SYNTHESIS OF CHIRAL PHOSPHINE-PHOSPHITE LIGANDS AND THEIR APPLICATIONS IN COPPER-CATALYZED 1,4-ADDITION OF GRIGNARD REAGENTS TO UNSATURATED CARBONYL COMPOUNDS

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Hamza ŞİMŞİR

SYNTHESIS OF CHIRAL PHOSPHINE-PHOSPHITE LIGANDS AND THEIR APPLICATIONS IN COPPER-CATALYZED 1,4-ADDITION OF GRIGNARD REAGENT TO α,β-UNSATURATED CARBONYL COMPUNDS

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Hamza ŞİMŞİR

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FOR
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IN
DIVISION OF CHEMISTRY

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I certify that in my opinion the thesis submitted by Hamza ŞİMŞİR titled "SYNTHESIS OF CHIRAL PHOSPHINE-PHOSPHITE LIGANDS AND THEIR APPLICATIONS IN COPPER-CATALYZED 1,4-ADDITION OF GRIGNARD REAGENT TO α,β-UNSATURATED CARBONYL COMPUNDS" is fully adequate in scope and in quality as a thesis for the degree of Master of Science.

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The degree of Master of Science by the thesis submitted is approved by the Administrative Board of the Graduate School of Natural and Applied Sciences, Karabük University.

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"I declare that all the information within this thesis has been gathered and presented in accordance with academic regulations and ethical principles and I have, according to the requirements of these regulations and principles cited all those which do not originate in this work as well."

Hamza ŞİMŞİR

ABSTRACT

M.Sc. Thesis

SYNTHESIS OF PHOSPHINE-PHOSPHITE LIGANDS AND THEIR APPLICATIONS IN COPPER-CATALYZED 1,4-ADDITION OF GRIGNARD REAGENTS TO α,β-UNSATURATED CARBONYL COMPOUNDS

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This work focuses on Cu-catalyzed asymmetric 1,4-additions of organometallic reagents to different α,β-unsaturated carbonyl compounds in the presence of chiral phosphine-phosphite ligands. In a first part of the thesis, synthesis of different chiral phosphine-phosphite ligands is described. In a key step, a borane-protected phosphinite, prepared from an *o*-bromophenol by *o*-phosphanylation, is reacted with *n*-butyllithium to afford the corresponding *ortho*-phosphanylphenol through bromine-lithium exchange and anionic migration rearrangement. Treatment with phosphorus trichloride in the presence of a base and subsequent reaction of the in situ formed dichlorophosphite with a chiral diol (TARTROL) affords the target P,P ligands in good overal yield (up to 60% over 4 steps). TARTROL is synthesized

from the reaction of aromatic grignard reagent and dimethyl ester, which is obtained from the reaction of tartaric acid and diketone. In a second part of the thesis, the Cu-catalyzed asymmetric 1,4-addition of ethyl magnesium bromide and phenyl magnesium bromide to cyclohexenone is described. Under the optimezed conditions [$CuBr.SMe_2$ (4 mol%), ligand (6 mol%), 2-methyl-THF, -78 ^{0}C, slow addition of grignard reagent] the 1,4-product was obtained with high enantioselectivity (up to 84% ee) and good regioselectivity (r.r. = 92:8). It was founded that, enantiomeric excess values of the addition of ethyl magnesium bromide to cyclohexenone is higher than, enantiomeric excess values of the addition of phenyl magnesium bromide to cyclohexenone.

Key Words : Phosphine-phosphite ligands, 1,4-addition reactions, taddol, tartrol, Cu catalysis, ethyl magnesium bromide, phenyl magnesium bromide.

Science Code : 201.1.112

ÖZET

Yüksek Lisans Tezi

KİRAL FOSFİN-FOSFİT LİGANDLARIN SENTEZİ VE BAKIR-KATALİZE GRİGNARD REAKTİFLERİNİN α,β-DOYMAMIŞ KARBONİL BİLEŞİKLERİNE 1,4-KATILMASI UYGULAMALARI

Hamza ŞİMŞİR

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Ocak 2013, 86 sayfa

Bu çalışmada, kiral fosfin-fosfit ligandlar ile oluşan, simetrik olmayan bakır katalize organometalik bileşenlerin, α,β-doymamış karbonil bileşiklerine 1,4 katılma reaksiyonları üzerinde durulmuştur. Tezin birinci kısmında, farklı kiral fosfin-fosfit ligandların sentezleri açıklanmıştır. Kiral fosfin-fosfit ligandların sentezinde ilk basamakta fenol orto-pozisyonundan bromlanır. Ardından fenolun oksijenine difenilfosfin eklenir ve buradaki fosfor atomu boran ile korunur. Bu şekilde oluşturulan fosfinite *n*-BuLi ilave edilerek, brom-lityum değişimi ve bunu takip eden anyonik göç düzenlenmesi gerçekleştirilir. Bu yolla elde edilen boran ile korunmuş *o*-fosfonilfenol diklorofosfit ara ürünü oluşturulur. Bu diklorofosfitin yeterli miktarda kiral diol (TARTROL) ile reaksiyonundan (4 basamakta 60% verim) P,P ligandlar elde edilmiştir. Doğada bulunan ve tartarattan senztezlenen tartarik asid ve diketonun

reaksiyonundan elde edilen, dimetil ester ile aromatik grignard bileşenin reaksiyonundan TARTROL sentezlenir. Tezin ikinci bölümünde, etil magnezyum bromid ve fenil magnezyum bromidin siklohekzenona, bakır katalize simetrik olmayan 1,4 katılma reaksiyonları açıklanmıştır. En iyilenmiş koşullarda, [$CuBr.SMe_2$ (4 mol%), ligand (6 mol%), 2-metil-THF, -78 ^0C, grignard bileşenin yavaşça ilavesi] yüksek enantiyomerik seçicilik (84% es'e kadar) ve iyi bölgesel seçicilik (b.s. = 92:8) elde edilmiştir. Siklohekzenona, etil magnezyum bromid katılması sonucu elde edilen enantiyomerik seçicilik değerlerinin, siklohekzenona fenil magnezyum bromid katılması sonucu elde edilen enantiyomerik seçicilik değerlerinden daha yüksek olduğu bulunmuştur.

Anahtar Sözcükler : Fosfin-fosfit ligandlar, 1,4-katılma reaksiyonları, taddol, tartrol, bakır kataliz, etil magnezyum bromid, fenil magnezyum bromid.

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LIST OF SYMBOLS AND ABBREVIATIONS

SYMBOLS

C : Celcius

n-BuLi : *n*-Butyllithium

BH_3 : Borane

DIOP : 2,3-*o*-isopropylidene-2,3dihydroxy-1,4-bis(diphenylphosphino)butane

Ee : enantiomeric excess

CH_2CI_2 : Dichloromethane

CO_2 : Carbon dioxide

eq : Equivalent

EtOAc : Ethyl acetate

F : Fluorine

g : Gram

Me-THF : Methyl tetrahydrofurane

DABCO : 1,4-diazabicyclo[2,2,2]octane

ph : Phenyl

mmol : Millimole

N : Nitrogen

Na : Sodium

TADDOL : Tetraaryl- 1,3-dioxolane-4,5-dimethanole

TARTROL : Tetraaryl- 1,4-dioxane-2,3-dimethanole

NaOH : Sodium Hydroxide

NEt_3 : Trietilamin

O : Oxygen

OH : Hydroksil

R_f : Retention Factor

SiO_2 : Silicium Dioxide

THF : Tedrahydrofuran

ABBREVIATIONS

GC-MS : Gas Chromatography-Mass Spectrometry

FTIR : Fourier Transform Infrared Spectroscopy

NMR : Nuclear Magnetic Rezonans

TLC : Thin Layer Chromatography

CHAPTER 1

INTRODUCTION

1.1. STREOCHEMISTRY AND CHIRALITY

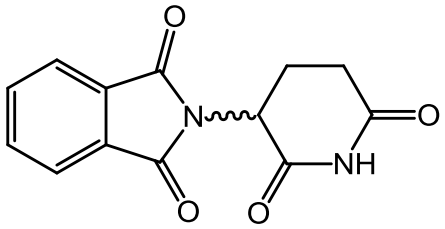
Stereochemistry mention to chemistry in three dimensions. The foundations of stereochemistry were laid by Louis Pasteur who described the first the stereochemistry in 1848 [1]. He realized that two diffirent kind of crystaline structure of tartrate salts which have diffirent optical activity. Later, Jacobous Van't Hoff [2] and Joseph Achille Le Bell [3] recognised the stereochemistry in 1874. Independetly of each other, Van't Hoff and Le Bell proposed that, the four bond of carbon were directed toward the corner of tetrahedron [4].

Every object has a mirror image, but not all of them are superpose on their mirror image. If one molecule can not superpose on its mirror image, it is called chiral molecule. On the contrary, if one molecule is a superposable, it is called achiral molecule. One of the chiral molecule and its mirror image are called enantiomers. This isomers recognized to being a R(+) or S(-) isomers. If one molecule have the same proportion of two enantiomers, (%50 R and %50 S) it is called racemic mixture [5].

Enantiomers have same physical properties. On the other hand biological properties of enantiomers, interaction with the other chiral molecules and optical activity of enantiomers are different. So many cruial molecules for a human life are chiral. For example, amino acids, proteins, natural sugars. are chiral molecules. Most pharmaceuticals are chiral molecules. While, one mirror image form a drug provide desired effect, the other mirror image form of drug caused to be side effect.

The importance of chiralty can be seen with the example of thalidomide (1) (Figure 1.1). Thalidomide is a drug which prescribed for treating morning sickness in

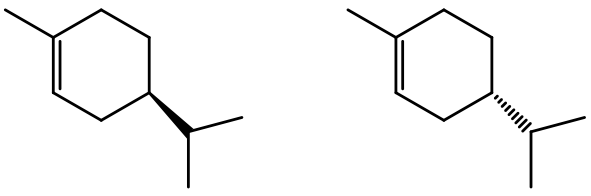
pregnant women but even later evidience indicated that enantiomers of thalidomide have different biological effect. One of the enantiomer cured morning sickness, on the other side, the other enantiomer cause of serious genetic damage to early embryonic growth and development. Due to the fact that, using of this drug, more than 10000 children in 46 countries were born with deformities such as phocomelia in the late 1950s [6].



2-(2,6-dioxopiperidin-3-yl)isoindoline-1,3-dione
Thalomid
1

Figure 1.1. Structure of Thalomid molecule.

Our sense of taste and smell also depend on chirality. Two different mirror image can be caused of different smells (Figure 1.2). An example of different properties of enantiomers is one enantiomer of (+)- limonene (2) is responsible for the smell of orange and beside, the other enantiomer of (-)- limonene (3) is responsible for the smell of lemons [7].



(+) - Limonene
(scent of orange)
2

(-) - Limonene
(scent of orange)
3

Figure 1.2. Enantiomers of limone molecule.

Three possible way can be used to acquiring non racemic compounds. The first of them is starting from a chiral molecule which seperate from natural source [8]. Only one enantiomer is produced by this way. It is named ‘chiral poll’. Disadvantage of

chiral poll is the other enantiomer can not be produced by this method. The second is seperation of them from a racemic mixture. Enantiomers can be seperated with appropriate method or kinetic resolution. Disadvantege of this method is that %50 of the substrate are wasted. The third of them is asymmetric synthesis. With the help of this methods, desired enantiomer can be produced using auxiliary and enantioselective catalysis with using chiral reagents.

1.2. ASYMMETRIC CATALYSIS

Asymmetric catalysis with transtion metals is considerably important field of chemical reactions. Most of the substances used as starting material for these syntheses are in general not chiral. The aim of these reactions is to produce a valuable chrial products [9]. The important point of these reactions is to use a chiral catalyst molecules. During the last decades, asymmetric syntheses have been the objective of organic chemistry. Knowles [10], Noyori [11] and Sharpless [12] was awarded to Nobel Prize 2001, for their working about asymetric catalysis.

In the 1960s, Knowles succeed the hydrogenation of α-phenyacrlic acid (5) with an enantioselectivity of %15 ee (Figure 1.3) [13] using metal catalyst $[RhCl(PPh_3)]_3$ and chiral phoshine (6). Although acquired enantioselectivity was low, his work was the first step of asymetric synhtheses and his result gave inspriation to improvment of asymmetric hydrogenation.

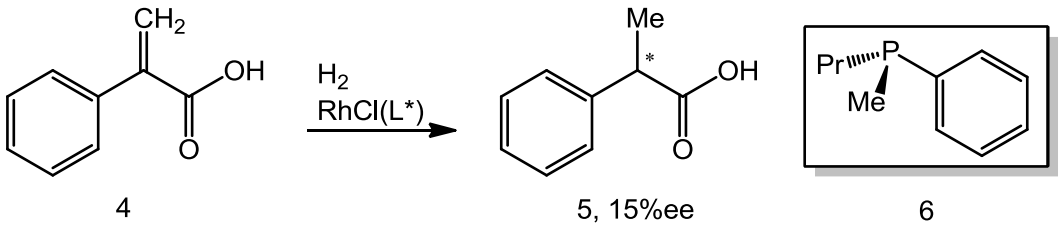


Figure 1.3. The first working about asymmetric catalytic hydrogenation.

In the 1966s, Noyori's work was another important example of homogeneous asymmetric carbon bond formation catalyzed by transtion metal complex [14]. Noyori's catalysts are widely used for the synthesis of fine chemicals and

pharmaceutical products. In his work, he gained cis- and trans-cylopropanecarboxylates (9) and (10) with %6 ee and %10 ee respectively (Figure 1.4). Noyori used a chiral Shiff base- Cu(II) complex (11) as a homogenous catalyst in the reaction of styrene (7) with ethyl diazoacetate (8).

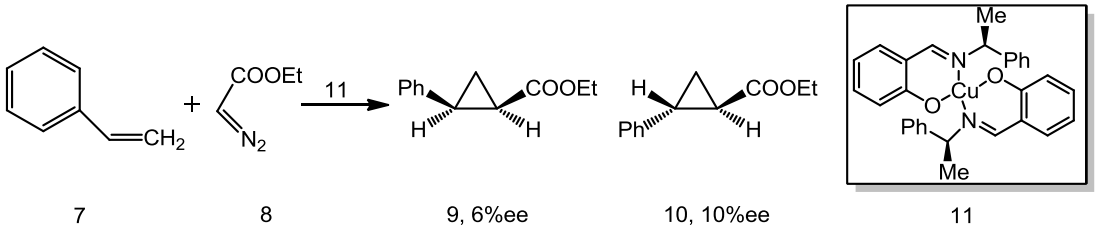


Figure 1.4. An example of catalytic asymmetric cylclopropanation.

After a few years later, Sharpless has made several important development, such as for the titanium-catalyzed asymetric epoxidation of allyclic alchol (12) [15]. Epoxides are useful intermediate products for various types of synthesis, including the production of drugs. In his work, he obtained (S)-oxiran-methanol (13) with 90% ee (Figure 1.5). Sharples used Ti(IV) alcoholate being an metal catalyst and enantiopure diethly tartrate (14).

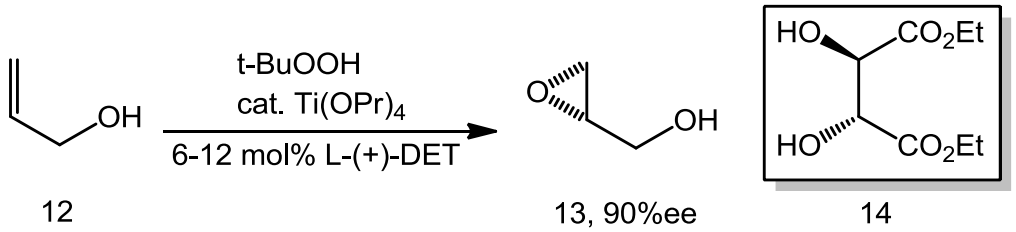
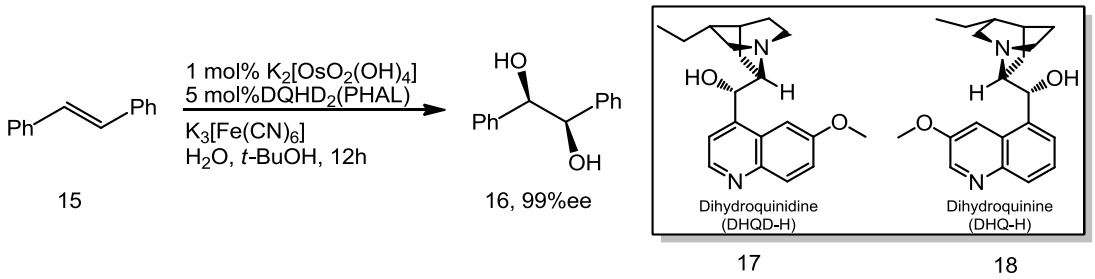


Figure 1.5. Asymmetric epoxidation of allylic alcohols reported by Sharples.

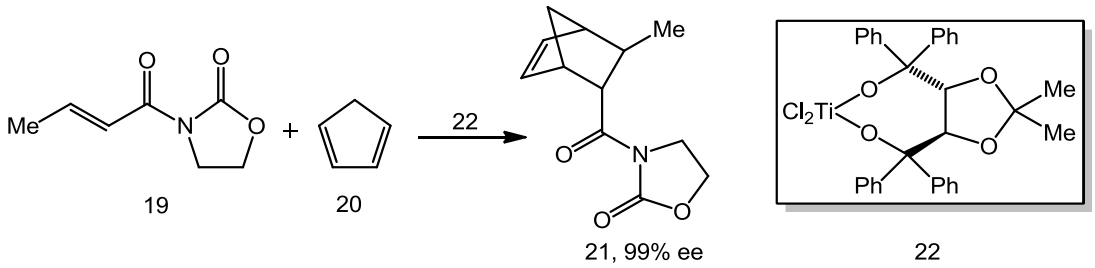
Another example is asymetric dihydroxylation. In this reaction, dihydroxyl groups added to trans-stilbene (15) with high enantioselectivity of 99%ee (Figure 1.6) [16]. Osmium tetraoxide is used to as a metal catalys. Being a chiral reagent dihydroqhinidine DHQD-H (17) and dihydroquinie DHQ (18) can be used.



15 16, 99%ee 17 18

Figure 1.6. Asymmetric dihydroxylation reported by Sharples.

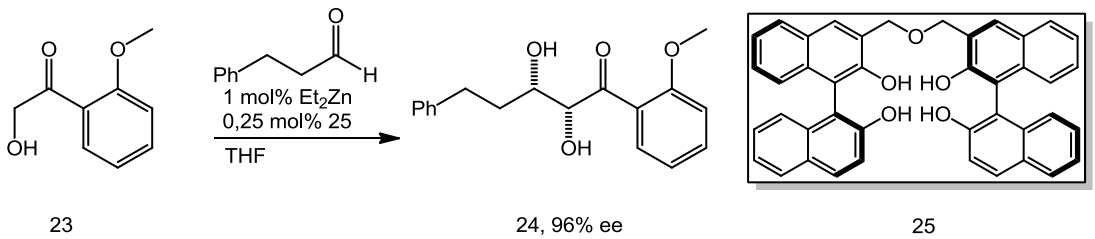
Another example of an asymetric carbon-carbon bond formation was reported by Narsaka [17]. The group conducted a highly enantioselective Diels-Alder reaction of the unsaturated acyloxazolidinone (19) and cyclopentadiene (20) catalyzed by chiral titanium complex (22) which derived from the widely applied TADDOL ligand which resulted in high enantioselectivity of up to 99% ee (Figure 1.7).



19 20 21, 99% ee 22

Figure 1.7. An example of asymmetric catalysis of Diels-Alder-reaction.

Another important example, the aldol reaction is regarded as a reliable carbon-carbon bond formation reaction. Shibasaki and co-workers reported the first catalytic enantioselective aldol reaction using diethylzinc with the presence of a chiral (S,S)-linked BINOL ligand (25) with an enantioselectivity of 96% ee (Figure 1.8) [18].



23 24, 96% ee 25

Figure 1.8. Enantioselective catalysis of the aldol reaction.

CHAPTER 2

THEORETICAL BASES

2.1. PHOSPHORUS LIGANDS

Trivalent phosphorus compounds play as ligands major role in asymmetric catalysis. Since, their ligating properties, from stable complexes with catalytically active metals which is their activity in several crucial chemical transformation and their great potential for steric and electronic modification. These trivalent P-compounds offer to chemists unique position in asymmetric catalysis.

Owing to the free electron pair, trivalent phosphorus compounds behave as Lewis bases and can, therefore, ligate to metals. Such as rhodium, ruthenim, palladium, nickel, copper. Substituents at the phosphorus are responsible for σ-donating and π-accepting properties of the P-ligand and can be used for electronic ‘fine tuning’ of the catalyst.

Trivalent P-ligands can be based on different general structures. For example phosphines are characterized by there P-C bonds. Depending on the type of the C-substituent, the basicity of the phosphine is different. Subtle differences can be carried out by using electron-poor or electron-rich aromatics (Figure 2.1).

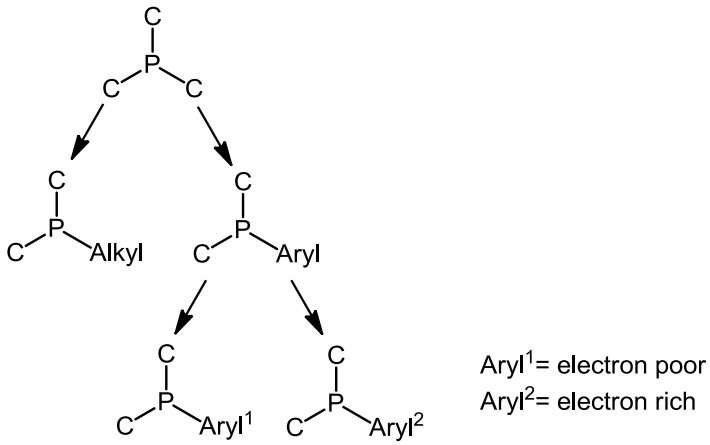


Figure 2.1. Variations of phosphine by different C-substituents.

The more important changes in the electronic structure, especially in the π-accepting properties, can be realized by replacement of P-C bond by P-O or P-N bonds. In this manner phosphinites, phosphonites and phosphites and their corresponding P-N analogues are formed (Figure 2.2).

