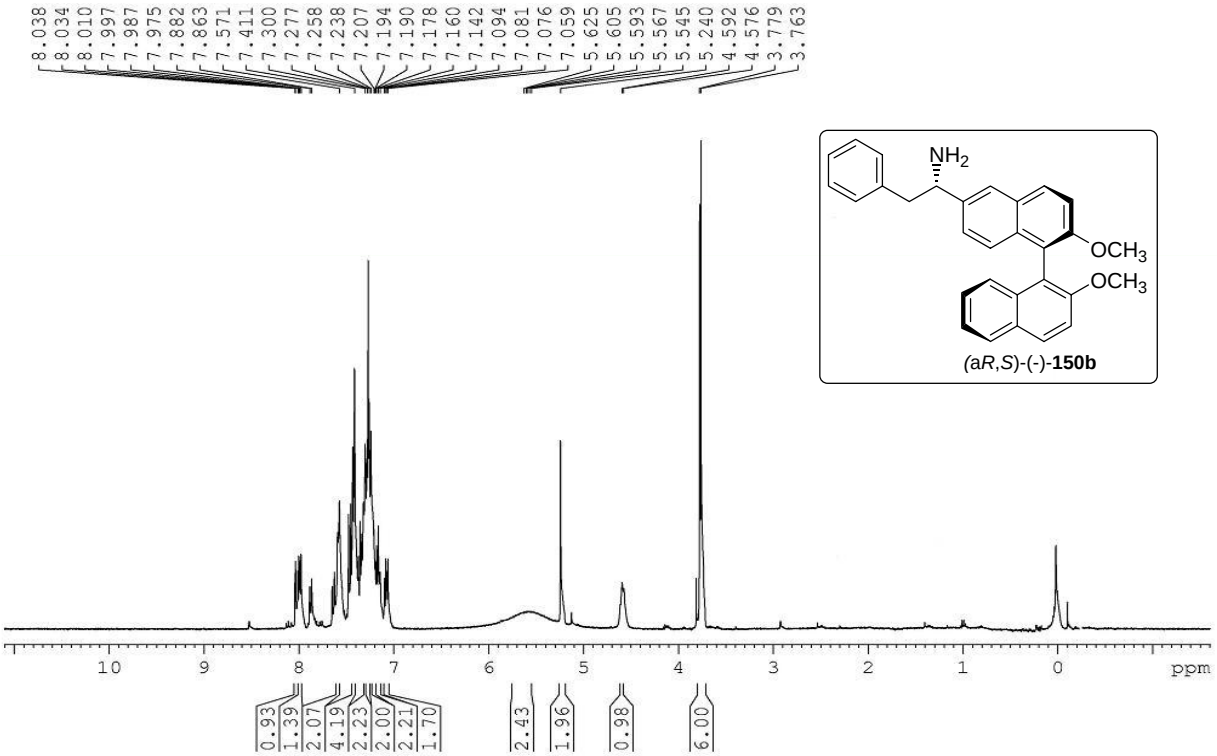
Spectrum No. 51 (Chapter 2, Section 2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



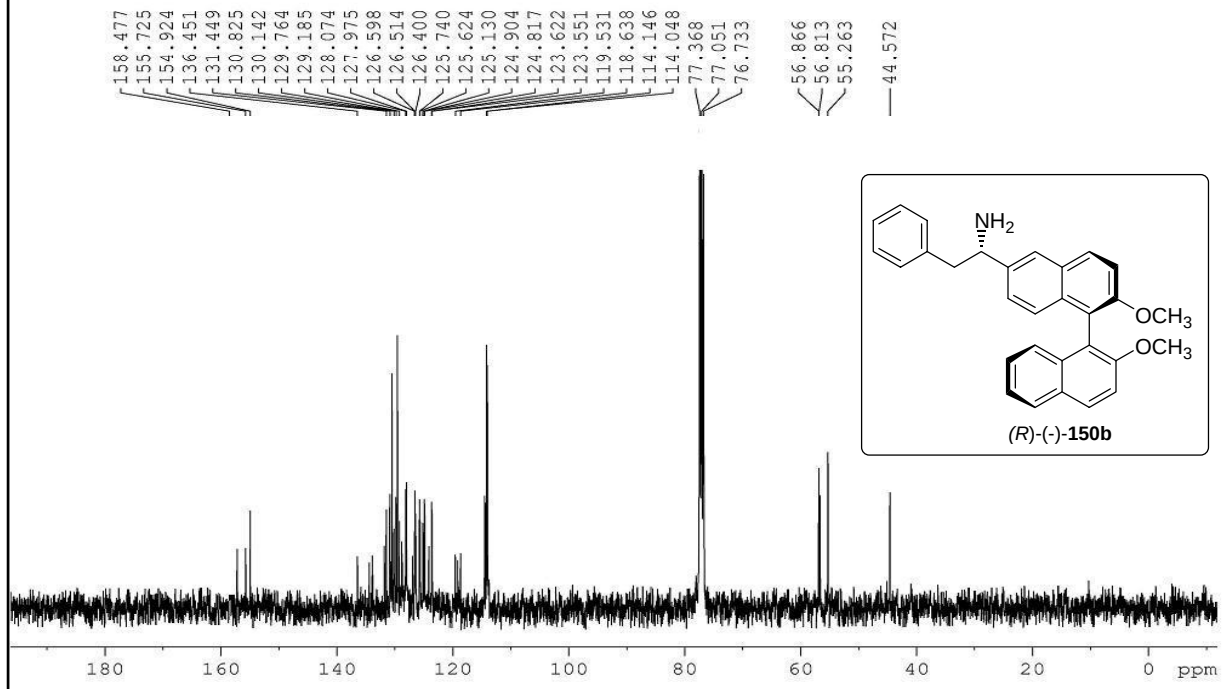
Spectrum No. 52 (Chapter 2, Section 2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