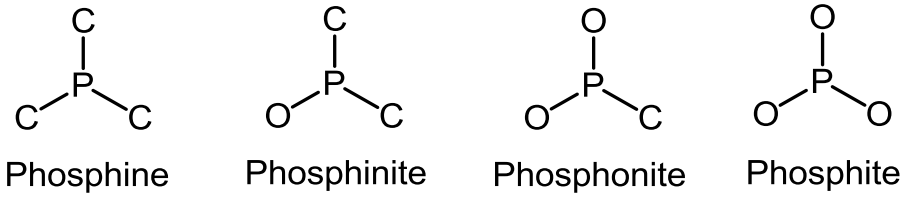


Figure 2.2. Various trivalent phosphorus ligand families.

Trivalent P-ligands can also be differentiated in monodentate, bidentate, polydentate and mixed bidentate ligands (Figure 2.3).

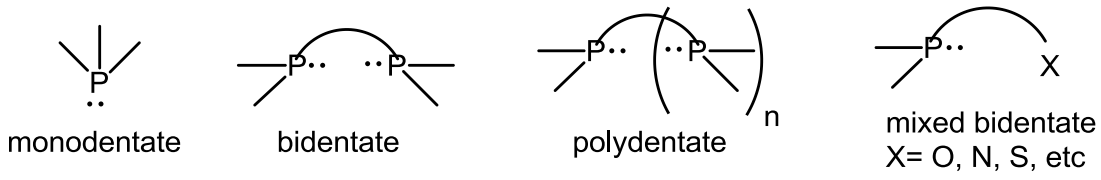


Figure 2.3. Variations of P ligands due to different coordination modes and ligating groups.

A critical subject in asymmetric catalaysis is the source of chirality, which is transfered during the catalytic step from the chiral catalyst to the prochiral substrate.

Chiral information can be derived from all types of chirality residing in the backbone of the P-ligand. The trivalent phosphorus itself can also be chiral centre, provided it is surronded by three different substituents. Its chiral unity remains stable under most catalytic conditions, which is an important advantage over related trivalent N-ligands. Moreover, achiral P-ligands can be used to construct chiral metal complexes, where the chirality is attributed to metal center. A special methodolgy incorporates P-ligating groups in the substrate. After intermediate coordination to the catalytically active metal these groups can direct the stereodiscriminating attack of a chiral catalyst (Figure 2.4) [19].

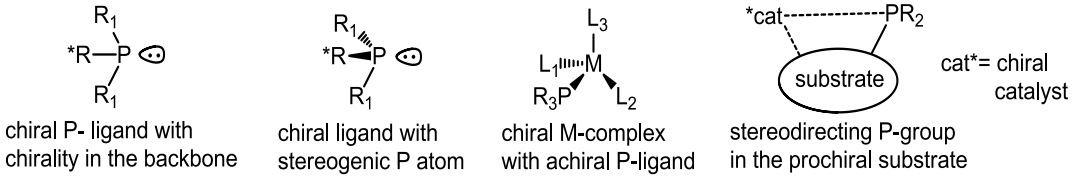


Figure 2.4. Source of chirality in asymmetric transformation with trivalent P-compounds.

Phosphours ligands are so important for asymmetric synthesis. After the early discoveries which are developed by Knowles a number of improved asymmetric catalysts based on metal complexes were developed. Knowles's hydrogenation reaction with a phosphorus ligand inspired the development of other type of phosphorus ligands which are chiral bidentate ligands for application in asymmetric hydrogenation. In this manner, in 1972, Kagan devised *C2*-symmetric chealating diphosphine (DIOP) (28). His work demonstrate that rhodium complexes of DIOP catalyzed asymmetric hydrogenation of C=C bonds with %80 ee (Figure 2.5) [20].

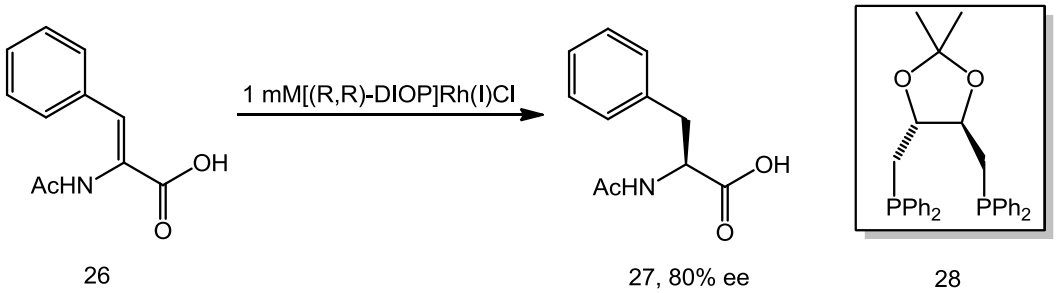
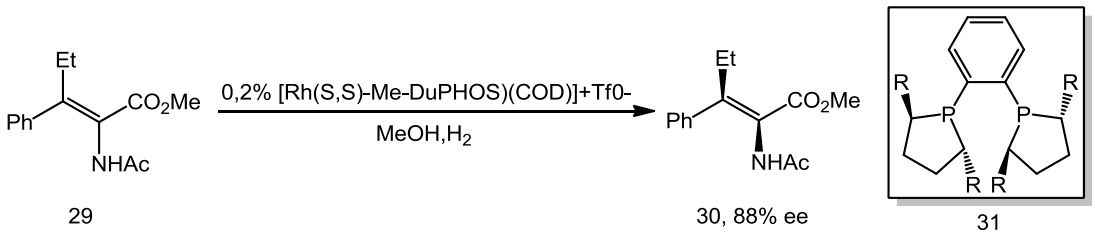


Figure 2.5. Assymetric hydrogenation with using bidentate phospine ligand.

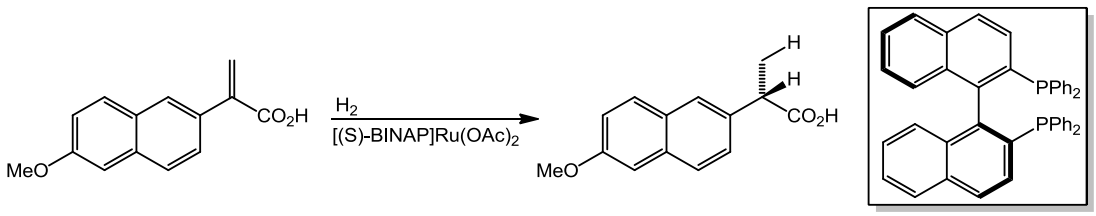
Kagan's works gave the inspriation to other scientists. After a few years later, another important bidentate ligand was used for asymmetric hydrogenation which was DUPHOS (31). With the using to DUPHOS %88 ee supplied for asymmetric hydrogenation (Figure 2.6) [21].



29 30, 88% ee 31

Figure 2.6. Asymmetric hydrogenation with using bidentate phospine ligant.

Synthesis of naproxen (33) is another example of asymmetric hydrogenation which is reported by Noyori in 1987 [22]. Naproxen is obtained with high enantioselectivity is 97%ee. This reaction is occured with the using of (S)-BINAP (34) which is an important bidentate phosphine ligand. It was used with Ru transtion metal catalyzer (Figure 2.7).



32 33, 97%ee 34

Figure 2.7. Asymmetric hydrogenation with using bidentate phosphine ligant.

2.1.1. Synthesis of TARTROL-derived P-P Ligands

Enantioselective metal-catalyzed processes are the objective to the development of new and effecient chiral ligands to achive high levels of reactivity and enantioselectivity. Several reaction parameters need to be optimized in order to obtain the highest level of reactivity and selectivity in catalytic enantioselective reactions. It has been shown that the desing of the chiral ligand is of crucial impact [23]. During the last few years, significant advances were made towards the design and preparation of chiral ligands used in the 1,4-addition of organometallics.

Desirable attributes for chiral ligands are assembled in a modular fashion from cheap, readily available precursors. The long known TADDOLs (tetraaryl-1,3-dioxolane-4,5-dimethanols) and TARTROLs (tetraaryl-1,4-dioxane-2,3-dimethanols) were first indtroduced by Seebach [24] and co-workers, and are readily obtained from inexpensive, naturally occurring tartarate, which is available in both enantiomeric forms. TARTROL is a significant tartaric acid-derivate. TARTROL (38) can be obtained from different dimethyl ester derivaties (37), (Figure 2.8).

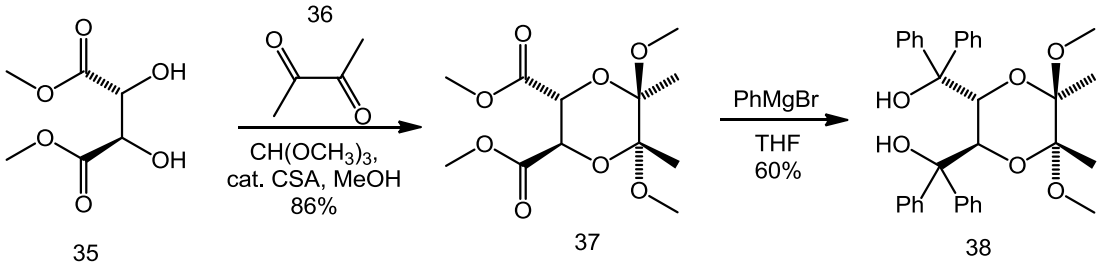


Figure 2.8. Synthesis of TARTROL form tartaric acid reported by Seebach.

TADDOL and TARTROL-derived ligands are the important group of chiral ligands, for useful transformations. Despite the large amount of these ligands used in the 1,4-addition reactions, only few provided good to high enantioselectivities. In contribution to this field, the Schmalz group, have recently developed a new family of highly modular bidentate phosphine-phosphite ligands derived from substituted phenols (39) and chiral diols (TADDOL or TARTROL) as a source of chirality as shown (Figure 2.9) [25].

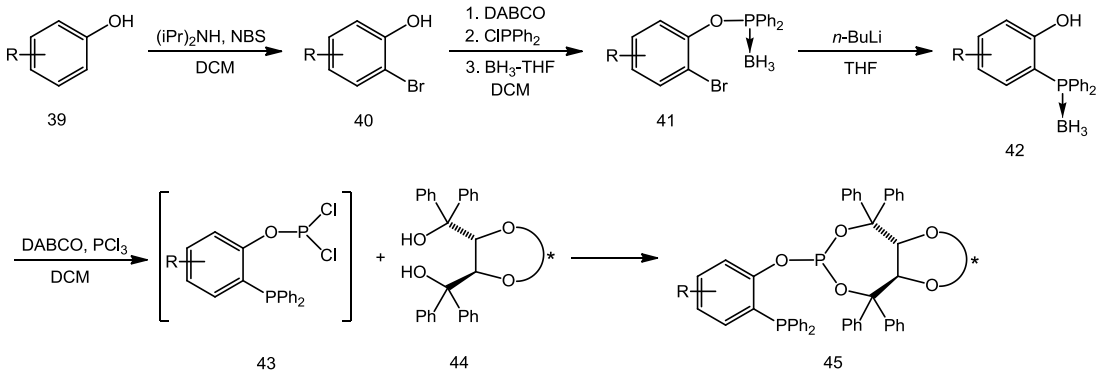


Figure 2.9. Synthesis of chiral phoshine- phosphite ligands according to Schmalz.

A small library of these ligands is shown (Figure 2.10). Some of these ligands have been proven to be privileged in different asymmetric metal-catalyzed reactions [25] such as the Rh-catalayzed hydroboration [26], hydroformylation [27], or in the Cu-catalyzed allylic substitution reactions[28]. Several of these ligands also have been shown to induce high levels of selectivity in the Cu-catalyzed asymmetric 1,4-addition of various Grignard reagents to cyclhexenone [29].

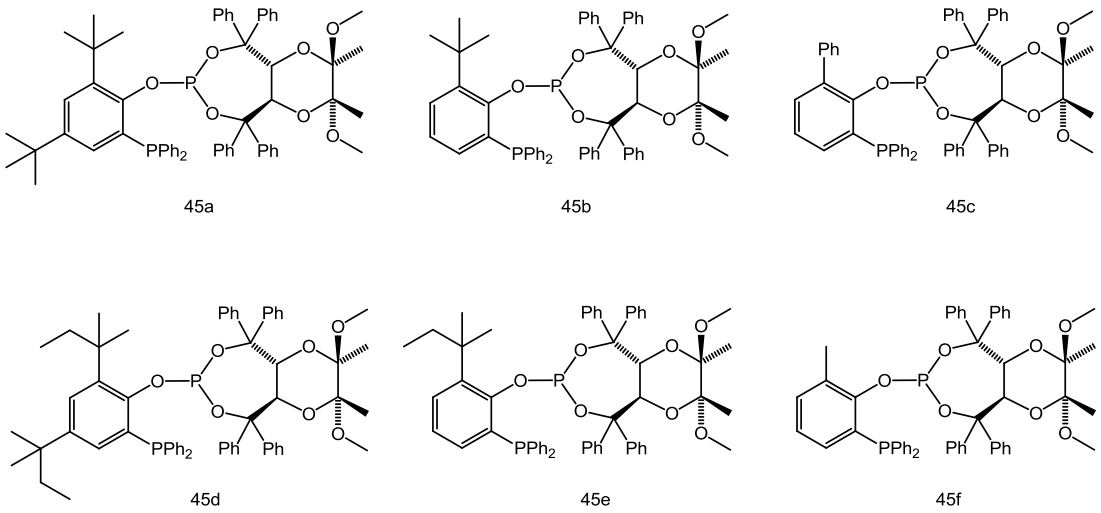


Figure 2.10. Phosphine-phosphite ligands synthesized in the Schmalz group.

2.2. CONJUGATE 1,4 ADDITION REACTIONS

The asymmetric conjugate 1,4-addition of organometallic reagent is a powerful methodology for the carbon-carbon bond formation giving β-substituted functionalized compounds, which are versatile synthons for further organic transformations [30].

When α,β-unsaturated aldehydes and ketones react with nucleophilic reagents, they may so in two ways. They may react by a simple addition, that is, one in which the nucleophile adds across the double bond of the carbonyl group; or they may react by conjugate addition. These two processes resemble 1,2-addition **A** and 1,4-addition **B** reactions of conjugated dienes (Figure 2.11).

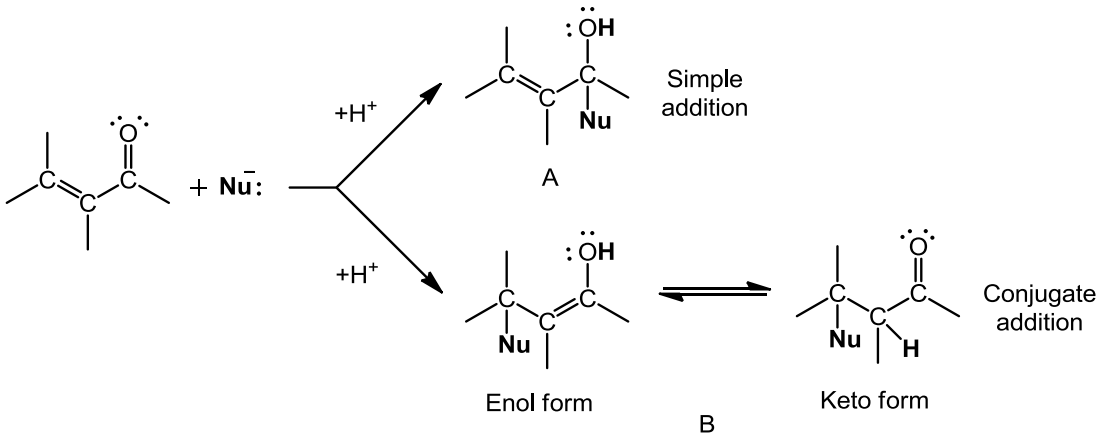


Figure 2.11. Nucleophile addition to α,β-unsaturated carbonyl compounds.

It can be examined the resonance structures that contribute to the overall hybrid for an α,β-unsaturated aldehyde and ketone(A-C), it is demonstrated that a better position to understand these reactions (Figure 2.12).

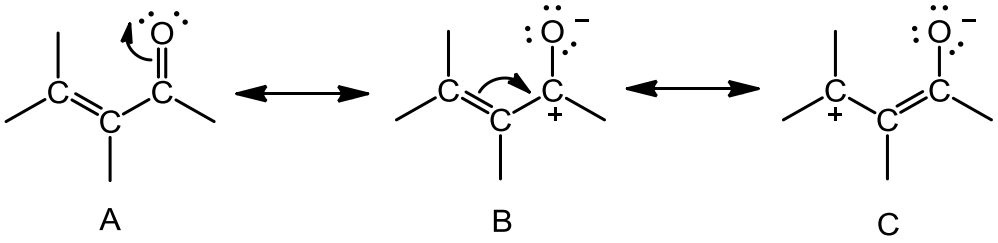


Figure 2.12. Resonance structure of α,β-unsaturated carbonyl compounds.

Although structures (B) and (C) involve separated charges, they make a significant contribution to the hybrid because, in each, the negative charge is carried by electronegative oxygen. Structures (B) and (C) also indicate that both the carbonyl carbon and β carbon should bear a partial positive charge.

The 1,4-addition of carbon nucleophiles is a selective reaction. One reaction will be occured either 1,2-addition or 1,4-addition depending several parameters. One of these parameters is reaction conditions. Treating an enone (B) with cyanide and an acid catalyst at low temperature gives a cyanohydrin (A) by direct attack at C=O, while heating the reaction mixture leads to conjugate addition (C) (Figure 2.13).

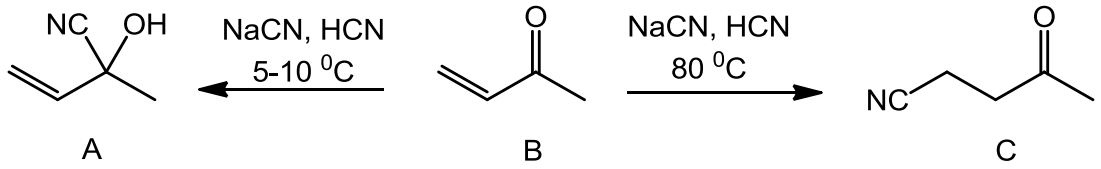


Figure 2.13. Nucleophile addition in different temparature to α,β-unsaturated carbonyl compounds.

Using of soft nucleophiles or hard nucleophiles is another significant parameter. Soft nucleophiles preferably add to the β-position of the enone (B) and the 1,4-addition product (C) is formed after protonation. On the other hand if hard nucleophiles are used, the regioselectivity of the reaction shifts and carbonyl atom is attached giving the 1,2-addition product (A) after protonation (Figure 2.14.) [31].

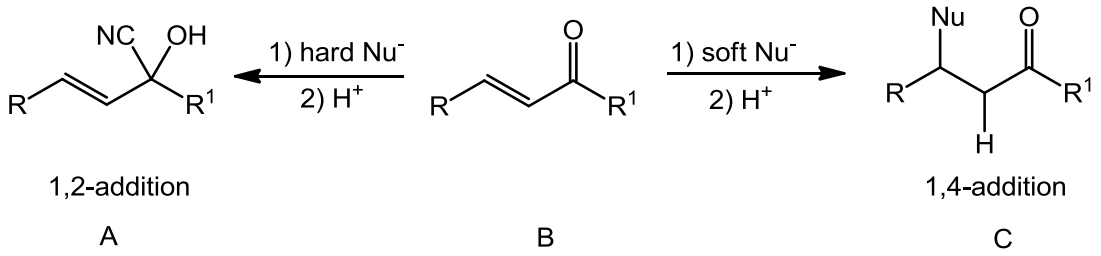


Figure 2.14. Hard and soft nucleophile addition to α,β-unsaturated carbonyl compounds.

2.3. ASYMMETRIC 1,4-ADDITION USING TRANSTION METAL CATALYSIS

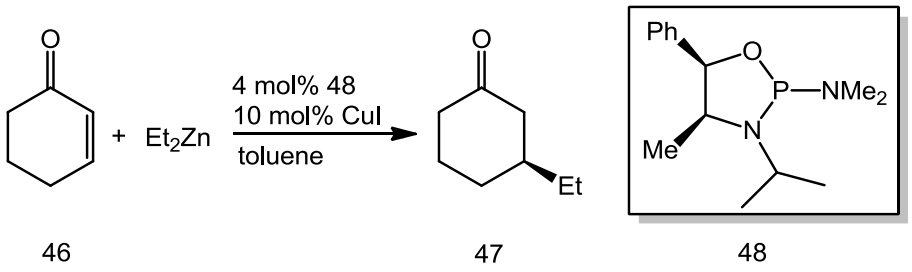
The transition metal catalyzed asymmetric 1,4-addition of organometallics to α,β-unsaturated carbonyl compounds is considered as a fundamental methodology for organic synthesis [32]. With the presence of transition metals (e.g copper, nickel, rhodium, palladium, cobalt etc.) the 1,4-addition reaction of organometallic reagents take place. In these reactions, stoichiometric amount of chiral reagents should be used in order to obtain high enantioselectivities.

2.4. COPPER-CATALYZED 1,4-ADDITION OF ORGANOMETALLIC REAGENTS

The advantage of enantioselective Cu-catalyzed 1,4-addition of organometallic reagent is compatibility of with many functional groups, the low cost of copper salts and often high regioselectivities and enantioselectivities. During the last decade, there have been important in the field of catalytic asymmetric 1,4-addition of organocopper reagents to α,β-unsaturated carbony compounds. The Cu-catalyzed asymmetric 1,4-addition has been successfully developed with a wide variety of substrate such as enones, α,β-unsaturated esters, nitroalkenes etc. and organomettalic nucleophiles. These addition reactions are so important for the synthesis of numerous biological active compounds and natural products [9].

2.4.1. Copper-Catalyzed Enantioselective 1,4-Addition of Organozinc Reagents

Enantioselective carbon-carbon bond formation reactions applying organozinc reagents have played an important role in the field of asymmetric 1-4-additon [33]. The reason is that, when organometallic reagents are compared with organozinc reagents, it is shown that, organometallic regants are more basic and less tolerant to variety of functional groups than organozinc reagents. Cu(I) and Cu (II) salts can be used. Cu(II) salts are oftenly used in these reactions as they are less hygroscopic, cheaper and not sensitive to oxidation. In 1993, Alexakis reported [34] the first example of catalytic asymmetric 1,4-addition of diethylzinc to cyclohexenone (46) using an ephenrine-based phosphorous ligand (48) with an enantioselectivity up to 32% ee (Figure 2.15).