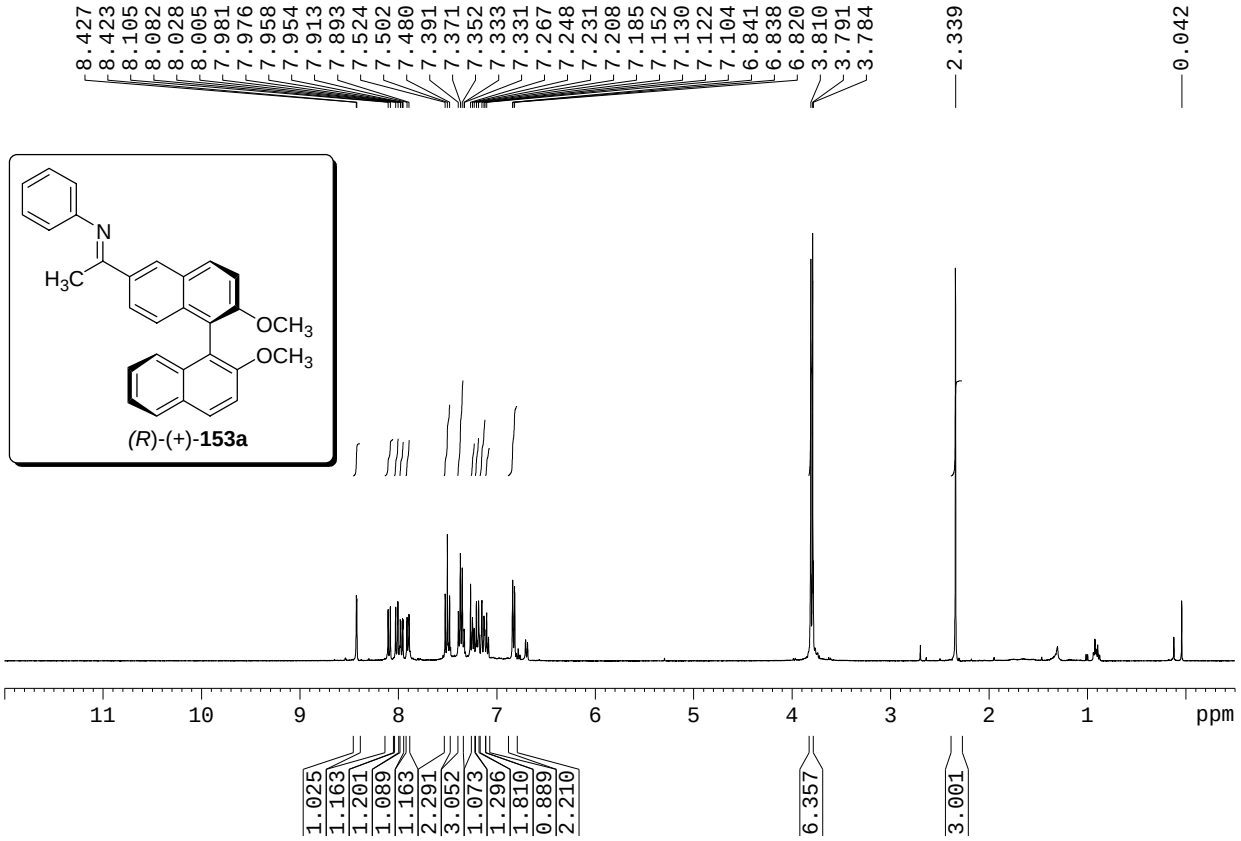
Spectrum No. 53 (Chapter 2, Section 2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



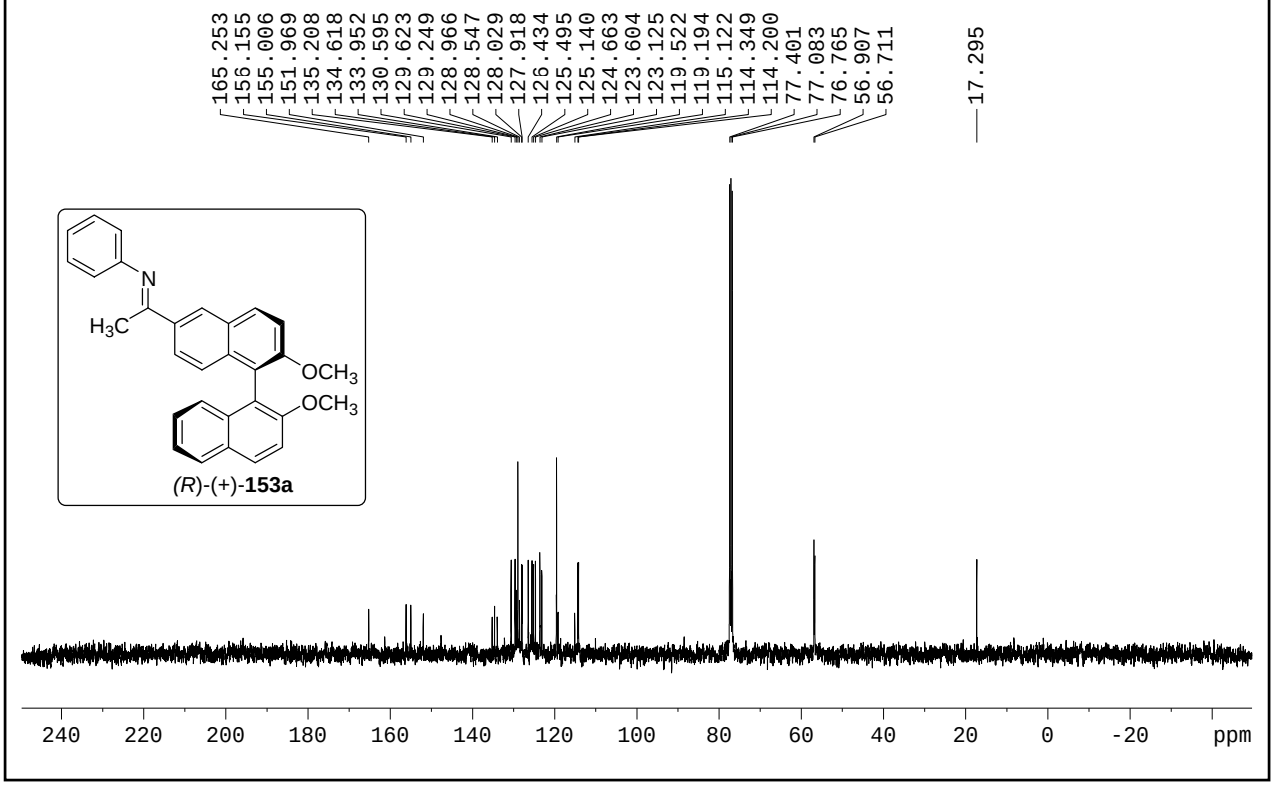
Spectrum No. 54 (Chapter 2, Section 2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