46 47 48

Figure 2.15. The first Cu-catalyzed 1,4-addition of diethylzinc to cyclohexenone.

After this important work, some research groups have reported that, enantioselective Cu-catalyzed 1,4 addition of organozinc reagents to α,β-unsaturated enones and with a wide range of copper based systems using phosphorus ligands, such as phosphoramidite, phosphites, phosphonites and phosphines and other phosphorus containing ligands. Pflatz reported the application of phosphate ligands with a BINOL backbone (52) in the Cu-catalyzed 1,4-addition of diethylzinc to to α,β-unsaturated carbonyl compounds with enantioselectivities of up to 83% ee [35]. With the using the diphosphite ligand (51) [36], Chan reached 89% ee. On the other side, Hoveyda and co-workers also reported the use of a new family of chiral peptide-based phosphine ligands in the Cu-catalyzed 1,4-addition of diethylzinc reagents with a broad substrate scope and high enantioselectivities (Figure 2.16) [37]

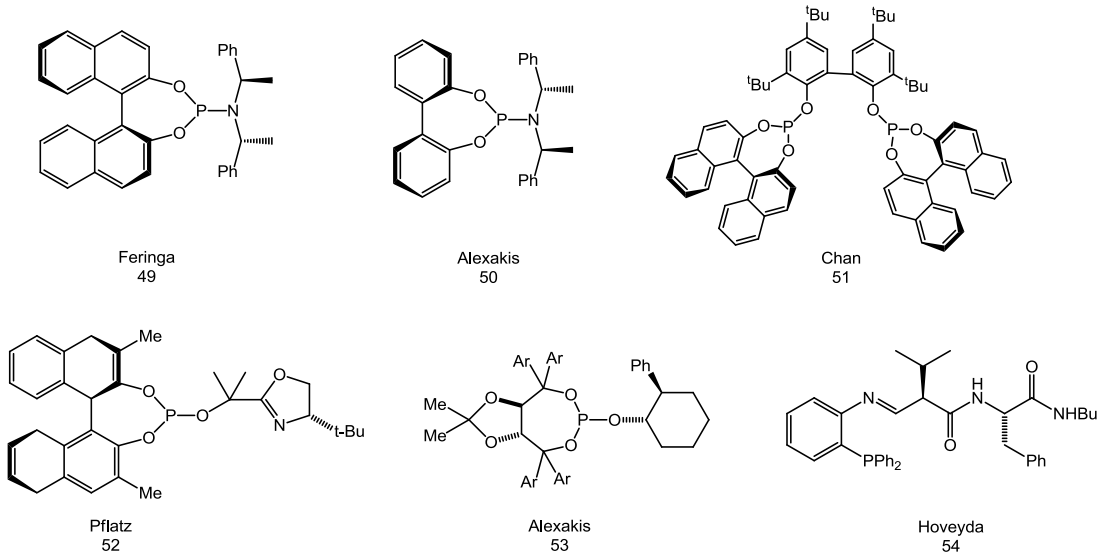


Figure 2.16. Ligands used in the copper-catalyzed 1,4-addition of Et_2Zn to α,β-unsaturated carbonyl compounds.

It is a possible mechanistic pathway for Cu-catalyzed 1,4-addition of dialkylzinc reagents which can contain the transfer of an alkyl fragment from R_2Zn (A) to copper atom followed by π-complexation of the resulting copper alkyl species to the double bond of enone and of the alkylzinc ion to enone carbonyl oxygen atom (C). The next alkyl transfer to the π-position of enone generates alkylzinc enolate (D) in a stereoselective fashion. Work up provides the substituted cyclohexanone (E) (Figure 2.17).

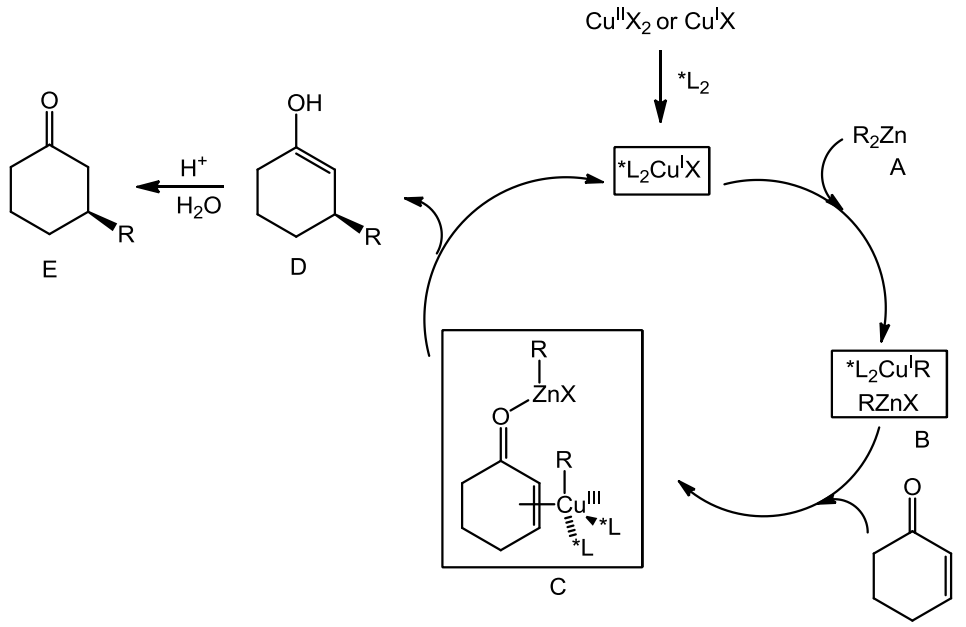


Figure 2.17. Proposed mechanism of the Cu-catalyzed 1,4-addition of R_2Zn.

In 1996, Feringa reported the asymmetric conjugate addition of diethylzinc to cylcohexanone (46) (Figure 2.18). He used the phosphoramidite ligand (49) and enantioselectivity up to %98 ee [38].

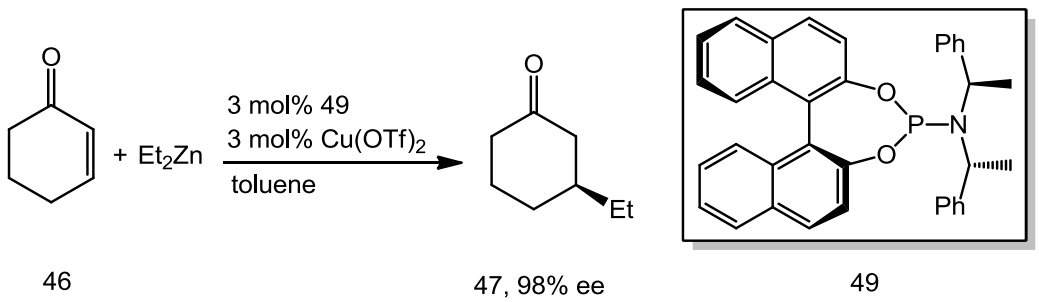


Figure 2.18. Copper-catalyzed 1,4-addition of Et_2Zn to cyclohexanone.

The conjugate 1,4-addition of diarylzinc reagents has recieved less attention than dialkylzinc reagents. After that Feringa, reported that high enantioselectivity can be obtained in the conjugate 1,4-addition of diphenylzinc, with the help of chiral phosphoramidite ligand (49) resulting in enantioselectivity up to %94 ee (Figure 2.19) [33].

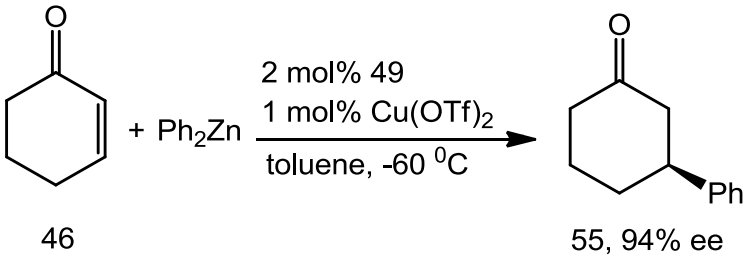


Figure 2.19. Conjugate 1,4-addition of diphenylzinc to cyclohexanone.

In 2005, Zhao et al [39] reported that Cu-catalyzed 1,4-addition of diphenylzinc to cyclohexanone. They used a phoshpine ligand and enantioselectivity was found to be %91. They demonstrated that with this method not only cyclohexanone, but also the other cyclic enones such as cyclopentenone can be obtained with the high enantioselectivity, with yields of %44 and %76ee. (Figure 2.20).

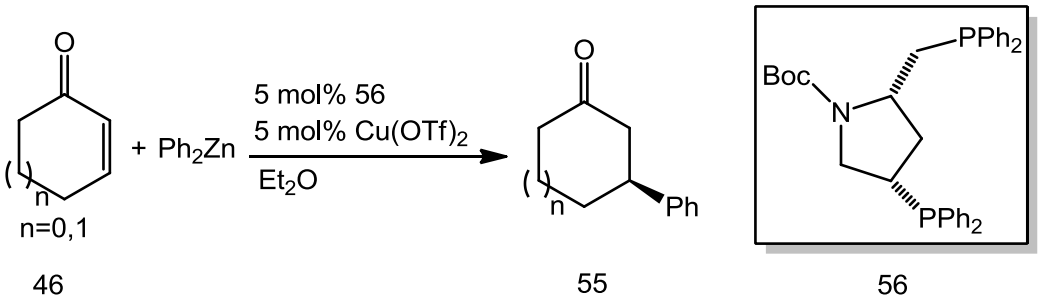


Figure 2.20. Copper-catalyzed 1,4-addition of Et_2Zn to cyclic enones.

2.4.2. Copper-Catalyzed 1,4-Addition of Organoaluminum Reagents

The asymmetric conjugate addition reactions using organoaluminum reagents are alternative to organozinc reagents, since they are more readily available [9]. Aluminum reagents depict strongly Lewis acidity due to the fact that they are coordinated with the oxygen atom of a carbonyl group of an enone and therefore make the β-position of the substrate more electrophilic. Chan and co-workers reported that Cu catalyzed 1,4-addition of trialkylaluminium species to cyclohexanone (46) [40] and cyclopentanone (59) [41] with the help of chiral diphosphine ligands (58) and (61) with an enantioselectivty of up to %96 ee (Figure 2.21) and %89 ee (Figure 2.22) respectively.

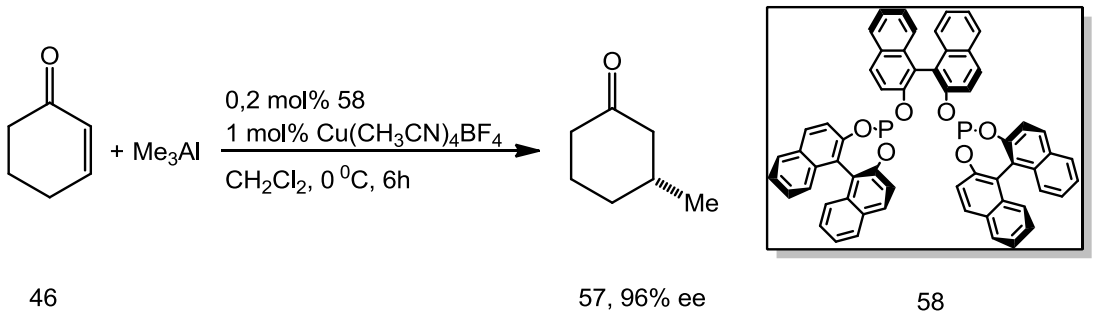


Figure 2.21. Cu-catalyzed 1,4-addition of triethylaluminium to cyclohexenone.

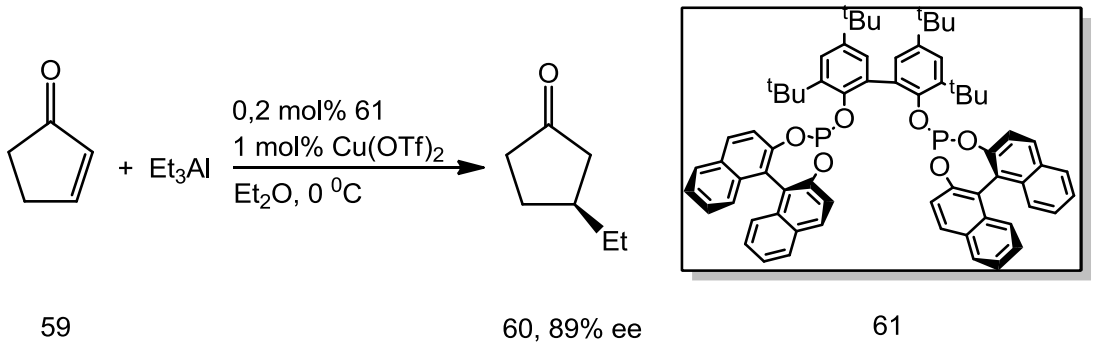


Figure 2.22. Cu-catalyzed 1,4-addition of triethylaluminium to cyclopentenone.

Fraser and Woodward also demonstrated that the utilization of organoaluminum reagents especially of AlR_3 (R = Me, Et) in the Cu-catalyzed 1,4-additions of aluminum reagents to various cyclic enones using phosphoramidite ligand (49) with high enantioselectivities (Figure 2.23) [42].

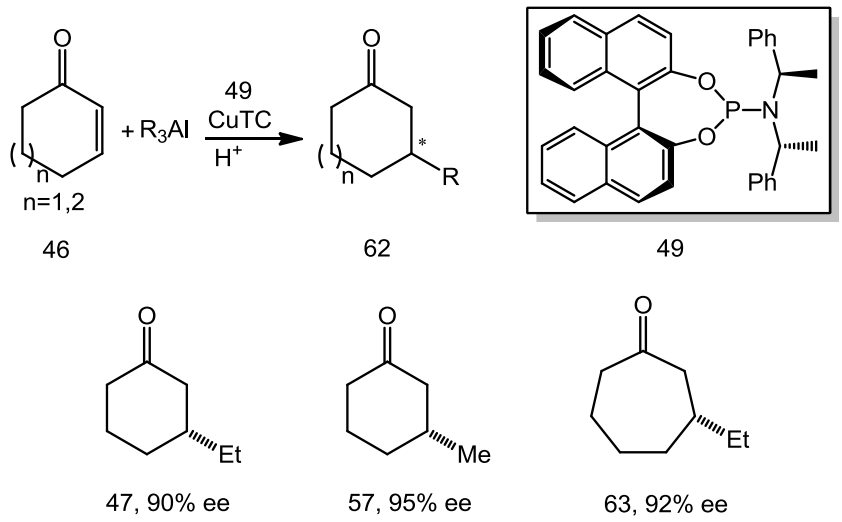


Figure 2.23. Cu-catalyzed 1,4-addition of aluminium to cyclic enones.

Additionally, organoaluminum reagents also provided a new efficient way to build chiral quaternary centers. For instance, Alexakis and co-workers [43] exploited this advantage in the asymmetric 1,4-addition of trialkylaluminium and triarylaluminum species to β-substituted cyclohexenone (Figure 2.24) in the presence of a chiral phosphoramidite ligand (66) with high yields and enantioselectivites (Table 1). The first step of the reaction is the generation of the $RAlEt_2$ by a halogen/Li exchange which is applicable for a wide range of nucleophiles.

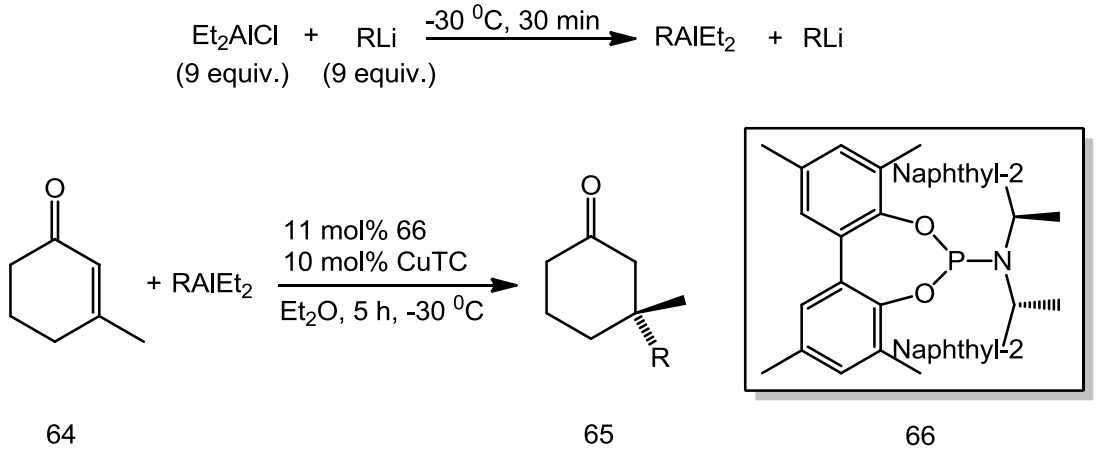


Figure 2.24. Cu-catalyzed 1,4-addition of triarylaluminium to to α,β-unsaturated cyclohexenone.

Table 2.1. Cu-catalyzed 1,4-addition of aryl aluminum reagents to 3-methyl cyclohexenone.

Entry	*R*	*Yield [%]*	*ee [%]*
1	Ph	75	96
2	*p*-MeC_6H_4	87	96
3	*p*-$OMeC_6H_4$	81	95
4	2-naphthyl	59	98
5	*p*-$CF_3C_6H_4$	74	98

2.4.3. Copper-Catalyzed 1,4-Addition Using Grignard Reagents

The asymmetric 1,4-addition of carbon nucleophiles to α,β-unsaturated carbonyl compounds represents to a powerful tool for carbon-carbon bond formation. Grignard reagents are cheaper and easier than dialkylzinc or aluminum reagents.

Moreover, transfer ability of many alkyl groups and the higher reactivity of the intermediate magnesium enolate considerable effort being undertaken to use Grignard reagents in the Cu-catalyzed asymmetric 1,4 addition [9]. Grignard reagents are used for highly active and enantioselective 1,4 addition to a wide variety of substrates. Although, in addition to cyclic and acyclic enones the less reactive α,β-unsaturated esters and thioesters can also be transformed with good enantioselectivies. In 1988, Lippard et al. [44] reported that asymmetric conjugate 1,4-addition reaction of *n*-BuMgCl to cyclohexanone (46) using a catalytic amount of Cu-amide complex (68) (Figure 2.25). With the addition either as HMPA or *t*-$BuPh_2SiCl$, enantioselectivy was obtained up to %74ee.

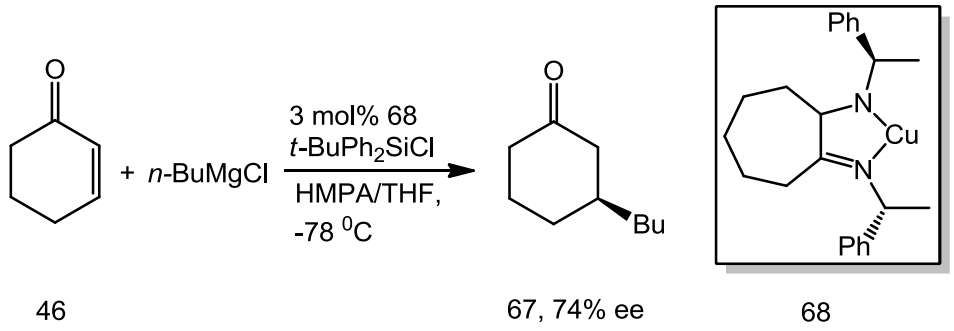


Figure 2.25. The first example of an enantioselective Cu-catalyzed 1,4-addition.

After Lippard's work, In 1991, Van Koten [45] reported that conjugate addition of MeMgI to 4-phenyl-3-butenone (69) using chiral bidentate aryl-thiolate Cu(I)-complex (71), enantioselectivity was up to %76 ee (Figure 2.26).

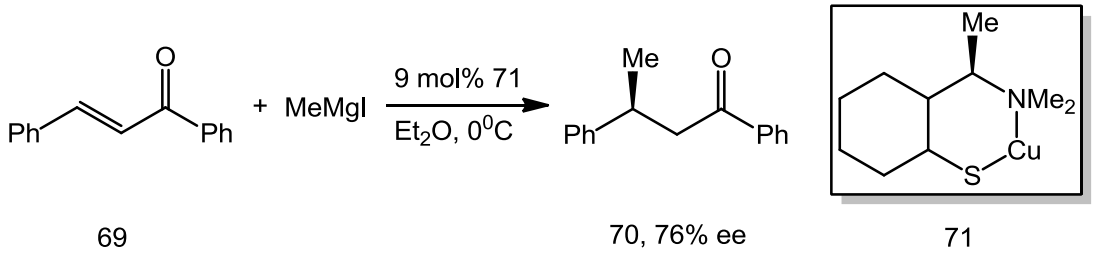


Figure 2.26. Enantioselective conjugate addition of MeMgI to phenyl-3-butenone.

Later, Rihs and Spescha reported [46] another chiral thiol-based catalyst for the conjugate addition of Grignard reagents to several α,β-unsaturated carbonyl

compounds. The catalyst in this transformation is prepared *in situ* from chiral thioglucofuranose (107), CuI-SBu_2 and *n*-BuLi. The conjugate addition reaction of *n*-BuMgCl to cyclohexenone (52) using 4 mol% of the catalyst in Et_2O at -78 °C delivered 1,4-addition product (102) in 60% ee. However, since the reaction was suffering from low reproducibility, they found that the use of TEMPO, which is proposed to react with the excess of *n*-BuLi, improved the reaction (Figure 2.27).