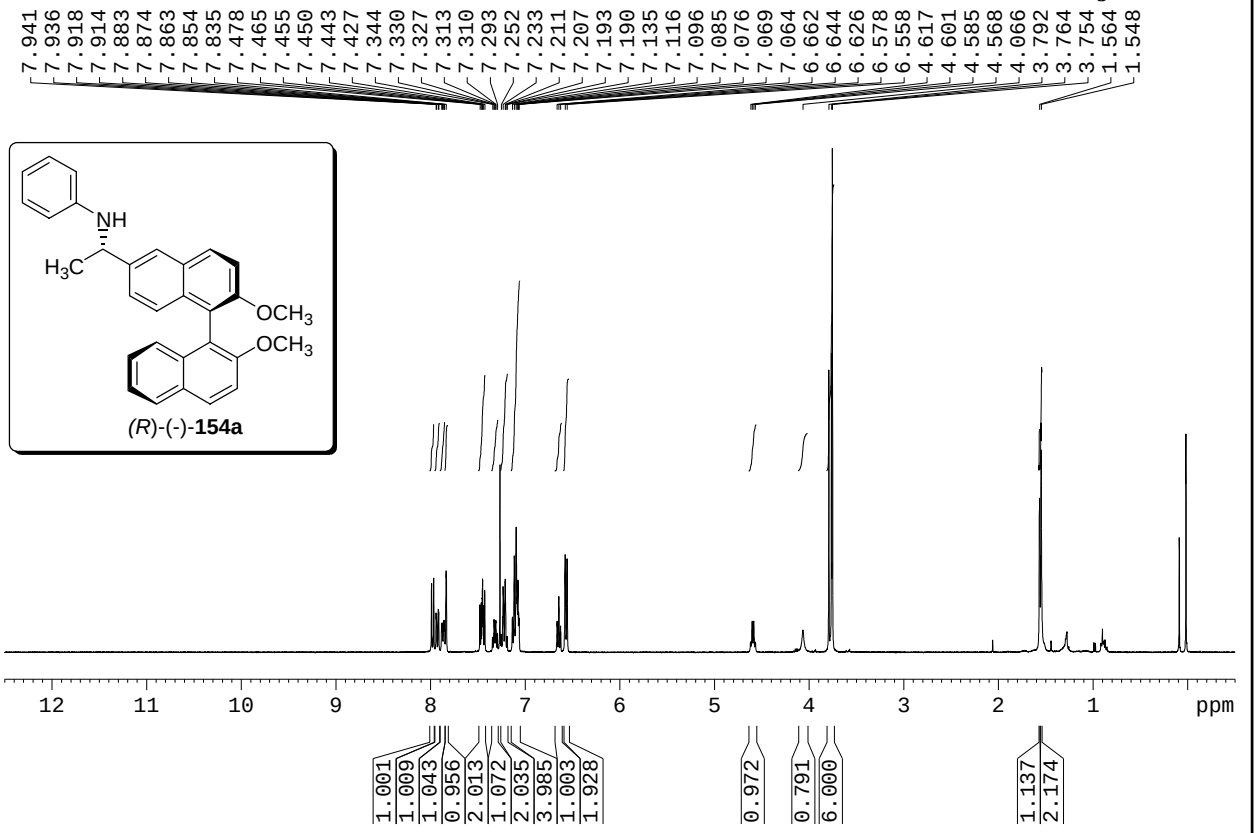
Spectrum No. 55 (Chapter 2, Section 2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



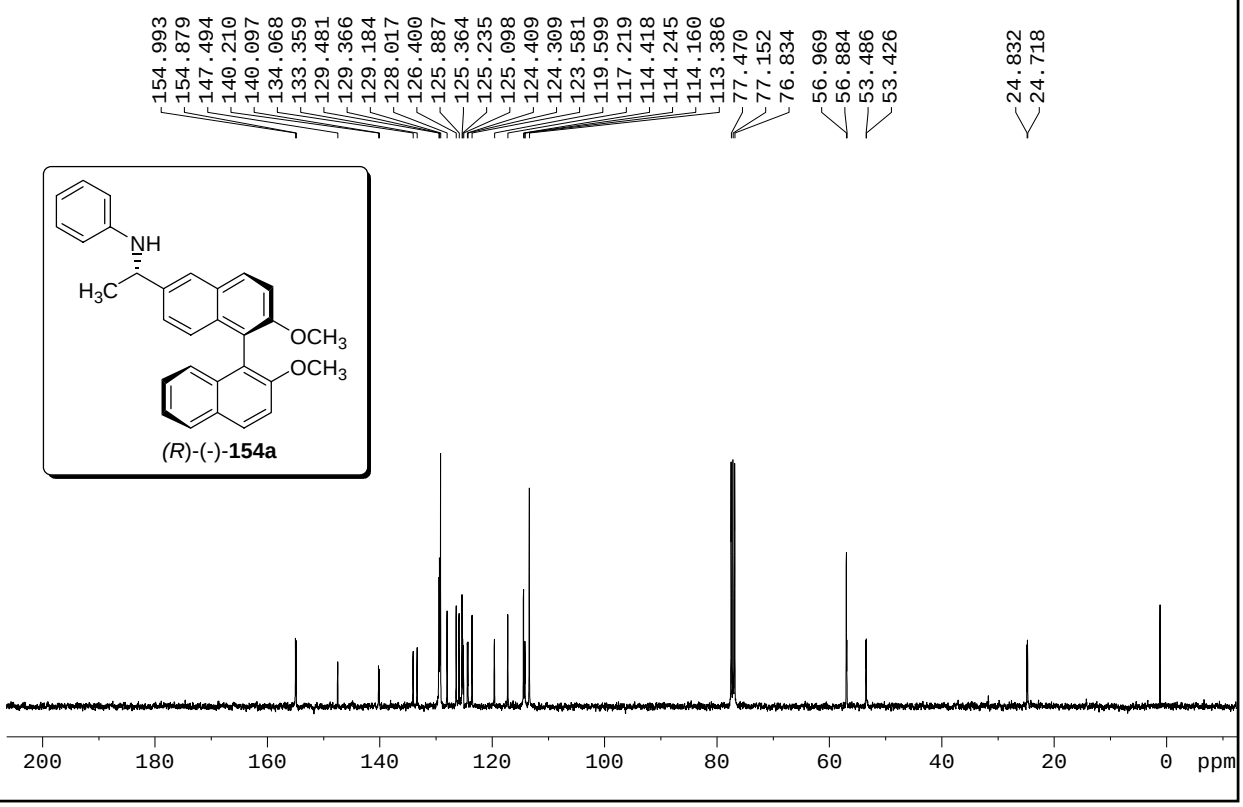
Spectrum No. 56 (Chapter 2, Section 2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



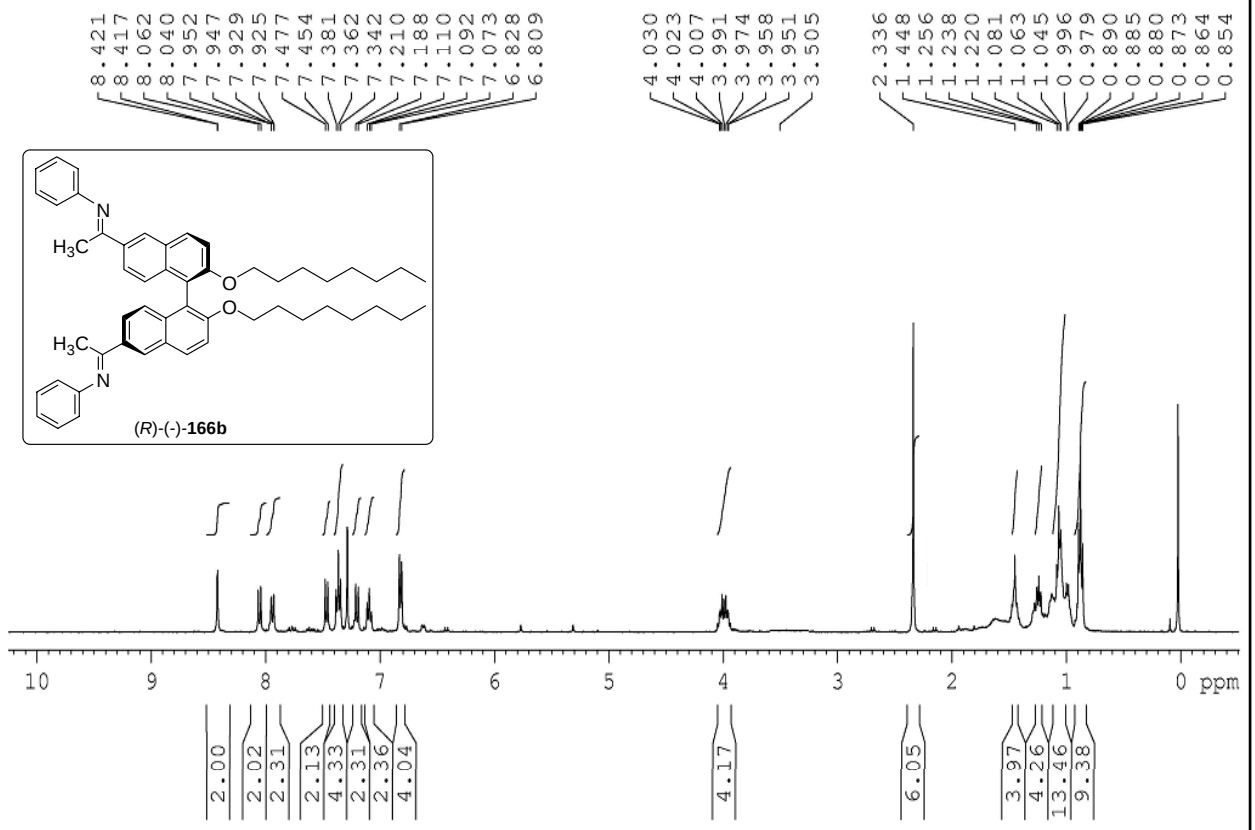
Spectrum No. 57 (Chapter 2 Section 2.3) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