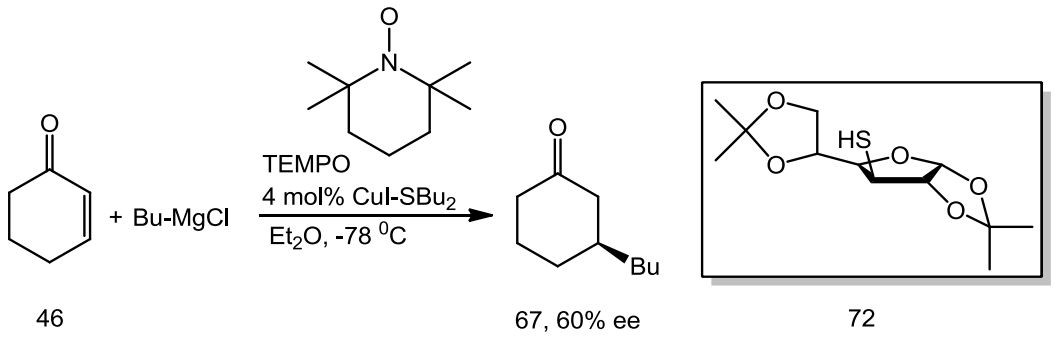


Figure 2.27. Copper-catalyzed 1,4-addition reported by Specha.

An important development in the Cu-catalyzed 1,4-addition of Grignard reagents to α,β-unsaturated carbonyl compounds was achieved by Pfaltz and Zhou [47]. They reported that enantioselective Cu-catalyzed 1,4-addition of *i-pr*MgCl using chiral Cu(I) thiolate-complex (75) with several α,β-unsaturated cyclic enones. And this reaction demonstrated that, the reactivity can be ordered as cyclopenatnone, cyclohexanone and cycloheptenone (Figure 2.28).

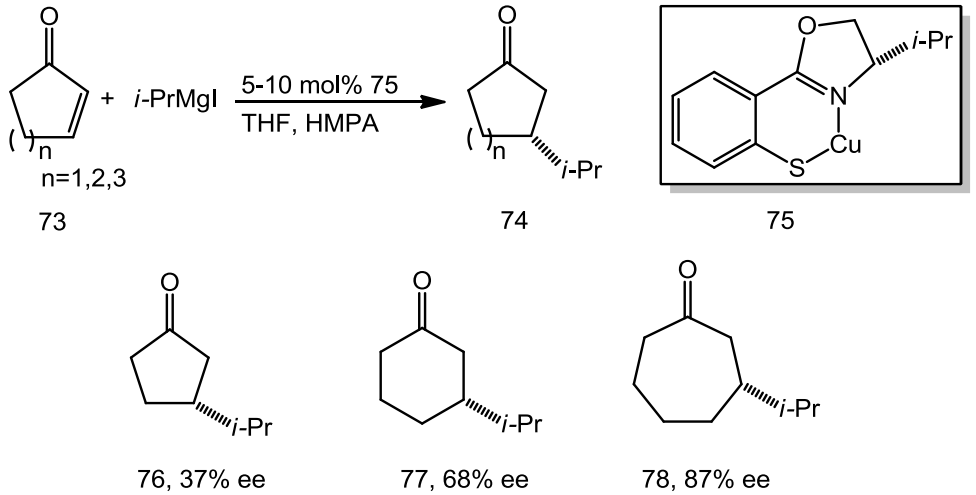


Figure 2.27. Cu-catalyzed 1,4-addition of *i-Pr*MgI to cyclic enones.

After that, Tomika reported [48] that conjugate addition of *n*-BuMgCl to cycloheptanone (79) using aminophospine ligand (81), enantioselectivity up to %92 ee. After this work, several cyclic and acylic α,β-unsaturated carbonyl compounds can be obtained using chiral aminophospine ligand and *n*-BuMgCl (Figure 2.29).

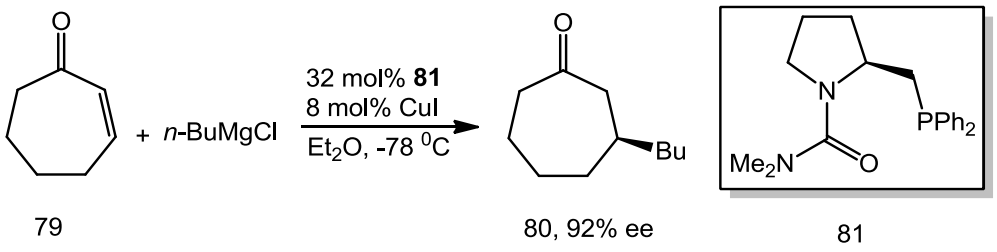


Figure 2.29. Cu-catalyzed 1,4-addition reported by Tomika.

In 1977, Sammiaka and Stangeland [49] examined the asymmetric Cu-catalyzed 1,4-addition of *n*-butyl Grignard reagents using a ferrocene-based phosphine-oxazoline ligand (84) for a range of cyclic enones. They observed an increased enantioselectivity depending on the variation of the ring size from cyclopentenone, cyclohexenone to cycloheptenone. With cyclopentenone, a low enantioselectivity 65% ee was obtained. Interestingly, the use of cyclohexenone delivered enantioselectivies up to 79% ee, while changing to cycloheptenone resulted in an enantioselectivity of 92% ee (Figure 2.30, Table 2.4).

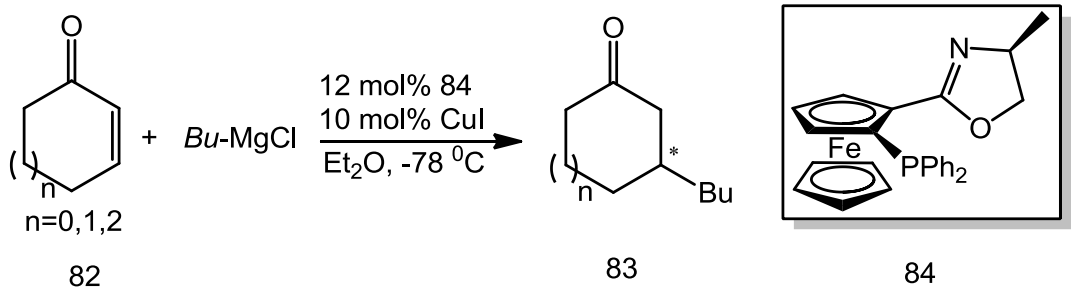


Figure 2.30. Cu-catalyzed enantioselective 1,4-addition of *n*-BuMgCl to cyclic enones.

Table 2.2. Enantioselective Cu-catalyzed 1,4-addition of Grignard reagents to cyclic enones.

Enone	*Cu [mol%]*	*L*[mol%]*	*1,4 : 1,2*	*Yield [%]*	*ee [%]*
cyclopentenone	10	12	99 : 1	82	65
cyclohexenone	10	6	99 : 1	97	83
cycloheptenone	10	12	99 : 1	82	92

Another important result in Cu-catalyzed 1,4-addition using Grignard reagent was reported by Seebach and co-workers [50]. They demonstrated that conjugate addition of *Bu*-MgCl to cyclohexanone (46) using chiral aminothiol ligand (85), enantioselectivity up to %80ee (Figure 2.31).

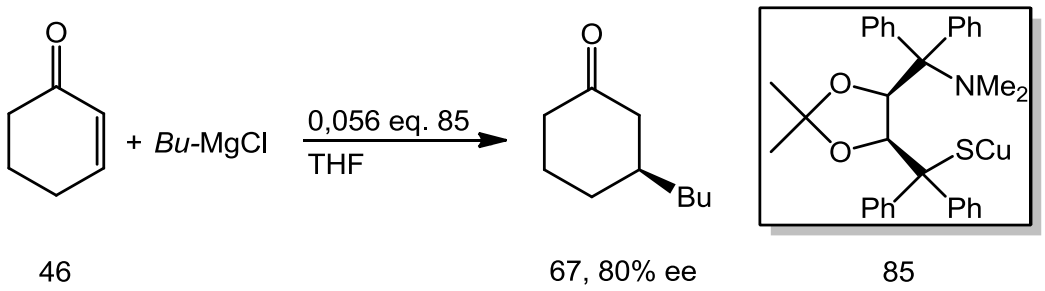


Figure 2.31. Cu-catalyzed 1,4-addition of Grignard reagents to cyclohexenone.

In 2004, Feringa and co-workers [51] reported that, Cu-catalyzed 1,4-addition using Grignard reagent to α,β-unsaturated carbonyl compound using two ferrocenyl based ligands TaniaPhos (88) and JosiPhos (89) enantioselectivity up to %96ee (Figure 2.32).

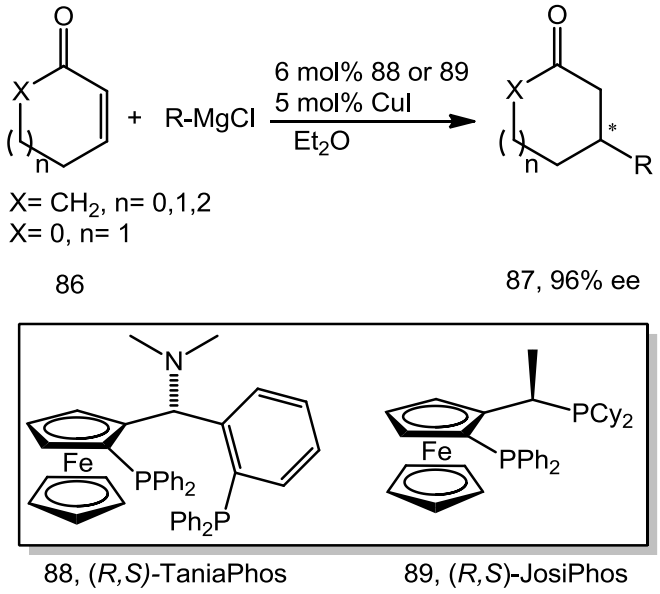


Figure 2.32. Cu-catalyzed enantioselective 1,4-addition of Grignard reagents.

Another significant development in Cu-catalyzed 1,4-addition using Grignard reagents to acyclic α,β-unsaturated carbonyl compounds was reported by Loh and co-workers [52]. They reported that conjugate addition of various alkyl magnesium bromides to α,β-unsaturated linear esters using CuI/Tol-BINAP **92**, enantioselectivities up to %93ee (Figure 2.33).

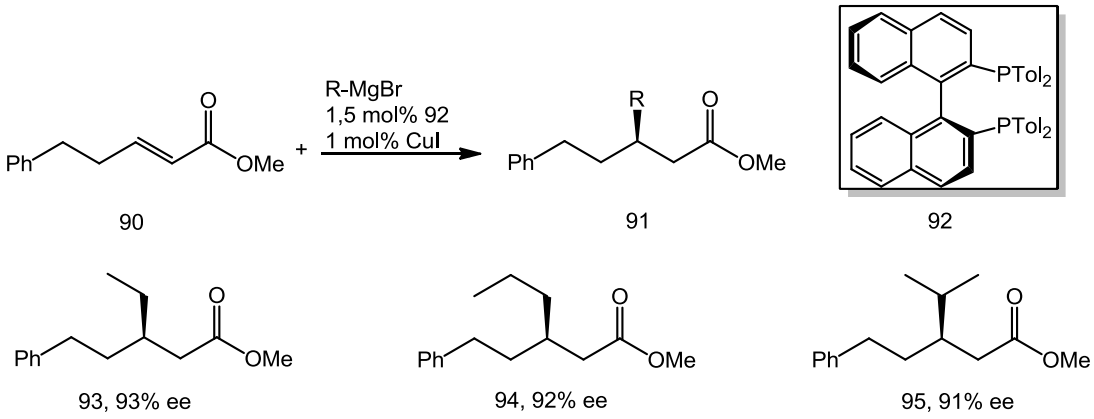


Figure 2.33 Cu-catalyzed 1,4-addition of Grignard reagents reported by Loh.

2.4.4. Copper-Catalyzed 1,4-Addition of Aryl and Alkenyl Grignard Reagents to β-Substituted Enones

The use of β-substituted α,β-unsaturated carbonyl compounds to create quaternary chiral centers. It is an continual challenge in transition metal-catalyzed 1,4-addition. Because of steric hinderance of the β-position. The solution is to create a quaternary chiral centers have been disclosed recently [32]. From other organometalic reagents, Grignard reagents are also able to undergo the Cu-catalyzed conjugate addition to β-substituted Micheal acceptors, producing an all-carbon quaternary center. The ferrocene-based ligands TaniaPhos (88) and JosiPhos (89) reported by Feringa were not able to induce high enantioselectivities Alexakis reported [53] the use of *C2*-symmetric imidazolidinium and alkoxy-NHCs ligands like (96) with Grignard reagents. Using these ligands, they were able to transfer a variety of alkyl Grignard reagents with high enantioselectivities up to 96% ee (Figure 2.34). By applying the same conditions to the addition of Ph-MgBr, the corresponding 1,4-addition product was achieved with a moderate enantioselectivity 70% ee.

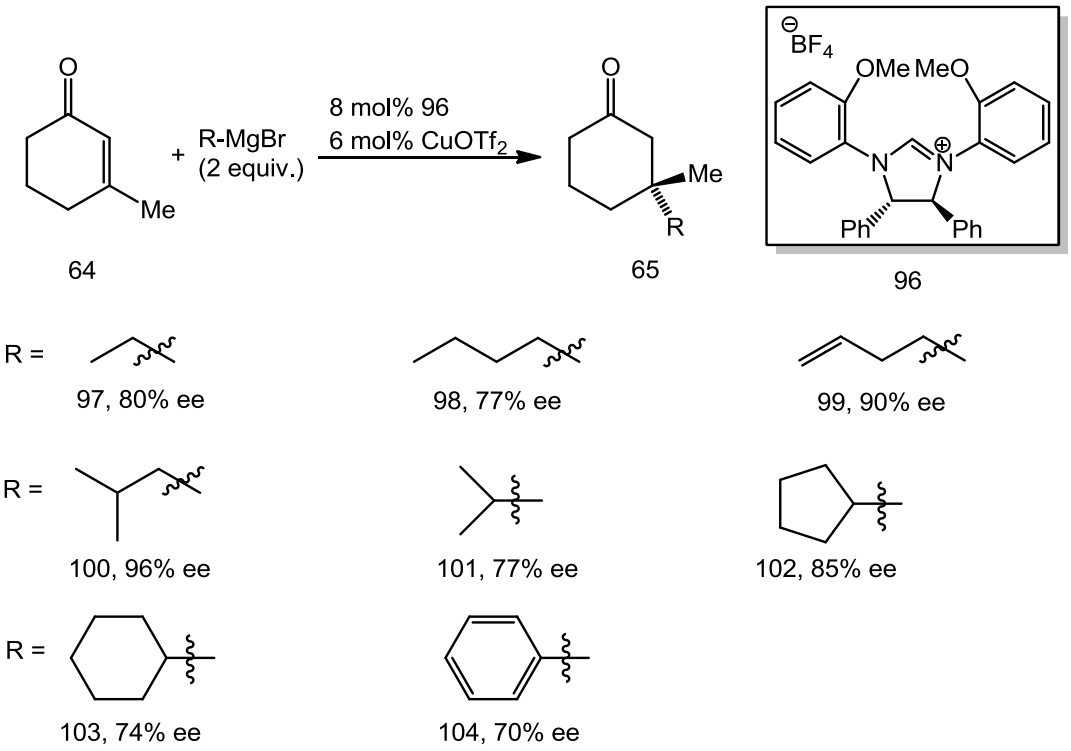


Figure 2.34. Cu-catalyzed 1,4-addition of Grignard reagents to β-substituted.

Alexakis's group reported that [53], Cu-catalyzed 1,4-addition of EtMgBr to β-substituted cyclic enones using phosphoramidites and *N*-heterocyclic carbens (107) with high enantioselectivities (Figure 2.35).

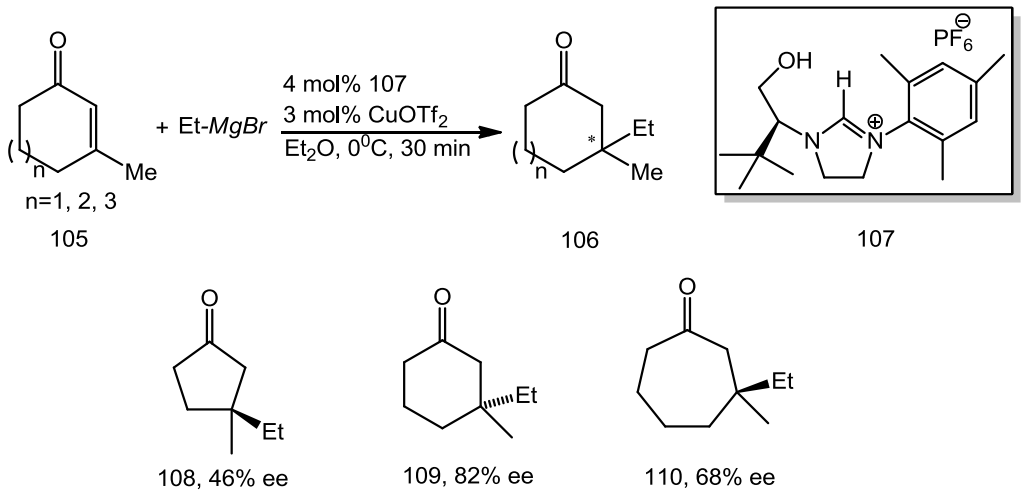


Figure 2.35. Cu-catalyzed 1,4-addition of Grignard reagents reported by Alexakis.

Matsumoto et al.[54] also used a C_2-symmetric NHC-ligand (112) to introduce various alkyl Grignard reagents with good enantioselectivities. They also examined the addition of Ph-MgBr, but only moderate yields and low enantioselectivities were obtained (Scheme 36). Alexakis demonstrated for the first time the Cu-catalyzed 1,4-addition of electron rich aryl Grignard regents to alkyl cyclohexenones using the NHC-ligand (117) with good enantioselectivities (Figure 2.36)

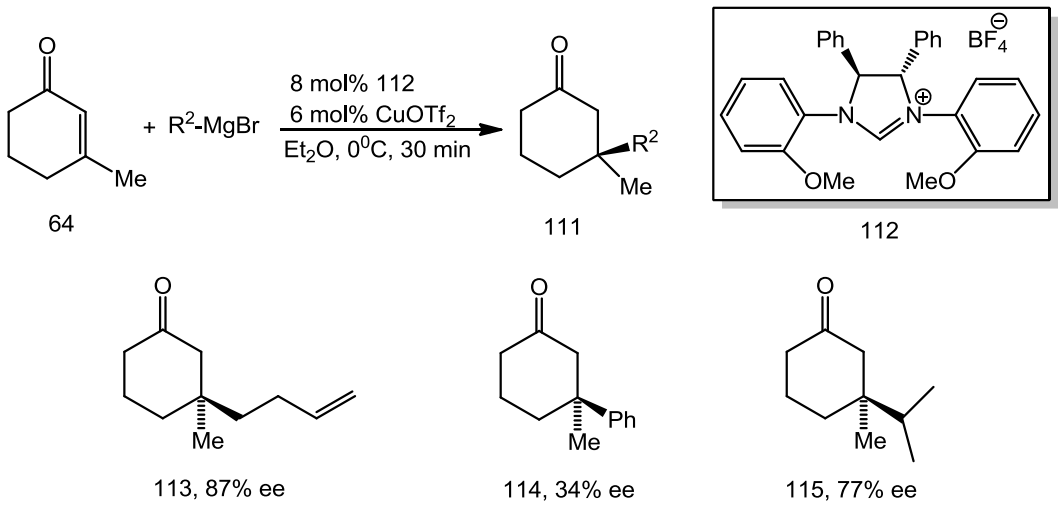


Figure 2.36. Use of C_2 symmetric NHC-ligands reported by Tomioka.

CHAPTER 3

EXPERIMENTAL PART

3.1. GENERAL INFORMATION

All reactions were conducted under an inert argon atmosphere and in heat-dried glassware using Standard Schlenk techniques. The glassware was flame dried at high vacuum (0.5-1 mbar) and allowed to cool down under argon atmosphere. Syringes, needles and transfer cannulas were dried in an oven at 80 ^{0}C and were flushed with argon directly before use.

Reagents and solvents were purchased from *Aldrich, Merck, Strem, Fluka, Acros* or *Lancaster* and were used without further purification except in the case of cyclopentenone, cyclohexenone, cycloheptenone. They were disstilled prior to use. Anhydrous solvents such as THF, Et_2O or Me-THF were dried by distillation from sodium benzophenone ketyl radical priour to use. Grignard solutions were either obtained from Chemetall or synthesized from the corresponding alkyl bromides in THF, Et_2O or Me-THF as solution. Content of Grignard reagents was determined based on the method reported by Knochel as follows: A 10 ml round-bottom flask equipped with a magnetic stirring bar and a septum was heated with a heat gun under reduced pressure and cooled to room temperature under an argon atmosphere. The dry flask was charged with accurately weighed iodine (254 mg, 1 mmol), fitted with a rubber septum and flushed with argon. A saturated solution of LiCl in THF (3-5 ml) was added and the solution was stirring. After the iodine was completely dissolved, the resulting brown solution was cooled to 0 ^{0}C in an ice bath and the Grignard reagent was added dropwise via a 1.00 ml syringe (0.01 ml graduations) until the brown color disappeared. The amount consumed contains 1 equiv of the Grignard reagent relative to iodine in the case of monoorganometallic reagents and 0.5 equiv for diorganometallic reagents.

Chormoatographic seperation and purification was performed using silica gel 60 M (0.04-0.063 mm/ 230-400 mesh) supplied by *Merk*.
Qualitative analysis of the reaction mixture through TLC was performed using Merck TLC-aluminium sheets coated with silica gel 60 F 254. The corresponding R*f* values were determined as the distance travelled by the compound (the middle of spot) divided by the distance travelled by solvent. The $KMnO_4$ solution was prepared from 3 g $KMnO_4$ mixed with 20 g K_2CO_3, 5 ml NaOH 5% aquiv and 300 ml of water.

The systematic 1,4-addition reactions were performed using a *Carousel Reaction* Station, which simultaneously performs up to twelve heated and stirred reactions. Depending on the size of the Carosuel, individual glass reaction tubes have a volume of 3 to 25 ml per tube to stir all the positions evenly and powerfully.

GC spectra were recorded on an Agilent HP6890 apparatus with a flame ionization detector (FID) and mass detector (MSD) 5937 N. Hydrogen was used as a carrier gas and a Optima 1 MS (Machere-Nagel) 30 m x 0.25 mm as a capillary column. GC data are given as followed: type of the colmn, flow of the carrier gas, method in following formula.

The solvent evaporation from reaction mixtures was done using a rotatory evaporator *R-114* from Büchi (vacuum of up to 10 mbar, water bath temperature: 40 ^{0}C). The advenced drying was performed at room temperature by appyling an oil pump vacuum.