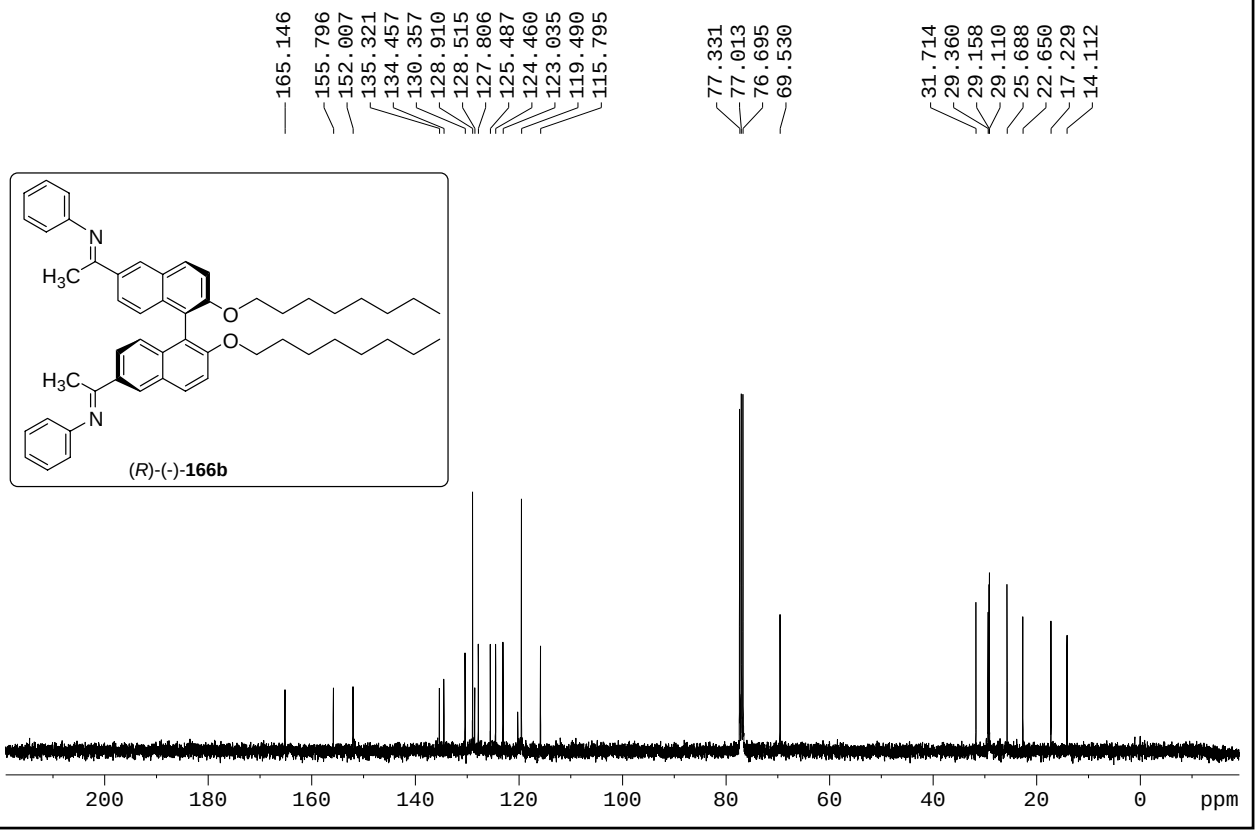
Spectrum No. 58 (Chapter 2, Section 2.3) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



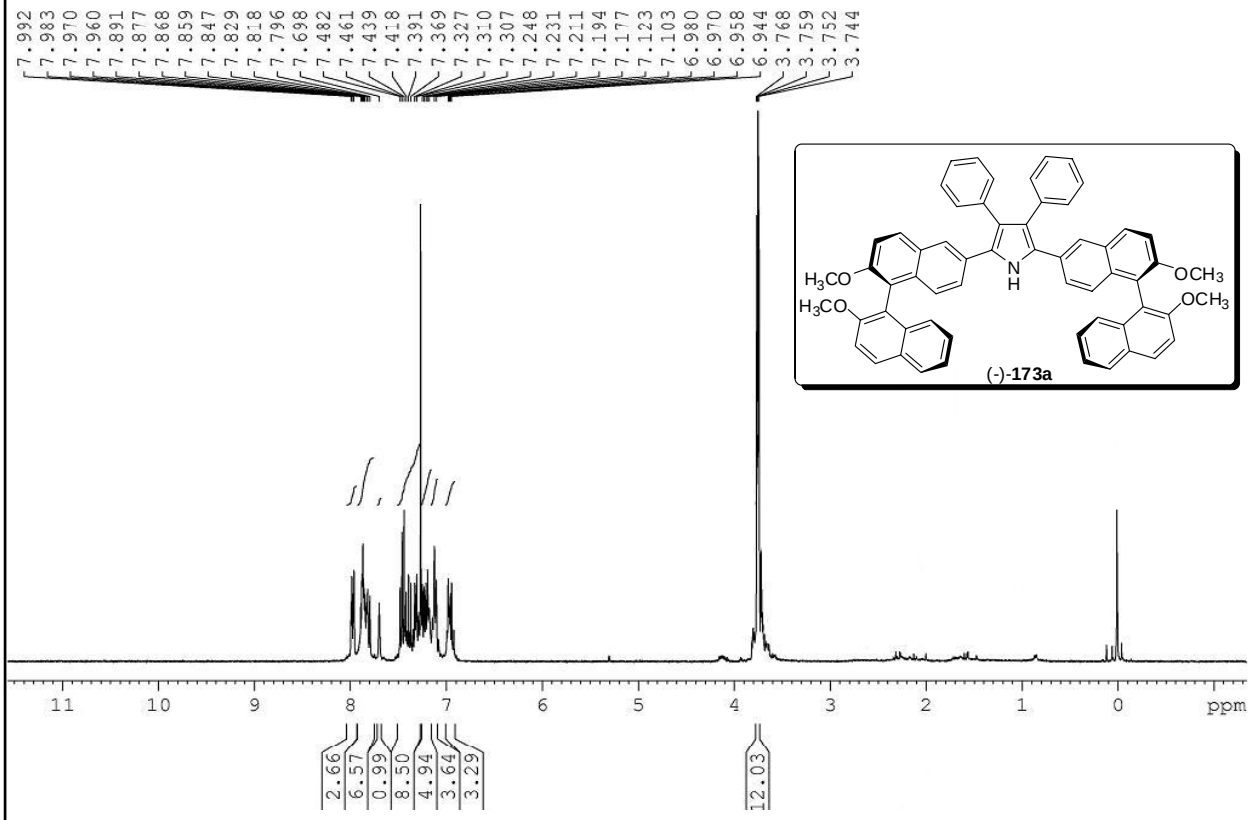
Spectrum No. 59 (Chapter 2 Section 2.5) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



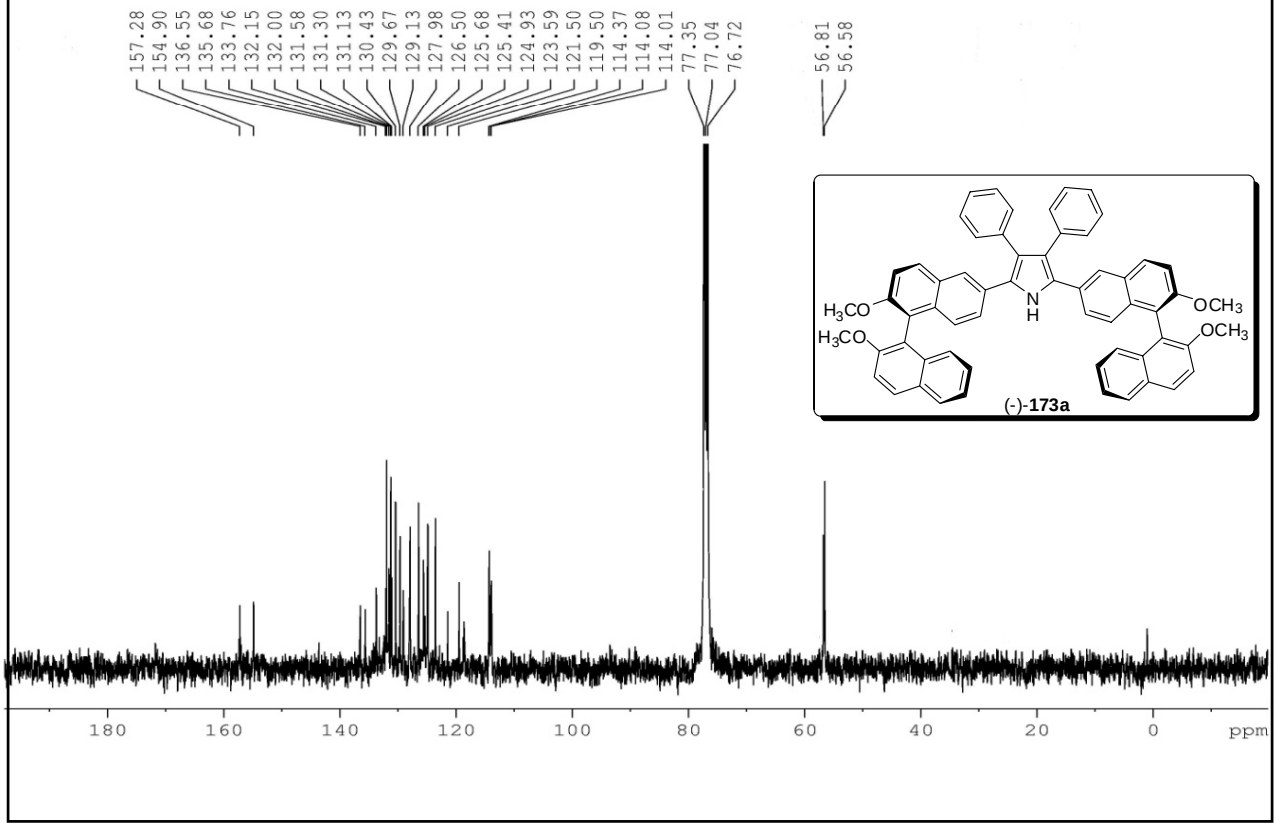
Spectrum No. 60 (Chapter 2, Section 2.5) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



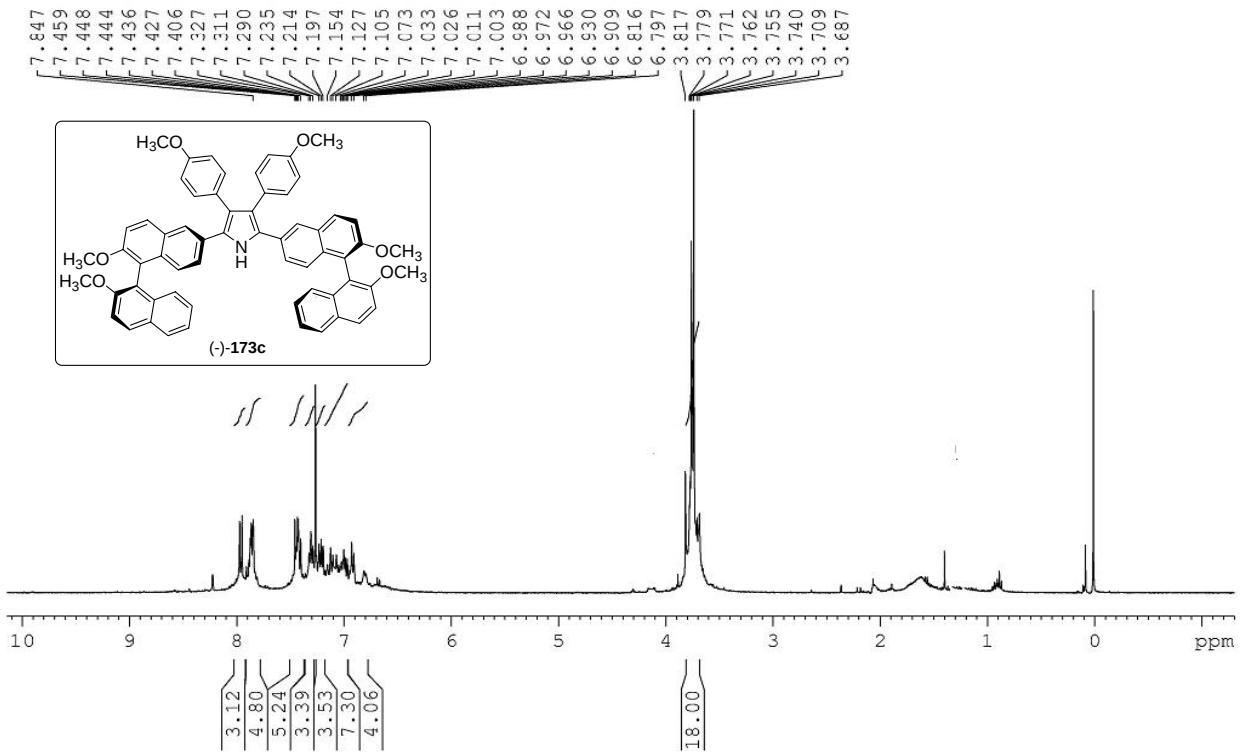
Spectrum No. 61 (Chapter 2, Section 2.6) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