^{1}H NMR spectra were recorded on a *Bruker* DPX 300 (300 MHz), *Bruker* DRX 500 (500 MHz) and a *Bruker* AV 600 (600 MHz) apparatus. Chemical shifts (δ) are given in ppm relative to the solvent reference as th internal Standard ($CDCl_3$, δ 7.24 ppm). Chemical multiplicity data reported as follows
s = Singlet
d = Dublett
t = Triplett
q = Quartett

dd = Dublett of Dubletts
m = Multiplett

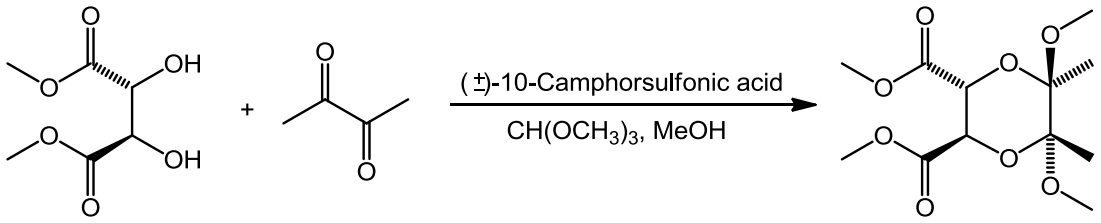
The ^{13}C NMR spectra were recorded on *Bruker* Avance II 600 (150 MHz) or *Bruker* Avance DRX 500 (125 MHz) apparatus. Chemical shifts (δ) are given in ppm relative to the solvent reference as the internal standard ($CDCl_3$: δ = 77.00ppm).

IR-spectra were recorded on Perkin Elmer FT-IR paragon 1000 spectrometer. Absorption bands are given in wave numbers (υ, cm^{-1}). Intensities of the bands are given as follows:
s = strong peaks
m = medium peaks
w = weak peaks

Melting points were measured on *Büchi* B-545 melting point apparatus and are uncorrected.

3.2. SYNTHESIS OF TARTARIC ACID DERIVATES

3.2.1. Synthesis of (2R, 3R, 5R, 6R)-dimethyl-5,6-dimethoxy-5,6-dimethyl-1,4-dioxane-2,3-dicarboxylat



35 36 37

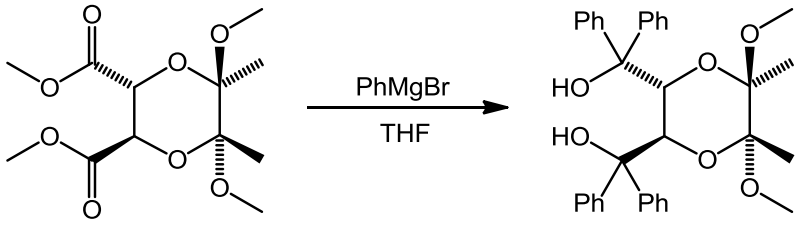
Figure 3.1. Synthesis of (*2R, 3R, 5R, 6R*)-dimethyl-5,6-dimethoxy-5,6-dimethyl- 1,4-dioxane-2,3-dicarboxylat.

17.82 g (0.1 mol, 1.0 eq.) (*R,R*)-tartaric acid-dimethylester (35) and 1.16 g (5 mmol, 0.05 eq.) (±)-10-Camphorsulfonic acid were dissolved in 100 ml dried methanol at room temparature. 44 ml (0.4 mol, 4 eq.) Trimethylorthoformat and 10.33 ml (0.12

mol, 1.2 eq.) 2,3-Butandione were filled on the reaction mixture. Yellow mixture was refluxed for 24 hours. After cooling to room temparature resulting mixture was treated with 16 g $NaHCO_3$ for 10 minutes. After filtration, solvent was removed. Orange product was purified by flash chromatograpy (CyHex:EtOAc / 5:1). After that 25.14 g (0.086 mol, 86%) (37) is obtained.

$C_{12}H_{20}O_8$	M = 292.28 g/mol
R_f	0.25 (CyHex:EtOAc / 5:1)
Melting Point	106 - 108 °C
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 4.51 (s, 2H, H3), 3.74 (s, 6H, H5), 3.30 (s, 6H, H6), 1.33 (s, 6H, H1).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 168.4 (C4), 99.2 (C2), 68.7 (C3), 52.5 (C5), 48.4 (C6), 17.3 (C1).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 2992 (w), 2951 (w), 2835 (w), 1742 (s), 1437 (m), 1377 (m), 1359 (m), 1285 (m), 1200 (s), 1172 (s), 1110 (s), 1032 (s), 950 (w), 886 (m), 853 (m), 809 (w), 773 (w), 741 (w).
GC-MS, 70 eV	m/z (%) = 261 (9), 229 (4), 144 (23), 113 (100), 73 (43), 59 (23).

3.2.2. Synthesis of (2R, 3R, 5R, 6R)-5,6-Dimethoxy-5,6-dimethyl- α, α, α', α'-tetraphenyl-1,4-dioxolane-2,3-dimethanol (TARTROL)



37 38

Figure 3.2. Synthesis of Tartrol.

16.0 g (55 mmol, 1.0 eq.) (37) in 180 ml dried THF was filled over 98 ml (275 mmol, 5.0 eq) 2.8 M Phenylmagnesiumbromide- solvent in 2-Me-THF, under -5 ^{0}C. Reaction mixture was refluxed 3 hours and then, the mixtured was cooled and stirred at room temparature 18 hours. Saturated NH_4Cl solvent was filled the mixture in ice-

bath. Later, HCl was filled the mixture until, pH-value were between 7 and 8. THF was removed. Water layers extracted with 150 ml. EtOAc two times. The combined organic layers were washed with saturated NaCl solvent and dried with $MgSO_4$. The solvent was removed and orange oil was obtained. Orange product was purified by flash chromatograpy (CyHex:EtOAc / 15:1). After that 19.62 g (36.3 mmol, 66%) (38) is obtained.

$C_{34}H_{36}O_6$	M = 540.65 g/mol
R_f	0.28 (CyHex:EtOAc / 10:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.98-7.96 (m, 4H, CH_{Ar}), 7.44-7.22 (m, 6H, CH_{Ar}), 7.14-7.02 (m, 10H, CH_{Ar}), 4.38 (s, 2H, H3), 4.33 (s, 2H, OH), 2.57 (s, 6H, H5), 0.99 (s, 6H, H1).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 146.0 (Cq_{Ar}), 142.8 (Cq_{Ar}), 127.9 (CH_{Ar}), 127.7 (CH_{Ar}), 127.2 (CH_{Ar}), 127.1 (CH_{Ar}), 126.8 (CH_{Ar}), 98.5 (C2), 79.4 (C4), 75.9 (C3), 47.6 (C5), 17.1 (C1).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3355 (br), 3057 (m), 3021 (m), 2992 (m), 2943 (m), 2830 (m), 2244 (w), 1598 (m), 1491 (s), 1446 (s), 1371 (s), 1318 (m), 1122 (s), 1034 (s), 908 (s), 847 (m).
GC-MS, 70 eV	m/z (%) = 325 (5), 297 (8), 269 (15), 207 (21), 183 (54), 165 (51), 105 (100), 77 (76), 51 (34).

3.3. SYNTHESIS OF *ORTHO*-BROMOPHENOLS

3.3.1. General Procedure I

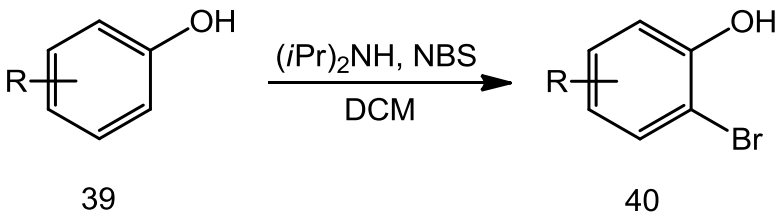


Figure 3.3. Synthesis of *ortho*-bromophenols.

In a flame-dried flask equipped with a Soxhlet apparatus and flushed with argon the substituted phenols (1 equiv.) (39) and diisopropylamine (0.1 equiv.) were dissolved in absolute DCM. The thimble was filled with NBS (1.1 equiv.) and system was heated to reflux for 16 h. During this time, the NBS was slowly consumed. After cooling to RT the resulting mixture was treated with 2M sulfuric acid. The layers were separated and aqueous layer was extracted with *tert*-butylmethylether. The combined organic layers were washed with water and brine and dried $MgSO_4$. The solvent was removed and the crude product was purified by flash chromatography.

3.3.2. Synthesis of 2-Bromo-4,6-di-*tert*-butylphenol

According to the *general procedure (I)*, 2,4-di-*tert*-butylphenol (39a) (20.60 g, 0.10 mol) and diisopropylamine (1.4 ml, 0.01 mmol, 0.1 eq.) were dissolved in CH_2Cl_2 (250 ml) and treated with NBS (19.58 g, 0.11 mol, 1.1 eq.) for 16 h at reflux. After cooling to RT the resulting mixture was treated with 2M sulfiric acid (200 ml). Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NaCl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (40a) (23.4 g, 82 mmol, 82%) as a pale yellow solid.

$C_{14}H_{21}BrO$	M = 285.22 g/mol
R_f	0.85 (CyHex:EtOAc / 50:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.32 (d, *J* = 2.3 Hz, 1H, H3), 7.24 (d, *J* = 2.4 Hz, 1H, H5), 5.65 (s, 1H, OH), 1.40 (s, 9H, H10), 1.28 (s, 9H, H8).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 148.0 (C1), 143.7 (C4), 136.7 (C6), 126.3 (C3), 123.7 (C5), 111.9 (C2), 35.6 (C9), 34.4 (C7), 31.5 (C8), 29.4 (C10).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3500 (m), 2953 (s), 2866 (m), 1776 (w), 1723 (w), 1563 (m), 1536 (w), 1473 (s), 1403 (s), 1363 (s), 1330 (s), 1280 (s), 1246 (s), 1166 (s), 1133 (m), 1083 (m), 1023 (w), 933 (w), 886 (w), 863 (s), 836 (s), 816 (m), 740 (s), 706 (s).
GC-MS, 70 eV	m/z (%) = 286 (10, $[M]^+$), 284 (10, $[M]^+$), 269 (41), 57 (90), 41

3.3.3. Synthesis of 2-Bromo-6-*tert*-butylphenol

According to the *general procedure (I)*, 2-*tert*-butylphenol (39b) (15.0 g, 0.10 mol, 1.0 eq.) and diisopropylamine (1.4 ml, 0.01 mol, 0.1 eq.) were dissolved in CH_2Cl_2 (250 ml) and treated with NBS (19.58 g, 0.12 mmol, 1.1 eq) for 16 h at reflux. After cooling to RT the resulting mixture was treated with 2M sulfiric acid (200 ml). Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NaCl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (40b) (21.2 g, 92.6 mmol, 93%) as a pale yellow solid.

$C_{10}H_{13}BrO$	M = 229.11 g/mol
R_f	0.8 (CyHex)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.33 (dd, *J* = 8.0, 1.4 Hz, 1H, H3), 7.21 (dd, *J* = 7.8, 0.9 Hz, 1H, H5), 6.73 (t, *J* = 7.9, Hz, 1H, H4), 5.79 (s, 1H, OH), 1.40 (s, 9H, $C(CH_3)_3$).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 150.4 (C1), 137.7 (C6), 129.6 (C3), 126.5 (C5), 120.9 (C4), 112.2 (C2), 35.3 (C7), 29.3 ($(CH_3)_3$).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3500 (s), 2955 (s), 2910 (m), 2870 (m), 1595 (m), 1472 (m), 1431 (s), 1390 (s), 1361 (s), 1330 (s), 1268 (m), 1239 (s), 1199 (m), 1185 (s), 1087 (s), 1074 (m), 853 (s), 820 (m), 772 (s), 733 (m), 680 (s).
GC-MS, 70 eV	m/z (%) = 230 (32, $[M]^+$), 228 (32, $[M]^+$), 213 (100), 185 (69), 150 (35), 135 (100), 107 (100), 91 (46), 77 (43), 63 (29), 51 (29).

3.3.4. Synthesis of 2-Bromo-1-naphthol

According to the *general procedure (I)*, 2-phenylphenol (39c) (17.0 g, 0.10 mol, 1.0 eq.) and diisopropylamine (1.4 ml, 0.01 mol, 0.1 eq.) were dissolved in CH_2Cl_2 (250 ml) and treated with NBS (19.58 g, 0.11 mol, 1.1 eq.) for 16 h at reflux. After cooling to RT the resulting mixture was treated with 2M sulfiric acid (200 ml).

Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NaCl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (40c) (22.01 g, 88.7 mmol, 89%) as a pale yellow solid.

$C_{12}H_9BrO$	M = 249.1 g/mol
R_f	0.4 (CyHex:EtOAc / 50:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.52-7.32 (m, 6H, H_{Ar}), 7.21 (dd, *J* = 7.6 Hz, 1.4 Hz, 1H, H_{Ar}), 6.84 (t, *J* = 7.8 Hz, 1H, H4), 5.66
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 149.1 (C1), 137.1 (Cq), 131.4 (CH_{Ar}), 130.1 (CH_{Ar}), 129.6 (Cq), 129.1 (CH_{Ar}), 128.5 (CH_{Ar}), 127.7 (CH_{Ar}), 121.6 (C4), 111.0 (C2).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3494 (m), 3057 (w), 3029 (w), 1598 (w), 1561 (w), 1496 (m), 1464 (s), 1452 (s), 1426 (s), 1391 (m), 1323 (s), 1228 (s), 1168 (s), 1123 (s), 1067 (s), 1040 (s), 1015 (s), 917 (m), 828 (s), 751 (s), 694 (s), 638 (s).
GC-MS, 70 eV	m/z (%) = 250 (69, $[M]^+$), 248 (69, $[M]^+$), 170 (100), 141 (78), 115 (76), 102 (10), 89 (20), 63 (38), 51 (23).

3.3.5. Synthesis of 2-Bromo-4,6-di-*tert*-pentylphenol

According to the *general procedure (I)*, 2,4-di-*tert*-pentylphenol (39d) (19.8 g, 84.3 mmol, 1.0 eq.) and diisopropylamine (1.2 ml, 8.4 mmol, 1.0 eq.) were dissolved in CH_2Cl_2 (250 ml) and treated with NBS (16.5 g, 92.7 mmol, 1.1 eq.) for 16 h at reflux. After cooling to RT the resulting mixture was treated with 2M sulfiric acid (200 ml). Aqueous layer was extracted with 3x100 ml MTBE. The combined organic layers were washed with 300 ml. saturated NaCl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (40d) (24.6 g, 78.5 mmol, 93%) as a pale yellow solid.

$C_{16}H_{25}BrO$	M = 313.27 g/mol
R_f	0.6 (CyHex)

^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.25 (s, 1H, H3), 7.10 (s, 1H, H5), 5.60 (s, 1H, OH), 1.85 (q, *J* = 7.5 Hz, 2H, C*H*$_2$CH$_3$), 1.58 (q, *J* = 7.4 Hz, 2H, C*H*$_2$CH$_3$), 1.35 (s, 6H, CH_3), 1.23 (s, 6H, CH_3), 0.69-0.61 (m, 6H, CH_2C*H*$_3$).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 147.8 (C1), 141.8 (C4), 134.9 (C6), 126.9 (C3), 125.7 (C5), 111.8 (C2), 39.1 (C_q), 37.6 (C_q), 36.9 (CH_2), 32.8 (CH_2), 28.5 ((CH_3)$_2$), 27.5 ((CH_3)$_2$), 9.4 (CH_2*C*H$_3$), 9.1 (CH_2*C*H$_3$).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3506 (m), 2966 (s), 2866 (m), 1726 (w), 1593 (w), 1566 (w), 1466 (s), 1400 (s), 1373 (m), 1360 (s), 1333 (m), 1296 (m), 1270 (m), 1246 (s), 1170 (s), 1126 (w), 1090 (m), 1056 (w), 1003 (w), 936 (w), 913 (w), 890 (w), 863 (m), 826 (w), 813 (w), 776 (m), 740 (m), 700 (s).
GC-MS, 70 eV	m/z (%) = 314 (8, [M]$^+$), 312 (8, [M]$^+$), 285 (95), 283 (100), 257 (8), 255 (8), 241 (4), 239 (4), 205 (6), 131 (5), 115 (6), 91 (5), 71 (9), 43 (10).

3.3.6. Synthesis of 2-Bromo-6-*tert*-pentylphenol

According to the *general procedure (I)*, 2-*tert*-pentylphenol (39e) (16.4 g, 0.10 mol, 1.0 eq.) and diisopropylamine (1.40 ml, 0.01 mol, 0.1 eq.) were dissolved in CH_2Cl_2 (250 ml) and treated with NBS (19.58 g, 0.11 mol, 1.1 eq.) for 16 h at reflux. After cooling to RT the resulting mixture was treated with 2M sulfiric acid (200 ml). Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NaCl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (40e) (19.9 g, 81.8 mmol, 82%) as a pale yellow solid.

$C_{11}H_{15}BrO$	M = 243.14 g/mol
R_f	0.85 (CyHex:EtOAc / 20:1)

^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.33 (dd, *J* = 8.0, 1.5 Hz, 1H, H3), 7.15 (dd, *J* = 7.9, 1.2 Hz, 1H, H5), 6.73 (t, *J* = 7.9 Hz, 1H, H4), 5.76 (s, 1H, OH), 1.87 (q, *J* = 7.5, Hz, 2H, H10), 1.35 (s, 6H, H8+H9), 0.64 (t, *J* = 7.5 Hz, 3H, H11).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 150.3 (C1), 136.0 (C6), 129.6 (C3), 127.9 (C5), 120.8 (C4), 112.1 (C2), 39.0 (C7), 32.7 (C10), 27.5 (C8+C9), 9.5 (C11) .
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3499 (s), 2960 (s), 2866 (m), 1592 (m), 1430 (s), 1380 (m), 1332 (s), 1266 (m), 1241 (s), 1182 (s), 1141 (s), 1089 (s), 843 (s), 769 (s), 734 (s), 678 (s).
GC-MS, 70 eV	m/z (%) = 244 (32, $[M]^+$), 242 (32, $[M]^+$), 213 (100), 185 (100), 134 (57), 115 (32), 77 (29), 51 (15).

3.3.7. Synthesis of 2-Bromo-6-methylphenol

According to the *general procedure (I)*, 2-methylphenol (39f) (10.80 g, 0.10 mol, 1.0 eq.) and diisopropylamine (1.40 ml, 0.01 mol, 0.1 eq.) were dissolved in CH_2Cl_2 (250 ml) and treated with NBS (19.58 g, 0.11 mol, 1.1 eq.) for 16 h at reflux. After cooling to RT the resulting mixture was treated with 2M sulfiric acid (200 ml). Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NaCl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (40f) (16.1 g, 86.04 mmol, 86%) as a pale yellow solid.

C_7H_7BrO	M = 187.03 g/mol
R_f	0.4 (CyHex)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.28 (d, *J* = 8.1 Hz, 1H, H3), 7.05 (d, *J* = 7.5 Hz, 1H, H5), 6.70 (t, *J* = 7.8 Hz, 1H, H4), 5.55 (s, 1H, OH), 2.29 (s, 3H, H7).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 150.3 (C1), 130.3 (C5), 129.3 (C3), 125.8 (C6), 121.1 (C4), 110.1 (C2), 16.6 (C7).

FT-IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3505 (s), 3069 (w), 3023 (w), 2949 (w), 2916 (m), 2849 (w), 1905 (w), 1843 (w), 1779 (w), 1598 (s), 1573 (m), 1461 (s), 1429 (s), 1396 (m), 1377 (m), 1324 (s), 1282 (s), 1233 (s), 1217 (m), 1161 (s), 1119 (s), 1073 (s), 1035 (m), 992 (s), 845 (s), 756 (s), 717 (s), 688 (m), 614 (s).

GC-MS, 70 eV m/z (%) = 188 (28, $[M]^+$), 186 (30, $[M]^+$), 107 (100), 77 (61), 51

3.4. SYNTHESIS OF 2-BORANATODIPHENYLPHOSPHANYL PHENOL

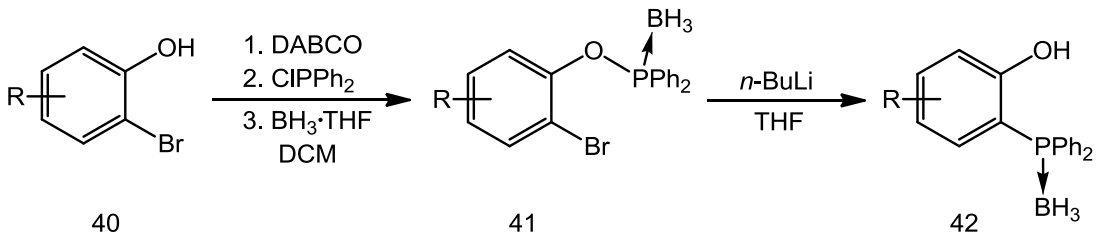


Figure 3.4. Synthesis of 2-borantodiphenylphosphanyl phenol.

3.4.1. General Procedure II

A flame-dried Schlenk flask was charged under argon with a substituted 2-bromo-phenol (40) (1 equiv.) and DABCO (1.2 equiv.) and dissolved in CH_2Cl_2. This solution was stirred for 5 min at RT then cooled 0^0C and chlorophosphine (1.2 equiv.) was added dropwise via syringe. The resulting suspension was stirred 10 min at this temperature, warmed to RT and stirred for another 2 h. The reaction mixture was then cooled to 0^0C and solution BH_3 in THF (2 equiv.) was added. This resulting solution was stirred 15 min at 0^0C and 1 h at RT before it was quenched with H_2O (Caution! Strong H_2 gas formation) and extracted with tert-butyl-methylether. The ethereal phase was washed with brine and dried ($MgSO_4$). The solvent was evaporated to give the crude product (41) which was used without further purification.

3.4.2. General Procedure III

In a flame-dried Schlenk flask under argon a solution of a BH_3-protected phosphinite (41) (1 equiv.) in THF was cooled to 0^0C and treated with *n*-BuLi (1.5 equiv.). The mixture was stirred for 2 h at this temperature, then quanched with H_2O, extracted with *tert*-butyl-methylether and washed with NH_4Cl-solution. The organic layers were dried ($MgSO_4$) and concentrated under reduced pressure to give the crude product which was purified by flash chromatography to provide the phosphines (42) as white solids.

3.4.3. Synthesis of 2-Boranatodiphenylphosphanyl-4,6-di-*tert*-butyl-phenol

According to *procudure (II) and (III)*, bromophenol (40a) (23.3 g, 81.7 mmol, 1.0 eq.) and DABCO (11.0 g, 98.0 mmol, 1.2 eq.) were dissolved in CH_2Cl_2 (160 ml) and treated with chlorodiphenylphosphine (17.6 ml, 98.0 mmol, 1.2 eq.). After addition of BH_3 in THF (1 M, 164.0 ml, 164.0 mmol, 2.0 eq.) the reaction was quenched with 300 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 300 ml. saturated NaCl-solution. The crude product (41a) was dissolved in THF (150 ml) and treated with *n*-BuLi (1.6 M 77 ml, 122 mmol, 1.5 eq.) and quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NH_4Cl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (42a) (30.6 g, 75.7 mmol 93% over two steps) as a white solid.

$C_{26}H_{34}BOP$	M = 404.33 g/mol
R_f	0.7 (CyHex:EtOAc / 50:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.55-7.42 (m, 12H, OH, H_{Ar}, H3), 6.66 (dd, *J* = 11.5 Hz, 2.4 Hz, 1H, H5), 1.41 (s, 9H, H10), 1.11 (s, 9H, H8).

^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 157.1 (d, *J* = 9.8 Hz, Cq), 142.1 (d, *J* = 8.0 Hz, Cq), 138.0 (d, *J* = 5.8 Hz, Cq), 133.0 (d, *J* = 9.8 Hz, CH_{Ar}), 131.4 (d, *J* = 2.5 Hz, CH_{Ar}), 128.8 (d, *J* = 10.6 Hz, CH_{Ar}), 128.7 (d, *J* = 3.8 Hz, CH_{Ar}), 128.6 (d, *J* = 61.7 Hz, Cq), 128.5 (d, *J* = 2.0 Hz, CH_{Ar}), 111.3 (d, *J* = 59.2 Hz, Cq), 35.4 ($C(CH_3)_3$), 34.3 ($C(CH_3)_3$), 31.2 ($C(CH_3)_3$), 29.6 ($C(CH_3)_3$).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 13.67 (d, *J* = 54.4 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3360 (m), 3046 (w), 2953 (s), 2906 (m), 2866 (m), 2366 (m), 1960 (w), 1900 (w), 1810 (w), 1573 (w), 1463 (m), 1430 (s), 1390 (m), 1340 (m), 1286 (w), 1246 (m), 1216 (m), 1186 (s), 1140 (m), 1103 (s), 1063 (s), 1023 (w), 1000 (w), 910 (m), 853 (w), 816 (m), 733 (s), 693 (s).
GC-MS, 70 eV	m/z (%) = 390 (95, $[M\text{-}BH_3]^+$), 375 (71), 348 (30), 333 (27), 201 (24), 183 (100), 152 (18), 133 (19), 108 (43), 78 (86), 57 (81),

3.4.4. Synthesis of 2-Boranatodiphenylphosphanyl-6-*tert*-butyl-phenol

According to *procudure (II) and (III)*, bromophenol (40b) (19.4 g, 84.7 mmol, 1.0 eq.) and DABCO (11.4 g, 101.7 mmol, 1.2 eq.) were dissolved in CH_2Cl_2 (120 ml) and treated with chlorodiphenylphosphine (18.3 ml, 101.7 mmol, 1.2 eq.). After addition of BH_3 in THF (1 M, 170.0 ml, 169.0 mmol, 2.0 eq.) the reaction was quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NaCl-solution. The crude product (41b) was dissolved in THF (150 ml) and treated with *n*-BuLi (1.6 M 80 ml, 127 mmol, 1.5 eq.) and quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NH_4Cl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (42b) (26.5 g, 76.1 mmol 90% over two steps) as a white solid.

$C_{22}H_{26}BOP$	M = 348.23 g/mol
R_f	0.65 (CyHex:EtOAc / 50:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.75 (d, *J* = 2.0 Hz, 1H, H_{Ar}),

	7.55-7.43 (m, 11H, H_{Ar}, OH), 6.81 (td, *J* = 7.7, 1.7 Hz, 1H, H_{Ar}), 6.73-6.66 (m, 1H, H_{Ar}), 1.40 (s, 9H, $C(CH_3)_3$).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 159.5 (d, *J* = 9.7 Hz, Cq), 138.9 (d, *J* = 5.4 Hz, Cq), 133.0 (d, *J* = 9.9 Hz, CH_{Ar}), 132.2 (CH_{Ar}), 132.1 (CH_{Ar}), 132.0 (CH_{Ar}), 131.5 (d, *J* = 2.5 Hz, CH_{Ar}), 131.2 (d, *J* = 1.9 Hz, CH_{Ar}), 131.0 (d, *J* = 2.4 Hz, CH_{Ar}), 128.9 (d, *J* = 10.5 Hz, CH_{Ar}), 128.8 (d, *J* = 10.5 Hz, CH_{Ar}), 127.9 (Cq), 120.1 (d, *J* = 8.7 Hz, CH_{Ar}), 112.3 (d, *J* = 59.0 Hz, Cq), 35.2 ($C(CH_3)_3$), 29.5 ($C(CH_3)_3$).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 12.87 (d, *J* = 73.1 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3350 (m), 3056 (w), 2999 (w), 2955 (m), 2375 (s), 1575 (m), 1481 (m), 1467 (m), 1434 (s), 1419 (s), 1389 (m), 1362 (m), 1341 (m), 1260 (m), 1232 (s), 1198 (s), 1155 (m), 1118 (s), 1103 (s), 1065 (s), 1026 (m), 998 (m), 907 (m), 828 (m), 735 (s), 689 (s), 635 (s).
GC-MS, 70 eV	m/z (%) = 334 (100, $[M\text{-}BH_3]^+$), 319 (78), 292 (100), 213 (24), 183 (54), 152 (15), 109 (26), 78 (23), 51 (15).

3.4.5. Synthesis of 2-Boranatodiphenylphosphanyl-6-phenyl-phenol

According to *procudure (II) and (III)*, bromophenol (40c) (22.0 g, 88.3 mmol, 1.0 eq.) and DABCO (11.9 g, 106.0 mmol, 1.2 eq.) were dissolved in CH_2Cl_2 (150 ml) and treated with chlorodiphenylphosphine (19.0 ml, 106.0 mmol, 1.2 eq.). After addition of BH_3 in THF (1 M, 176.0 ml, 176.0 mmol, 2.0 eq.) the reaction was quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NaCl-solution. The crude product (41c) was dissolved in THF (150 ml) and treated with *n*-BuLi (1.6 M 83 ml, 132 mmol, 1.5 eq.) and quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NH_4Cl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (42c) (30.6 g, 83.0 mmol 94% over two steps) as a white solid.

$C_{24}H_{22}BOP$	M = 368.22 g/mol
R_f	0.3 (CyHex:EtOAc / 50:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.65-7.59 (m, 4H, H_{Ar}), 7.55-7.33 (m, 12H, H_{Ar}), 7.15 (s, 1H, OH), 7.13-7.07 (m, 1H, H_{Ar}), 7.00 (dt, *J* = 7.6 Hz, 1.6 Hz, 1H, H_{Ar}).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 156.5 (d, *J* = 7.0 Hz, C1), 136.8 (Cq_{Ar}), 134.8 (CH_{Ar}), 134.2 (d, *J* = 5.7 Hz, CH_{Ar}), 133.0 (d, *J* = 9.9 Hz, CH_{Ar}), 131.4 (CH_{Ar}), 130.6 (d, *J* = 5.8 Hz, C6), 129.4 (CH_{Ar}), 128.8 (d, *J* = 10.6 Hz, CH_{Ar}), 128.6 (CH_{Ar}), 127.9 (Cq_{Ar}), 127.7 (CH_{Ar}), 120.8 (d, *J* = 9.4 Hz, CH_{Ar}), 113.2 (d, *J* = 57.2 Hz, C2).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 14.75 (d, *J* = 66.9 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3333 (m), 3053 (w), 2380 (m), 1963 (w), 1820 (w), 1576 (w), 1480 (m), 1433 (s), 1340 (m), 1223 (s), 1183 (m), 1146 (m), 1096 (s), 1063 (s), 1020 (m), 996 (m), 906 (m), 830 (m), 796 (m), 736 (s), 696 (s).
GC-MS, 70 eV	m/z (%) = 354 (100, $[M\text{-}BH_3]^+$), 275 (46), 257 (10), 199 (10), 183 (31), 170 (18), 152 (15), 108 (20), 78 (35), 51 (23).

3.4.6. Synthesis of 2-Boranatodiphenylphosphanyl-4-6-di-*tert*-pentyl-phenol

According to *procudure (II) and (III)*, bromophenol (40d) (23.5 g, 75.0 mmol, 1.0 eq.) and DABCO (10.1 g, 90.0 mmol, 1.2 eq.) were dissolved in CH_2Cl_2 (150 ml) and treated with chlorodiphenylphosphine (16.2 ml, 90.0 mmol, 1.2 eq.). After addition of BH_3 in THF (1 M, 150.0 ml, 150.0 mmol, 2.0 eq.) the reaction was quenched with 500 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 500 ml. saturated NaCl-solution. The crude product (41d) was dissolved in THF (200 ml) and treated with *n*-BuLi (1.6 M 70 ml, 112 mmol, 1.5 eq.) and quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NH_4Cl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (42d) (29.3 g, 67.8 mmol 91% over two steps) as a white solid.

$C_{28}H_{38}BOP$	M = 432.38 g/mol
R_f	0.35 (CyHex)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.55-7.41 (m, 11H, OH, H_{Ar}), 7.33 (d, *J* = 2.2 Hz, 1H, H_{Ar}), 6.57 (dd, *J* = 11.6 Hz, 2.3 Hz, 1H, H_{Ar}), 1.85 (q, *J* = 7.4 Hz, 2H, C*H*$_2$CH$_3$), 1.45-1.36 (m, 8H, C*H*$_2$CH$_3$, CH_3), 1.05 (s, 6H, CH_3), 0.64-0.53 (m, 6H, CH_2C*H*$_3$).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 157.0 (d, *J* = 9.8 Hz, Cq), 140.2 (d, *J* = 7.9 Hz, Cq), 136.2 (d, *J* = 5.8 Hz, Cq), 132.9 (d, *J* = 9.8 Hz, CH_{Ar}), 131.4 (d, *J* = 1.5 Hz, CH_{Ar}), 130.5 (d, *J* = 1.0 Hz, CH_{Ar}), 129.4 (d, *J* = 3.3 Hz, CH_{Ar}), 128.8 (d, *J* = 10.5 Hz, CH_{Ar}), 128.6 (d, *J* = 61.5 Hz, Cq), 110.9 (d, *J* = 59.5 Hz, Cq), 38.9 (Cq), 37.4 (Cq), 36.8 (CH_2), 32.9 (CH_2), 28.2 ((CH_3)$_2$), 27.8 ((CH_3)$_2$), 9.5 (CH_2*C*H$_3$), 9.0 (CH_2*C*H$_3$).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 13.60 (d, *J* = 51.4 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3361 (m), 3046 (w), 2959 (s), 2866 (m), 2375 (m), 1953 (w), 1883 (w), 1810 (w), 1586 (w), 1570 (w), 1453 (m), 1435 (s), 1380 (m), 1361 (m), 1340 (m), 1296 (w), 1236 (m), 1187 (m), 1133 (m), 1104 (s), 1066 (m), 1026 (m), 998 (m), 906
GC-MS, 70 eV	m/z (%) = 418 (83, $[M\text{-}BH_3]^+$), 403 (55), 389 (100), 375 (61), 362 (25), 347 (16), 333 (19), 311 (22), 205 (13), 183 (33), 108 (20), 87 (18).

3.4.7. Synthesis of 2-Boranatodiphenylphosphanyl-6-*tert*-pentyl-phenol

According *procudure (II) and (III)*, bromophenol (40e) (19.0 g, 78.1 mmol, 1.0 eq.) and DABCO (10.5 g, 93.7 mmol, 1.2 eq.) were dissolved in CH_2Cl_2 (150 ml) and treated with chlorodiphenylphosphine (16.8 ml, 93.7 mmol, 1.2 eq.). After addition of BH_3 in THF (1 M, 156.0 ml, 156.0 mmol, 2.0 eq.) the reaction was quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NaCl-solution. The crude product (41e) was dissolved in THF (180 ml) and treated with *n*-BuLi (1.6 M 73 ml, 117 mmol, 1.5 eq.) and quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated

NH_4Cl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (42e) (26.1 g, 72.0 mmol 92% over two steps) as a white solid.

$C_{23}H_{28}BOP$	M = 362.25 g/mol
R_f	0.3 (CyHex)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.64 (d, *J* = 2.0 Hz, 1H, H_{Ar}), 7.56-7.38 (m, 11H, H_{Ar}, OH), 6.82 (td, *J* = 7.7, 1.6 Hz, 1H, H_{Ar}), 6.71-6.64 (m, 1H, H_{Ar}), 1.86 (q, *J* = 7.5 Hz, 2H, CH_2CH_3), 1.36 (s, 6H, $C(CH_3)_2$), 0.62 (t, 3H, CH_2CH_3).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 159.3 (d, *J* = 9.5 Hz, Cq), 137.2 (d, *J* = 5.4 Hz, Cq), 133.0 (d, *J* = 9.9 Hz, CH_{Ar}), 132.6 (d, *J* = 1.9 Hz, CH_{Ar}), 132.0 (d, *J* = 3.4 Hz, CH_{Ar}), 131.5 (d, *J* = 2.5 Hz, CH_{Ar}), 128.9 (d, *J* = 10.6 Hz, CH_{Ar}), 128.6 (Cq), 127.8 (Cq), 120.0 (d, *J* = 8.7 Hz, CH_{Ar}), 112.3 (d, *J* = 59.2 Hz, Cq), 38.9 (d, *J* = 1.4 Hz, Cq), 32.8 (CH_2), 27.8 ($C(CH_3)_2$), 9.6 (CH_2CH_3).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 12.95 (d, *J* = 73.8 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3352 (m), 3056 (w), 2958 (m), 2872 (w), 2375 (m), 1576 (m), 1480 (m), 1467 (m), 1435 (s), 1419 (s), 1383 (m), 1360 (m), 1341 (m), 1225 (s), 1199 (s), 1158 (m), 1120 (m), 1104 (s), 1068 (s), 1027 (m), 998 (m), 909 (w), 827 (m), 741 (s), 699 (s), 690 (s).
GC-MS, 70 eV	m/z (%) = 348 (80, $[M\text{-}BH_3]^+$), 333 (77), 319 (85), 305 (100), 300 (85), 221 (15), 199 (15), 183 (80), 152 (18), 107 (31), 78 (30), 51 (15).

3.4.8. Synthesis of 2-Boranatodiphenylphosphanyl-6-methyl-phenol

According to *procudure (II) and (III)*, bromophenol (40f) (16.0 g, 85.5 mmol, 1.0 eq.) and DABCO (11.5 g, 102.6 mmol, 1.2 eq.) were dissolved in CH_2Cl_2 (150 ml) and treated with chlorodiphenylphosphine (18.4 ml, 102.6 mmol, 1.2 eq.). After addition of BH_3 in THF (1 M, 171.0 ml, 171.0 mmol, 2.0 eq.) the reaction was quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE.

The combined organic layers were washed with 250 ml. saturated NaCl-solution. The crude product (41b) was dissolved in THF (150 ml) and treated with *n*-BuLi (1.6 M 80 ml, 128 mmol, 1.5 eq.) and quenched with 250 ml water. Aqueous layer was extracted with 3x150 ml MTBE. The combined organic layers were washed with 250 ml. saturated NH_4Cl-solution. The crude product was purified by flash chromatography (CyHex:EtOAc 50:1) to afford (42a) (25.1 g, 82.0 mmol 96% over two steps) as a white solid.

$C_{19}H_{20}BOP$	M = 306.15 g/mol
R_f	0.3 (CyHex:EtOAc / 50:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.63 (s, 1H, OH), 7.55-7.40 (m, 10H, H_{Ar}), 7.27 (d, *J* = 7.2 Hz, 1H, H_{Ar}), 6.81-6.68 (m, 2H, H_{Ar}), 2.25 (s, 3H, CH_3).
^{13}C-NMR (APT)	(75 MHz, $CDCl_3$): δ [ppm] = 158.7 (d, *J* = 9.5 Hz, Cq), 135.0 (CH_{Ar}), 133.0 (d, *J* = 9.9 Hz, CH_{Ar}), 131.9 (d, *J* = 3.1 Hz, CH_{Ar}), 131.5 (d, *J* = 2.5 Hz, CH_{Ar}), 128.9 (d, *J* = 10.7 Hz, CH_{Ar}), 128.6 (Cq), 127.8 (Cq), 127.5 (d, *J* = 6.2 Hz, Cq), 120.2 (d, *J* = 8.4 Hz, CH_{Ar}), 110.9 (d, *J* = 58.7 Hz, Cq), 16.3 (CH_3).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 12.47 (d, *J* = 66.9 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3359 (s), 3054 (w), 2953 (w), 2924 (w), 2856 (w), 2374 (s), 1585 (m), 1481 (m), 1456 (s), 1434 (s), 1422 (s), 1378 (m), 1343 (m), 1222 (s), 1180 (s), 1149 (m), 1102 (s), 1063 (s), 1027 (m), 998 (m), 863 (m), 827 (m), 739 (s), 690 (s), 647 (m).
GC-MS, 70 eV	m/z (%) = 292 (100, $[M\text{-}BH_3]^+$), 213 (55), 199 (28), 183 (34), 165 (17), 152 (14), 107 (20), 77 (17), 51 (18).

3.5. SYNTHESIS OF CHIRAL PHOSPHINE-PHOSPHITE LIGANDS

3.5.1. General Procedure IV

A flame-dried Schlenk flask was put under argon and phoshine (42) (1.0 equiv.) and DABCO (8 equiv.) were dissolved in absolute CH_2Cl_2. The resulting solution was stirred for 10 min at RT, then cooled to 0^0C and a solution of PCl_3 in CH_2Cl_2 (1.2

equiv.) was added drop wise via syringe. The reaction mixture was stirred for 30 min at this temperature, warmed to RT and stirred for 3 h. The milky suspension was cooled to 0^0C and a solution of the chiral diol (44) (1,5 equiv.) in CH_2Cl_2 was added. After 30 min the resulting solution was allowed to warm to RT and stirring was continued for another 20 h. The solvent was evaporated to give the crude product, which was purified by flash chromatography to afford ligands (45) as white foams.

3.5.2. Synthesis of 7-(2,4-di-*tert*-butyl-6-diphenylphosphinophenoxy)-2,3-dimethoxy-2,3-dimethyl-5,5,9,9-tetraphenyl-hexahydro-[1,4]dioxino [2,3-e][1,3,2] dioxaphosphepine

According to *general procedure (IV)*, a solution of (42a) (2.02 g, 5.0 mmol, 1.0 eq.) was treated with DABCO (4.49 g, 40.0 mmol, 8 eq.) and PCl_3 (2M, 3.0 ml, 6.0 mmol, 1.2 eq.) in CH_2Cl_2 (25 ml) and TARTROL (38) (4.05 g, 7.5 mmol, 1.5 eq.) in CH_2Cl_2 (25 ml). The crude product was purified by flash chromatography (CyHex:DCM 4:1) to afford (45a) (2,97 g, 3.1 mmol, 62%) as white foam.

$C_{60}H_{64}O_7P_2$	M = 959.09 g/mol
R_f	0.4 (CyHex:DCM / 4:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.88 (s, 2H, H_{Ar}), 7.51 (d, *J* = 7.6 Hz, 2H, H_{Ar}), 7.33-7.04 (m, 21H, H_{Ar}), 6.94-6.79 (m, 6H, H_{Ar}), 6.70 (dd, *J* = 3.6 Hz, 2.6 Hz, 1H, H8), 4.86 (d, *J* = 10.8 Hz, 1H, H6), 4.75 (d, *J* = 10.8 Hz, 1H, H5), 2.60 (s, 3H, H3), 2.33 (s, 3H, H4), 1.20 (s, 9H, H9), 1.07 (s, 9H, H10), 1.06 (s, 3H, H2), 1.02 (s, 3H, H1).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 138.2 (d, *J* = 115.8 Hz, $P(OR)_3$), -15.7 (d, *J* = 106.8 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3054 (w), 2957 (m), 2868 (w), 2831 (w), 1583 (w), 1492 (m), 1476 (m), 1445 (s), 1432 (s), 1418 (s), 1391 (m), 1372 (s), 1361 (m), 1283 (w), 1258 (w), 1202 (s), 1128 (s), 1029 (s), 983 (s), 905 (s), 856 (s), 837 (s), 810 (s), 776 (s), 732 (s), 694 (s), 671 (s), 649 (s).

3.5.3. Synthesis of 7-(2-*tert*-butyl-6-diphenylphosphinophenoxy)-2,3-dimethoxy-2,3-dimethyl-5,5,9,9-tetraphenyl-hexahydro-[1,4]dioxino[2,3-e][1,3,2] dioxaphosphepine

According to *general procedure (IV)*, a solution of (42b) (1.74 g, 5.0 mmol, 1.0 eq.) was treated with DABCO (4.49 g, 40.0 mmol, 8 eq.) and PCl_3 (2M, 3.0 ml, 6.0 mmol, 1.2 eq.) in CH_2Cl_2 (25 ml) and TARTROL (38) (4.05 g, 7.5 mmol, 1.5 eq.) in CH_2Cl_2 (25 ml). The crude product was purified by flash chromatography (CyHex:DCM 4:1) to afford (45b) (2,07 g, 2.3 mmol, 46%) as white foam.