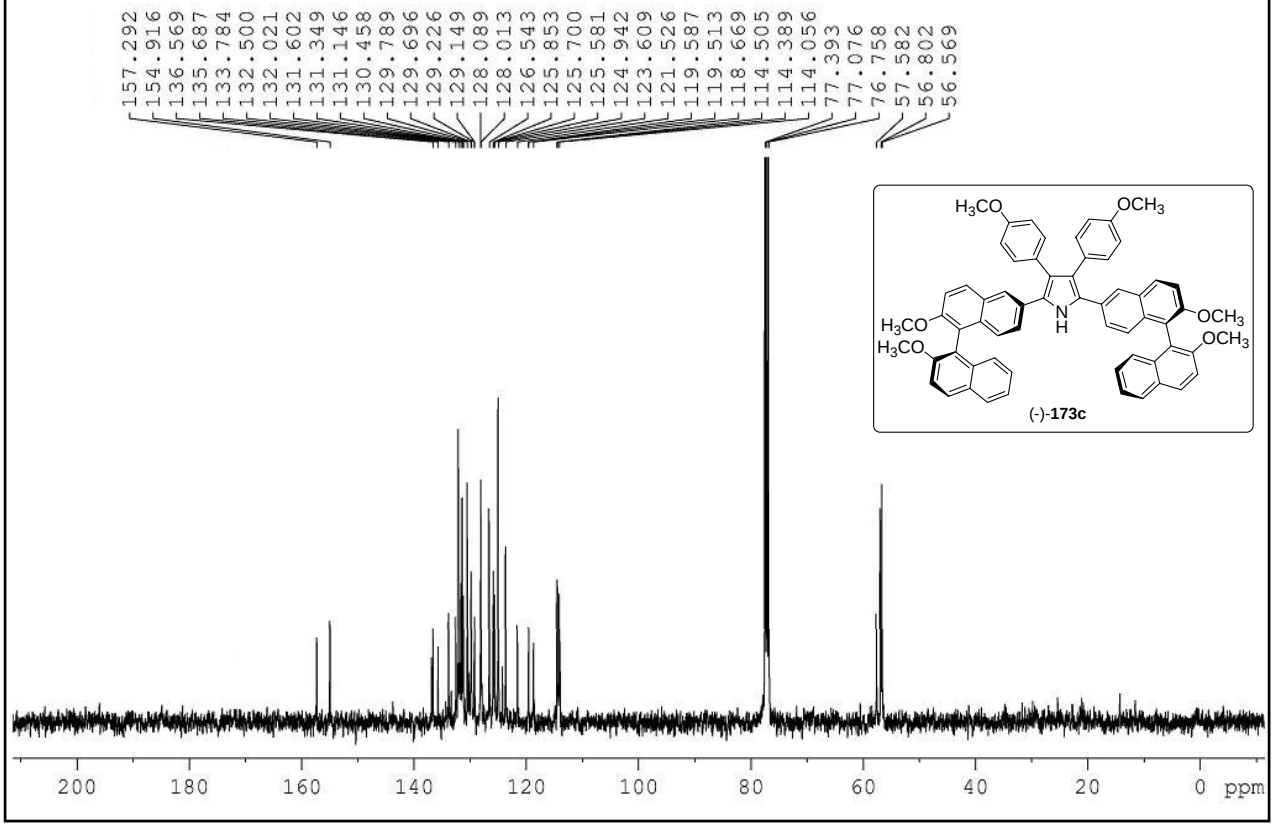
Spectrum No. 62 (Chapter 2, Section 2.6) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



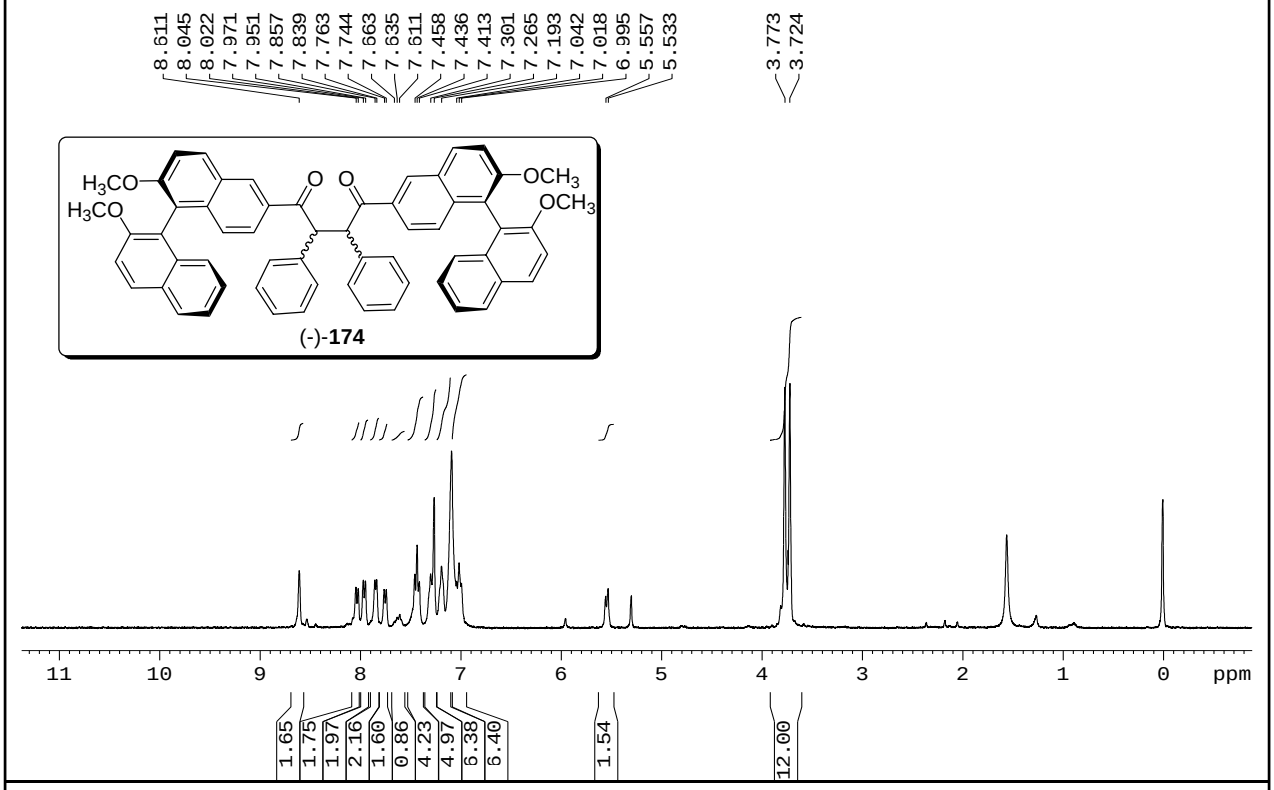
Spectrum No. 63 (Chapter 2, Section 2.6) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



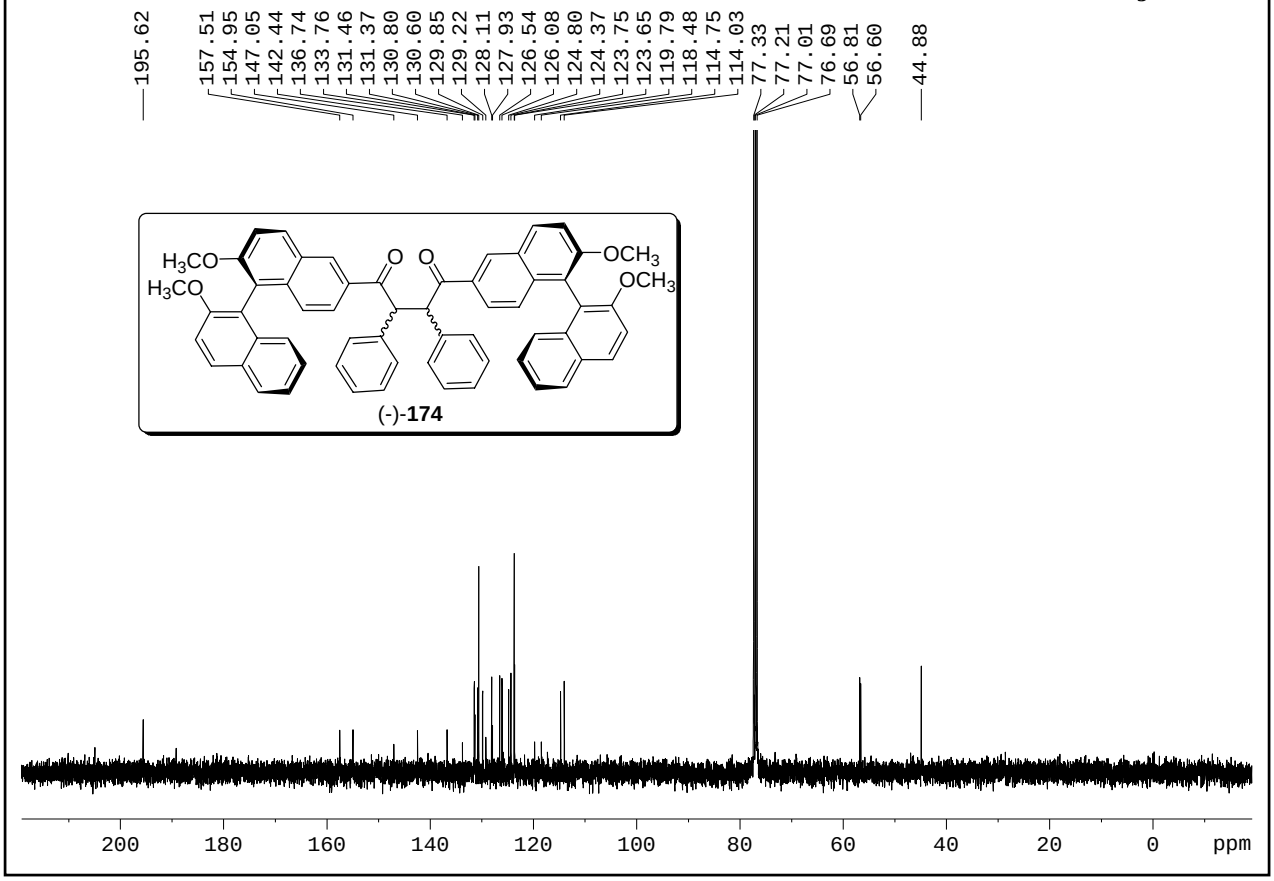
Spectrum No. 64 (Chapter 2, Section 2.6) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



Spectrum No. 65 (Chapter 2, Section 2.6) ^{1}H NMR Spectrum (400 MHz, $CDCl_3$)



Spectrum No. 66 (Chapter 2, Section 2.6) ^{13}C NMR Spectrum (100 MHz, $CDCl_3$)



LIST OF PUBLICATIONS

1. Convenient method for the synthesis of 6,6′-diacyl-bi-2-naphthyl ethers; Periasamy, M.; **Nagaraju, M**.; Kishorebabu, N. *Synthesis* **2007**, *24*, 3821.

2. Convenient method for the synthesis of 6-monoacyl-bi-2-naphthyl ethers and 6,6′-heteroacyl-bi-2-naphthyl ethers. Periasamy, M.; **Nagaraju, M**. *To be communicated.*

3. Convenient methods for diastereoselective reduction of 6-acyl-bi-2-naphthyl ethers and diastereoselective reductive amination of 6-acyl-bi-2-naphthyl ethers; **Nagaraju, M**.; Periasamy, M. *To be communicated.*

4. Synthesis of novel chiral 2,5-bis(bi-2-naphthyl methyl ether) substituted pyrroles. **Nagaraju, M**.; Periasamy, M. *To be communicated*.

POSTERS PRESENTED IN SYMPOSIA AND INTERNSHIP

1. Presented a poster in the “Chemfest 2008” 5th in house symposium held at University of Hyderabad, Hyderabad; Title: Highly diastereoselective reduction of 6-acyl-bi-2-naphthyl methyl ethers.

2. Participated in a one year Internship program (Oct’2010 to Oct’2011) under Dr. S. Baskaran, Medicinal Chemistry Department, GSK, RTP, NC, USA.