$C_{56}H_{56}O_7P_2$	M = 902.99 g/mol
R_f	0.4 (CyHex:DCM / 4:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.87 (s, 2H, H_{Ar}), 7.53 (d, *J* = 7.8 Hz, 2H, H_{Ar}), 7.34-7.31 (m, 5H, H_{Ar}), 7.23-7.04 (m, 16H, H_{Ar}), 6.96-6.80 (m, 7H, H_{Ar}), 6.71 (ddd, *J* = 7.5 Hz, 3.0 Hz, 1.6 Hz, 1H, H_{Ar}), 4.86 (d, *J* = 10.8 Hz, 1H, CH), 4.75 (d, *J* = 10.8 Hz, 1H, CH), 2.61 (s, 3H, OCH_3), 2.33 (s, 3H, OCH_3), 1.21 (s, 9H, $((CH_3)_3)$, 1.06 (s, 3H, CH_3), 1.02 (s, 3H, CH_3).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 138.5 (d, *J* = 118.2 Hz, $P(OR)_3$), -16.5 (d, *J* = 118.2 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3054 (w), 2945 (w), 2829 (w), 1492 (w), 1445 (m), 1432 (m), 1400 (m), 1389 (m), 1372 (m), 1360 (w), 1204 (m), 1139 (s), 1128 (s), 1029 (s), 1013 (s), 981 (s), 924 (m), 904 (m), 839 (s), 814 (s), 747 (s), 695 (s), 666 (m), 650 (m).

3.5.4. Synthesis of 7-(3-diphenylphosphino-(1,1-biphenyl-2yl)oxy)-2,3-dimethoxy-2,3-dimethyl-5,5,9,9-tetraphenyl-hexahydro-[1,4]dioxino [2,3-e][1,3,2] dioxaphosphepine

According to *general procedure (IV)*, a solution of (42c) (1.84 g, 5.0 mmol, 1.0 eq.) was treated with DABCO (4.49 g, 40.0 mmol, 8 eq.) and PCl_3 (2M, 3.0 ml, 6.0 mmol, 1.2 eq.) in CH_2Cl_2 (25 ml) and TARTROL (38) (4.05 g, 7.5 mmol, 1.5 eq.) in

CH_2Cl_2 (25 ml). The crude product was purified by flash chromatography (CyHex:DCM 4:1) to afford (45c) (2,44 g, 2.64 mmol, 53%) as white foam.

$C_{58}H_{52}O_7P_2$	M = 922.98 g/mol
R_f	0.3 (CyHex:DCM / 2:1)
^{1}H-NMR	(600 MHz, $CDCl_3$): δ [ppm] = 7.70 (d, *J* = 7.1 Hz, 2H, H_{Ar}), 7.52 (d, *J* = 7.6 Hz, 2H, H_{Ar}), 7.30-7.28 (m, 4H, H_{Ar}), 7.25-7.19 (m, 8H, H_{Ar}), 7.17-7.12 (m, 9H, H_{Ar}), 7.07-7.04 (m, 6H, H_{Ar}), 7.02-6.97 (m, 2H, H_{Ar}), 6.89 (t, *J* = 7.7 Hz, 2H, H_{Ar}), 6.77 (ddd, *J* = 7.6 Hz, 3.3 Hz, 1.7 Hz, 1H, H_{Ar}), 6.29 (d, *J* = 7.3 Hz, 2H, H_{Ar}), 4.64 (d, *J* = 10.7 Hz, 1H, CH), 4.49 (d, *J* = 10.7 Hz, 1H, CH), 2.50 (s, 3H, OCH_3), 2.30 (s, 3H, OCH_3), 1.03 (s, 3H, CH_3), 1.02 (s, 3H, CH_3).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 137.1 (d, *J* = 106.4 Hz, $P(OR)_3$), -15.9 (d, *J* = 106.4 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3053 (w), 2945 (w), 2830 (w), 1599 (w), 1581 (w), 1492 (m), 1445 (s), 1432 (m), 1402 (s), 1372 (m), 1203 (m), 1127 (s), 1030 (s), 982 (s), 907 (s), 843 (s), 819 (s), 765 (s), 740 (s), 696 (s), 671 (s).

3.5.5. Synthesis of 7-(2-diphenylphosphino-4,6-di-*tert*-pentylphenoxy)-2,3-dimethoxy-2,3-dimethyl-5,5,9,9-tetraphenyl-hexahydro-[1,4]dioxino [2,3-e][1,3,2] dioxaphosphepine

According to *general procedure (IV),* a solution of (42d) (1.97 g, 4.56 mmol, 1.0 eq.) was treated with DABCO (4.09 g, 36.48 mmol, 8 eq.) and PCl_3 (2M, 2.8 ml, 5.47 mmol, 1.2 eq.) in CH_2Cl_2 (30 ml) and TARTROL (38) (3.70 g, 6.84 mmol, 1.5 eq.) in CH_2Cl_2 (30 ml). The crude product was purified by flash chromatography (CyHex:DCM 5:1) to afford (45d) (2,26 g, 2.29 mmol, 50%) as white foam.

$C_{62}H_{68}O_7P_2$	M = 987.15 g/mol
R_f	0.6 (CyHex:DCM / 2:1)

^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.91 (s, 2H, H_{Ar}), 7.59 (d, *J* = 7.6 Hz, 2H, H_{Ar}), 7.35-6.98 (m, 23H, H_{Ar}), 6.92 (t, *J* = 7.2 Hz, 2H, H_{Ar}), 6.80 (t, *J* = 7.4 Hz, 2H, H_{Ar}), 6.61 (s, 1H, H_{Ar}), 4.84 (d, *J* = 11.5 Hz, 1H, CH), 4.80 (d, *J* = 11.6 Hz, 1H, CH), 2.70 (s, 3H, OCH_3), 2.37 (s, 3H, OCH_3), 1.86-1.63 (m, 2H, CH_2), 1.42-1.40 (m, 2H, CH_2), 1.25 (s, 6H, $(CH_3)_2$), 1.10 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 0.58 (t, *J* = 7.2 Hz, 3H, $CH_2C\mathit{H}_3$), 0.51 (t, *J* = 7.1 Hz, 3H, $CH_2C\mathit{H}_3$).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 140.0 (d, *J* = 109.4 Hz, $P(OR)_3$), -15.0 (d, *J* = 109.3 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3054 (w), 2958 (m), 2872 (w), 2831 (w), 1583 (w), 1492 (m), 1445 (s), 1432 (s), 1419 (s), 1373 (s), 1360 (w), 1297 (w), 1263 (w), 1204 (s), 1128 (s), 1030 (s), 989 (s), 924 (s), 905 (s), 834 (s), 810 (s), 783 (s), 770 (m), 739 (s), 695 (s), 671 (s), 649 (s), 616 (w).

3.5.6. Synthesis of 7-(2-diphenylphosphino-6-*tert*-pentylphenoxy)-2,3-dimethoxy-2,3-dimethyl-5,5,9,9-tetraphenyl-hexahydro-[1,4]dioxino [2,3-e][1,3,2] dioxaphosphepine

According to *general procedure (IV),* a solution of (42e) (1.24 g, 3.43 mmol, 1.0 eq.) was treated with DABCO (3.08 g, 27.44 mmol, 8 eq.) and PCl_3 (2M, 3.0 ml, 6.0 mmol, 1.2 eq.) in CH_2Cl_2 (30 ml) and TARTROL (38) (2.78 g, 5.14 mmol, 1.5 eq.) in CH_2Cl_2 (30 ml). The crude product was purified by flash chromatography (CyHex:DCM 4:1) to afford (45e) (1,66 g, 1.8 mmol, 53%) as white foam.

$C_{57}H_{58}O_7P_2$	M = 917.01 g/mol
R_f	0.45 (CyHex:DCM / 4:1)

^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.87 (s, 2H, H_{Ar}), 7.54 (d, *J* = 7.4 Hz, 2H, H_{Ar}), 7.31-6.98 (m, 23H, H_{Ar}), 6.88 (t, *J* = 6.7 Hz, 3H, H_{Ar}), 6.76 (t, *J* = 7.1 Hz, 2H, H_{Ar}), 6.65 (d, *J* = 6.6 Hz, 1H, H_{Ar}), 4.79 (d, *J* = 11.9 Hz, 1H, CH), 4.76 (d, *J* = 11.7 Hz, 1H, CH), 2.67 (s, 3H, OCH_3), 2.32 (s, 3H, OCH_3), 1.64-1.57 (m, 2H, CH_2), 1.20 (s, 6H, $(CH_3)_2$), 1.06 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 0.47 (t, *J* = 7.0 Hz, 3H, $CH_2C\mathit{H}_3$).
^{31}P-NMR {^{1}H}	(121 MHz, $CDCl_3$): δ [ppm] = 140.4 (d, *J* = 111.2 Hz, $P(OR)_3$), -15.5 (d, *J* = 111.2 Hz, PR_3).
FT-IR (ATR)	$\tilde{\nu}$ [cm^{-1}] = 3053 (w), 2953 (m), 2872 (w), 2830 (w), 1583 (w), 1492 (m), 1445 (s), 1432 (s), 1400 (s), 1373 (s), 1301 (w), 1264 (w), 1203 (s), 1140 (s), 1128 (s), 1030 (s), 1014 (s), 989 (m), 924 (m), 905 (m), 837 (s), 811 (s), 739 (s), 717 (m), 696 (s), 671 (m).

3.5.7. Synthesis of 7-(2-diphenylphosphino-6-methylphenoxy)-2,3-dimethoxy-2,3-dimethyl-5,5,9,9-tetraphenyl-hexahydro-[1,4]dioxino[2,3-e][1,3,2] dioxaphosphepine

According to *general procedure (IV)*, a solution of (42f) (1.53 g, 5.0 mmol, 1.0 eq.) was treated with DABCO (4.49 g, 40.0 mmol, 8 eq.) and PCl_3 (2M, 3.0 ml, 6.0 mmol, 1.2 eq.) in CH_2Cl_2 (25 ml) and TARTROL (38) (4.05 g, 7.5 mmol, 1.5 eq.) in CH_2Cl_2 (25 ml). The crude product was purified by flash chromatography (CyHex:DCM 4:1) to afford (45f) (2,19 g, 2.54 mmol, 51%) as white foam.

$C_{53}H_{50}O_7P_2$	M = 860.91 g/mol
R_f	0.3 (CyHex:DCM / 4:1)
^{1}H-NMR	(300 MHz, $CDCl_3$): δ [ppm] = 7.85 (d, *J* = 8.0 Hz, 2H, H_{Ar}), 7.66 (t, *J* = 7.9 Hz, 3H, H_{Ar}), 7.48-7.39 (m, 2H, H_{Ar}), 7.33-7.26 (m, 7H, H_{Ar}), 7.19-7.16 (m, 6H, H_{Ar}), 7.12-6.99 (m, 11H, H_{Ar}), 6.85 (t, *J* = 7.5 Hz, 1H, H_{Ar}), 6.55 (ddd, *J* = 7.3 Hz, 3.0 Hz, 1.3 Hz, 1H, H_{Ar}), 4.75 (d, *J* = 10.9 Hz, 1H, CH), 4.70 (d, *J* = 10.9 Hz, 1H, CH), 2.67 (s, 3H, OCH_3), 2.33 (s, 3H, OCH_3), 2.14 (s, 3H, Ph-$C\mathit{H}_3$), 1.07 (s, 3H, CH_3), 1.00 (s, 3H, CH_3).

^{31}P-NMR (^{1}H} (121 MHz, $CDCl_3$): δ [ppm] = 139.3 (d, *J* = 69.4 Hz, $P(OR)_3$), -16.6 (d, *J* = 69.4 Hz, PR_3).

FT-IR (ATR) $\tilde{\nu}$ [cm^{-1}] = 3054 (w), 2945 (w), 2830 (w), 1583 (w), 1491 (m), 1445 (m), 1433 (m), 1408 (m), 1373 (m), 1255 (w), 1205 (m), 1176 (m), 1140 (s), 1128 (s), 1030 (s), 984 (m), 925 (m), 906 (s), 874 (m), 840 (s), 817 (m), 740 (s), 696 (s), 671 (m).

3.6. COPPER-CATALYZED ASYMMETRIC 1,4-ADDITION OF GRIGNARD REAGENTS TO CYCLOHEXENONE

3.6.1. General Procedure

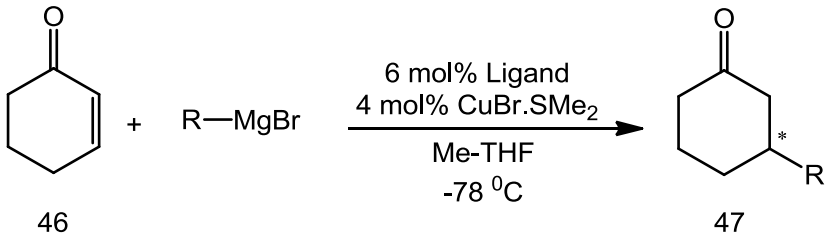


Figure 3.5. Copper-catalyzed asymmetric 1,4 addition of grignard reagent to cyclohexenone.

Under an argon atmosphere, CuBr.SMe_2 (0.04 equiv) and a chiral ligand (0.06 equiv) were dissolved in dry MeTHF and the resulting mixture was allowed tos tir for 15 min at room temperature. After the addition of the α,β-unsaturated carbonyl compound (46) (1.0 equiv) the mixture was stirred for another 30 min and then cooled to -78^{0}C. Then a diluted solution of the Grignard reagent (1.5 equiv, [RMgX] = 0.1-0.5 mol%) was slowly added by means of a syringe pump over a period of 2 h. The mixture was stirred for another 1 hour and then quenched by the addition of MeOH (2 ml) and a 1 M aqueous NH_4Cl solution (3ml). The layers were separated and the aqueous phase was extracted with *tert*-butylmethylether (MTBE). The combined organic layers were dried over $MgSO_4$, filtered through a short pad of silica and the solvent was evaporated under reduced pressure. The product was identified by GC-MS and Chiral-GC.

CHAPTER 4

RESULTS AND DISCUSSION

4.1. STRUCTURE OF TARTROL

TARTROLs compounds, as well as various derivates in which one or both of the OH groups is derivatized or replaced by another functional group. The OH groups are subject to the usual chemical reactions: ether formation, esterification, silylation and treatment with $ClPR_2$, Cl_2PR, Cl_3P or Cl_2SO, in the course of which bicylclic compounds may be produced.

It is useful that speak in a formal sense of a "TARTROL auxiliary system". The term "chiral auxiliary" could be understood in the broadest possible sense, that is as a way of describing a compound or a class or family of compounds with the aid of which it becomes possible to "introduce chirality". Such a material should be capable of creating a "chiral environment" not only around a specific reaction center, but also-through supramolecular interactions-in solution, within a liquid crystalline system, or in the solid state [24].

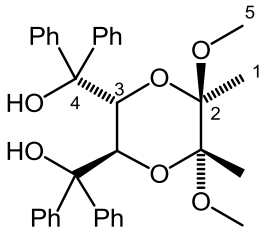


Figure 4.1. Structure of TARTROL molecule.

^{1}H-NMR Spectroskopy is presented to some information about the structure of TARTROL molecule. H1 peak (singlet) is seen at 0,99 ppm in the spectrum This mean that H1 hydrogens are not affected from any electronegative atom. The lenght

of the peak has depicted that, this molecule has contained six hydrogen atoms which belong to two overlapping CH_3 molecules.

H3 peak (singulett) is seen at 4.38 ppm in the spectrum. This mean that, H3 hydrogen is affected from electronegative molecules. Carbon atom bounded to H3 hydrogen is neigbour of an oxygen atom. In addition to, H3 hydrogen is affected from phenol molecules and OH molecule. These molecules are not neighbour of carbon atom bounded to H3 hydrogen. But all of these molecules affect to hydorgen of H3. Therefore H3 hydrgen are shown in low field region in the spectrum. The lenght of the peak has depicted that, this molecule has contained two hydrogen atoms which belong to two overlapping CH molecules.

H5 peak (singulett) is seen at 2.57 ppm in the spectrum. This mean that H5 hydrogen is affected from an electronegative molecule. Carbon atom bounded to H5 hydrogen is neigbour of an oxygen atom. The lenght of the peak has depicted that, this molecule has contained two hydrogen atoms which belong to two overlapping CH molecules.

OH peak (singulett) is seen at 4.33 ppm in the spectrum. The lenght of the peak has depicted that, this molecule has contained two hydrogen atoms which belong to two overlapping OH molecules.

Aromatic hydrogen peaks (multiplett) are seen at different areas in the spectrum. The reason of is that, different interactions with electronegative groups. Aromatic hydrogen peaks are calculated and it should be twenty hydrogen atoms in this molecule. When it is compared to the spectrum it is seen that, the number is correct.

FT-IR results demonstrate that, when the results of dimethyl ester and the results of TARTROL are compared, it is seen two differences. First of them is about at 1742 cm^{-1} peak in the spectrum. This peak mean that, the molecule has contained a ketone group. This pek is not seen in TARTROL spectrum. The second difference is about at 1200 cm^{-1} peak in the spectrum. This peak mean that, the molecule has contained an ester group. This peak is not seen in TARTROL spectrum. This peak converted to

another peak, at 3355 cm^{-1} peak which mean that the molecule has contained an OH group.

4.2. STRUCTURE OF BROMOPHENOL

Several methods for direct *ortho*-bromination and *ortho*-dibromination of phenols have been reported. It is founded that, treatment of phenols with bromine in the presence of a large excess of *t*-butyl amine at -70 ^{0}C gave 2-bromo- or 2,6-dibromophenols in good yields. The researchers demonstrate that, the reaction between phenol and *N*,*N*-dibromomethyl-amine efficiently affords 2,6-dibromophenol. But this reaction requires very low temperatures and using unstable brominating agent. *Ortho*-bromination reactions occured with the presence of *N*-bromosuccinimide (NBS) at the reflux temperature of solvent.

The *ortho*-bromination and *ortho*-dibromination of phenols are observed when secondary amines are added. Especially, diisopropylamine and dibutylamine depicted high *ortho*-selectivity. Even 0.1 molar amount of diisopropylamine is sufficiently effective for *ortho*-selectivity. From this result, it is understood that the amine worked catalytically in the selective *ortho*-bromination of phenol (Figure 4.2.).

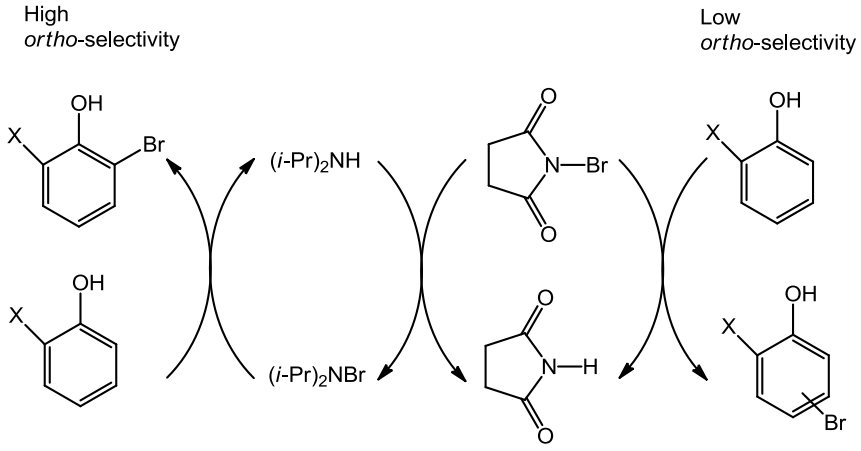


Figure 4.2. Reaction mechanism of *ortho*-bromination.

The mechanismm of *ortho*-bromination of phenol is considered that, *N*-bromoamines generated from the reaction between NBS and amines, then they from strong hydrogen bonding with phenols to cause bromination at one *ortho*-position of phenol and regeneration of the amines. Catalytic amount of the amines is sufficient because of the regeneration of the amines. The nucleophilicity of nitrogen atom of *N*-bromoamines is stronger than that of NBS. Therefore traces of *N*-bromoamines can react with phenols continuously.

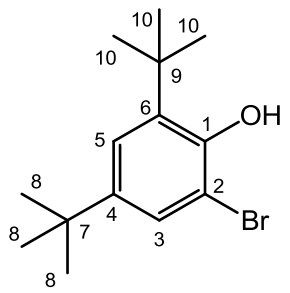


Figure 4.3. Structure of 2-bromo-4,6-di-*tert*-butylphenol molecule.

^{1}H-NMR Spectroskopy is presented to give some information about the structure of 2-bromo-4,6-di-*tert*-butylphenol molecule. H3 peak (dublett) is seen at 7.32 ppm in the spectrum. And H5 (dublett) peak is seen at 7.24 ppm in the spectrum. Both of the them are aromatic hydrogen atoms. They are affected from electronegative molecules differently. Therefore they are located in different places in the spectrum. H3 hydrogen is affected more from electronegative OH molecule than H5 hydrogen. Therefore, effect H3 peak is located in lower field region. The lenght of one peak has depicted that, this molecule has contained one hydrogen atom. And totally, this molecule has contained two aromatic hydrogen atoms.

H8 peak (singulett) is seen at 1.28 ppm in the spectrum. And H10 (singulett) peak is seen at 1.40 ppm in the spectrum. This mean that, these hydrogen atoms are affected by electronegative molecules. But this interaction is not directly. H10 hydrogen is affected more by electronegative OH molecule than H8 hydrogen but, this is indirect interaction. Therefore, effect H10 peak is located in lower field region. The lenght of one peak has depicted that, this molecule has contained nine hydrogen atoms which

belong to three overlapping CH_3 molecules. And totally, this molecule has conatined eighteen hydrogen atoms.

OH peak (singulett) is seen at 5.65 ppm in the spectrum. The lenght of peak has depicted that, this molecule has contained one hydrogen atom which belongs to one OH molecule.

4.3. STRUCTURE OF BORANE PROTECTED PHOSPHANYLPHENOL

Ortho-bromophenol is then converted into the borane-protected phosphinite by reaction with chlorodiphenylphosphine and with the presence of DABCO, and later with the addition of BH_3-THF. The boran-protected phosphities are under air atmosphere stable and in some cases they could be crystaline compounds. After that, borane-protected phosphinite is then converted into a borane-protected phosphanylphenol by treatment with *n*-BuLi. Addition of *n*-BuLi is so crucial at this step because of the two reasons.

The first reason is that, after the brominiation reaction with the NBS, always a side product which is dibromophenol is obtained. These broms are converted to lithiums with the presence of *n*-BuLi. During the work up these lithiums are converted to hydrogens.

The second reason is that, borane protected phosphinites are rearranged by *n*-BuLi. After this anionic fries-type process, borane protected phsophanyl phenols are obtained. (Figure 4.4.) [55].

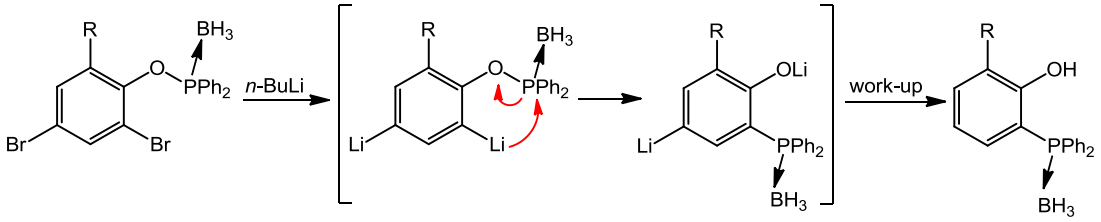


Figure 4.4. Rearrangement mechanism of borane protected phosphanylphenol.

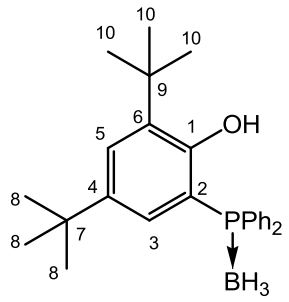


Figure 4.5. Structure of boranatodiphenylphosphanyl-4,6-di-*tert*-butyl-phenol.

^{1}H-NMR Spectroskopy is presented to give some information about the structure of Boranatodiphenylphosphanyl-4,6-di-*tert*-butyl-phenol. H5 peak (dublett) is seen at 6.66 ppm in the spectrum. This mean that, this is an aromatic hydrogen atom. But H5 molecule is affected from phosphorus molecule which is more electropositive than carbon molecule. Therefore, H5 molecule is located in higher field region. The lenght of peak has depicted that, this molecule has contained one hydrogen atom.
H8 peak (singulett) is seen at 1.11 ppm in the spectrum. And H10 (singulett) peak is seen at 1.41 ppm in the spectrum. This mean that, these hydrogen atoms are affected by electronegative molecules. But this interaction is not directly. H10 hydrogen is affected by more electronegative OH molecule than H8 hydrogen but, this is indirect interaction. Therefore effect H10 peak is located in lower field region. The lenght of one peak has depicted that, this molecule has contained nine hydrogen atoms which belong to three overlapping CH_3 molecules. And totally, this molecule has conatined eighteen hydrogen atoms.

H3, OH and aromatic hydrogen peaks are seen at 7.75-7.42 ppm. All of this peaks are calculated and there should be twelve hydrogen atoms in this molecule. When it is compared with the spectrum it is seen that, the number is correct.

^{31}P-NMR is another significant method to determine the structure. One peak is seen at 13.67 ppm in the spectroskopy. This mean that the molecule has contained one PR_3 molecule.

4.4. STRUCTURE OF PHOSPHİNE-PHOSPHİTE LİGAND

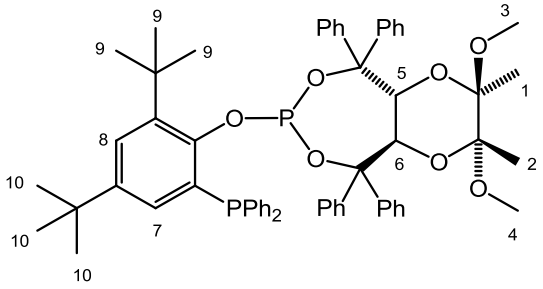


Figure 4.6. Structure of 7-(2,4-di-tert-butyl-6-diphenylphosphinophenoxy)-2,3-dimethoxy-2,3-dimethyl-5,5,9,9-tetraphenyl-hexahydro-[1,4]dioxino [2,3-e][1,3,2] dioxaphosphepine.

Modular nature of phosphine-phosphite ligands facilitated their optimization and and a gain in the understanding of many reactions. Additionally, in the other asymmetric transformations, phosphine-phosphite ligands are sometimes better ligands than more traditional bidentate or monodentate phosphorus compounds.

^{1}H-NMR Spectroskopy is presented to give some information about the structure of 7-(2,4-di-tert-butyl-6-diphenylphosphinophenoxy)-2,3-dimethoxy-2,3-dimethyl-5,5,9,9-tetraphenyl-hexahydro-[1,4]dioxino[2,3-e][1,3,2] dioxaphosphepine. H2 peak (singulett) is seen at 1.06 ppm in the spectrum, and H1 (singulett) peak is seen at 1.02 ppm in the spectrum. H1 molecule is affected from phosphorus molecule which is more electropositive than carbon molecule. But this interaction is not directly, this is an indirect interaction. Therefore H1 molecule is located in higher field region The lenght of the each peak has depicted that, this molecule has contained three hydrogen atoms.

H3 peak (singulett) is seen at 2.60 ppm in the spectrum, and H4 (singulett) peak is seen at 2.33 ppm in the spectrum. This mean that H3 and H4 hydrogens are affected by an electronegative molecule. Carbon atom bounded to H3 hydrogen and other carbon atom bounded to H4 hydrogen are neigbour of an oxygen atom. But H4 molecule is affected by phosphorus molecule which is more electropositive than carbon molecule. And this interaction is not directly, this is an indirect interaction.

Therefore H4 molecule is located in higher field region The lenght of the each peak has depicted that, this molecule has contained three hydrogen atoms.

H5 peak (dublett) is seen at 4.75 ppm in the spectrum, and H6 (dublett) peak is seen at 4.86 ppm in the spectrum. This mean that H5 and H6 hydrogens are affected by an electronegative molecule. Carbon atom bounded to H5 hydrogen and other carbon atom bounded to H6 hydrogen are neigbour of an oxygen atom. H5 hydrogen and H6 hydrogen are affected by both phenol molecules and OH molecule. These effects are make a contribution to be located in low field region. But on the other hand H5 molecule is affected from phosphorus molecule which is more electropositive than carbon molecule. And this is an indirect interaction. Therefore H5 molecule is located in higher field region The lenght of the each peak has depicted that, this molecule has contained one hydrogen atom.

H8 peak (dublett) is seen at 6.70 ppm in the spectrum. This mean that, this is an aromatic hydrogen atom. But H8 molecule is affected by phosphorus molecule which is more electropositive than carbon molecule Therefore H6 molecule is located in higher field region. The lenght of the peak confirmed that, this molecule has contained one hydrogen atom.

This ligand molecule has contained thirty two different aromatic hydrogens. And these hydrogens are affected by electro negative oxygen and phenyl groups on the other side electropositive phosphorus molecules. Some of them has so weak effects Therefore some structures can not be determined profoundly. When NMR spectrum of this ligand is compared with the designed ligand it is seen that this which molecule is obtained.

In the ^{31}P-NMR results, two different peaks are seen. First peak is seen at 15.7 ppm in the spectrum. This mean that, the molecule has contained one PR_3 molecule, and the second peak is seen at 138.2 ppm in the spectrum. This mean that, the molecule has contained one PO_3 molecule.

FT-IR results demonstrate that, when the results of TARTROL and the results of ligand are compared, a peak which is at 3355 cm^{-1} is not seen in the ligand spectrum. This mean that , the molecule has not contained any OH groups.

4.5. CU-CATALYZED 1,4-ADDITON TO CYCLOHEXANONE

Conjugate additions of carbon nucleophiles to α,β-unsaturated carbonyl compounds one of the most valuable methods for carbon-carbon bond formation in organic synthesis. Because a new chirality center could be formed during the reaction. Cu catalyzed addition of organometallic reagents to cyclic enones is a cornerstone reaction in the development of new efficient catalyst systems.

The results of the addition of EtMgBr to cyclohexenone in the presence of (45) ligands are summarized in Table 4.1.

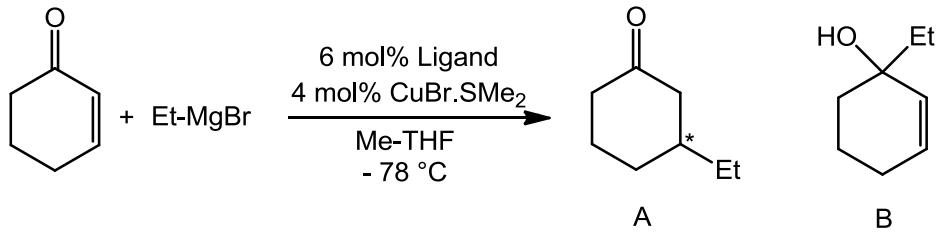


Figure 4.7. Addition of EtMgBr to cyclohexenone.

Table 4.1. Result of (45) ligands screening in the addition of EtMgBr to cyclohexenone.

Ligand	*Yield*	*A : B*	*ee*
45a	61	85:15	84
45b	63	84:16	78
45c	80	92:08	30
45d	48	78:22	77
45e	57	82:18	60
45f	52	83:17	76

According to results, 1,4-addition products were obtained with high regioselectivities. The minor 1,2-addition products were always formed as racemic mixture, and 1,4-addition products were obtained with the high enantioselectivities, except in the presence of (45c) ligand. The best result with respectively both enantioselectivity and conversion was obtained with the (45a) ligand. Under the optimized conditions (A) product was synthesized, and this product was isolated after the seperation of by product rac-(B) by careful flash chromatography with 61% yield.

The results of the addition of PhMgBr to cyclohexenone in the presence of 45 ligands are summarized in Table 4.2.

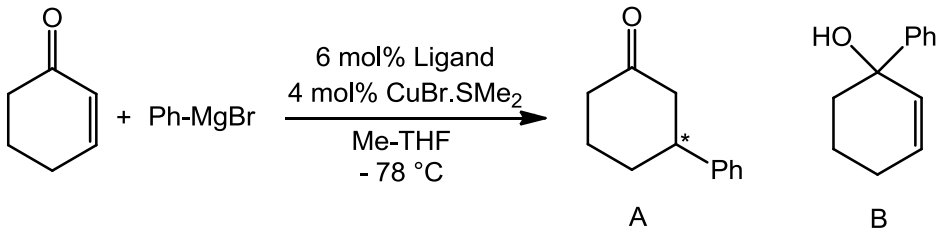


Figure 4.8. Addition PhMgBr to cyclohexenone.

Table 4.2. Result of (45) ligands screening in the addition of EtMgBr to cyclohexenone.

Ligand	*Yield*	*A : B*	*ee*
45a	73	86:14	14
45b	68	86:14	4
45c	78	92:08	4
45d	75	89:11	10
45e	82	90:10	8
45f	46	67:33	10

According to results, 1,4-addition products were obtained with high regioselectivities. The minor 1,2-addition products were always formed as racemic mixture. But 1,4-addition products were obtained with the absolutely low enantioselectivity results. The best result with respectively both enantioselectivity and conversion was obtained with the (45a) ligand. Under the optimized conditions, (A) product was synthesized, and this product was isolated after the seperation of by product rac-(B) by careful flash chromatography with 73% yield.

4.6. MECHANISM OF THE CU-CATALYZED 1,4-ADDITION OF GRIGNARD REAGENTS

The structure of chiral ligands and transtion metals are so importanat for asymmetric catalysis. The key step in metal-catalyzed asymmetric reaction is the formation of a new species around the metalic center which involves the substrate, the reagents, and a ligand usually bound to the metal center through one or more functional groups. The ligand modulates the reactivity of the metal and also creates an asymmetric enviroment around the metal center.

The mechanism of the conjugate addition reaction of organocopper reagents has been the subject of debates for a long time. During the last decades, a wide variety of conjugate addition reactions were performed successfully and good results were obtained using organometallic compounds. Although there is structural and mechanistic information on organocuprate chemistry, relatively few studies have been performed on catalytic asymmetric transformations. Woodward et al. proposed the Cu-catalyzed enantioselective conjugate addition of organometallic compounds may follow a similar path as the noncatalytic organocuprate addition. On the basis of previous mechanistic studies by Woodward et al. a possible reaction mechanism is outlined in Figure 4.7. [56].

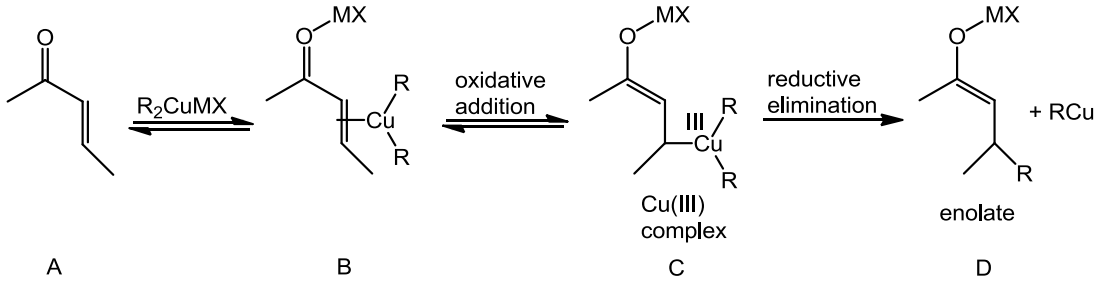


Figure 4.9. Propesed mechanism for 1,4-cuprate addition of enones.

4.7. SOLVENT EFFECT IN THE CU-CATALYZED 1,4-ADDDITION

The optimization of the asymmetric conjugate addition reactions depend on various parameters. The most important one is the effect of solvent and nature of the copper salts. Alexakis et al. [53] described that using stronger coordinating solvents such as THF and EtOAc is resulted high levels of enantioselectivity in the Cu-catalyzed $Cu(OTf)_2$ conjugate addition of ET_2Zn to cyclohexanone. On the other hand, when compared, these solvents (THF and EtOAc reaction time 5h) with toluene or dichlorometane, the reaction time is longer approximately 2h. Schmalz's group reported that the first Cu-catalyzed 1,4-addition of Grignard reagents to different α,β-unsaturated carbonyl compounds using chiral phospine-phosphite ligands [55]. According to this report, in the presence of Me-THF in combination with $CuBr.SMe_2$ gived the highest ee. As a consequence, THF, EtOAc and Me-THF are appropiote solvent, for the Cu-catalyzed 1,4-addition of Grignard reagents.

CHAPTER 5

CONCLUSION AND OUTLOOK

In this work, TARTROL-derived phoshine-phosphite ligands are synthesized with 50-70% yield. These ligands structures are identified with ^{1}H, ^{13}C, ^{31}P NMR and FT-IR spectroskopies. These ligands are performed to Cu-catalyzed 1,4-addition of EtMgBr and PhMgBr to cyclohexenone. The best result for the 1,4-addition of EtMgBr to cyclohexenone was obtained with the presence of (45a) ligand (84% ee). Also, the best result for the 1,4-addition of PhMgBr to cyclohexenone was obtained with the presence of (45a) ligand (14% ee).

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APPENDIX

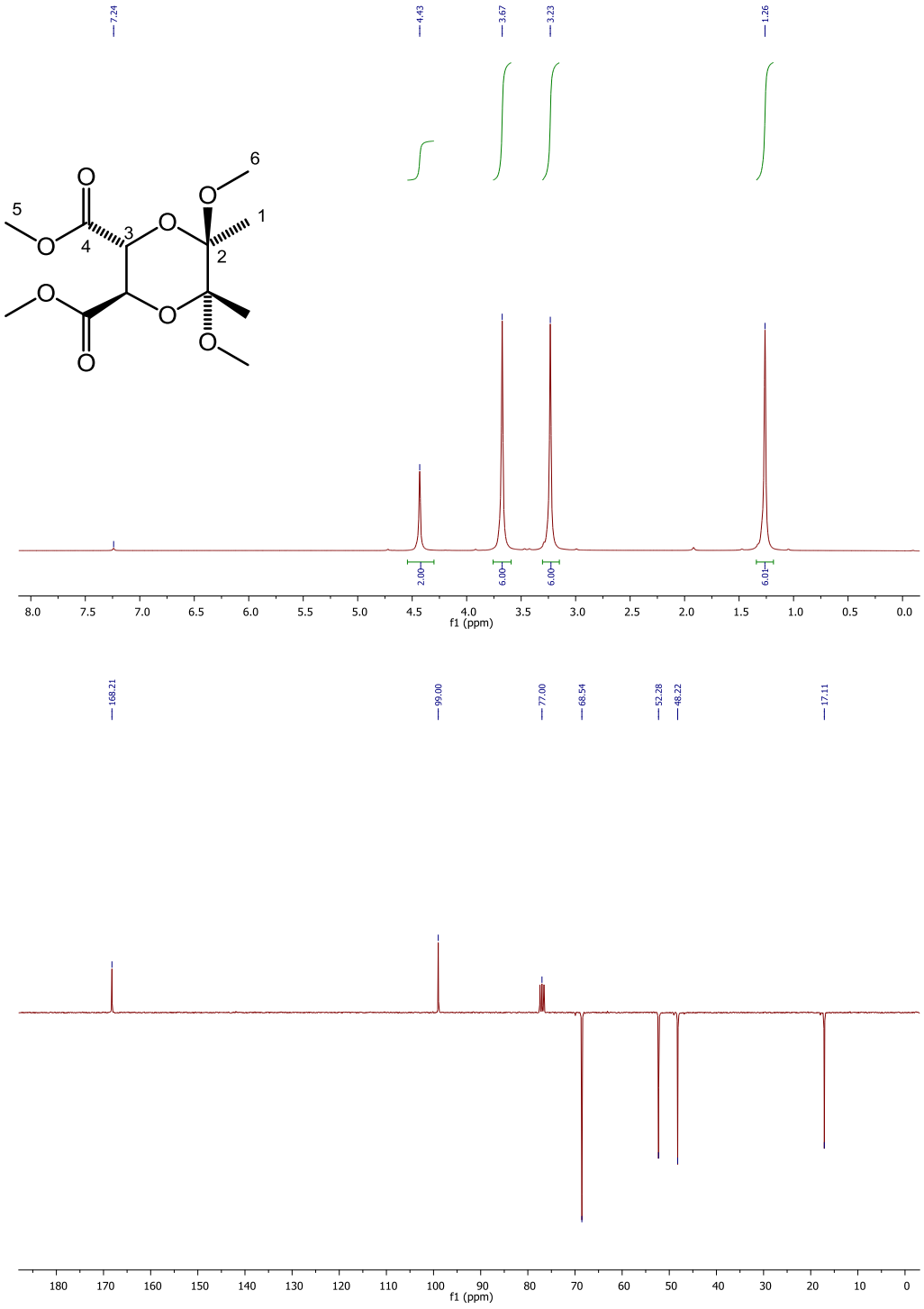

Figure 5.1. ^{1}H-NMR and ^{13}C-NMR of Molecule 37

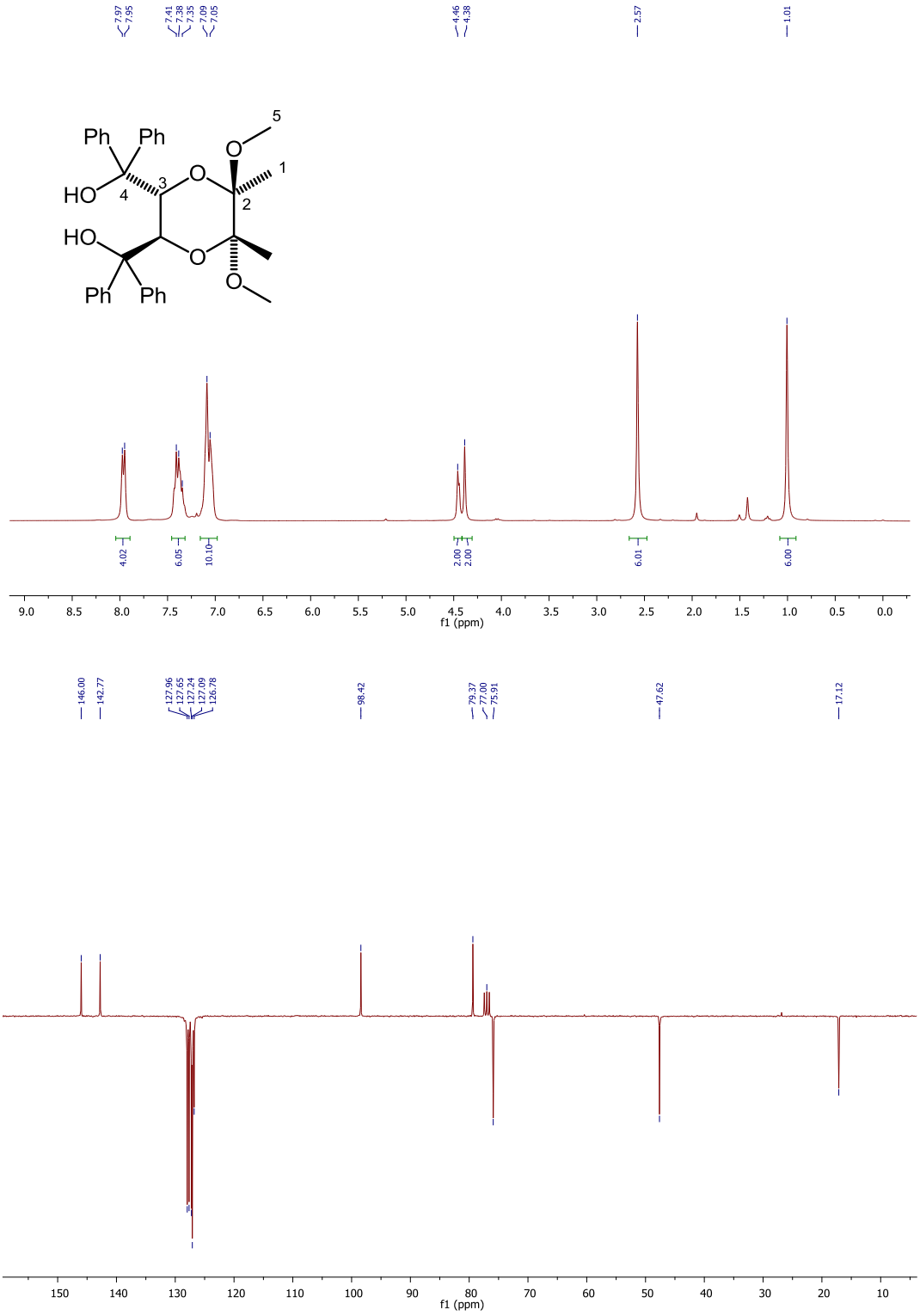

Figure 5.2. ^{1}H-NMR and ^{13}C-NMR of Molecule 38

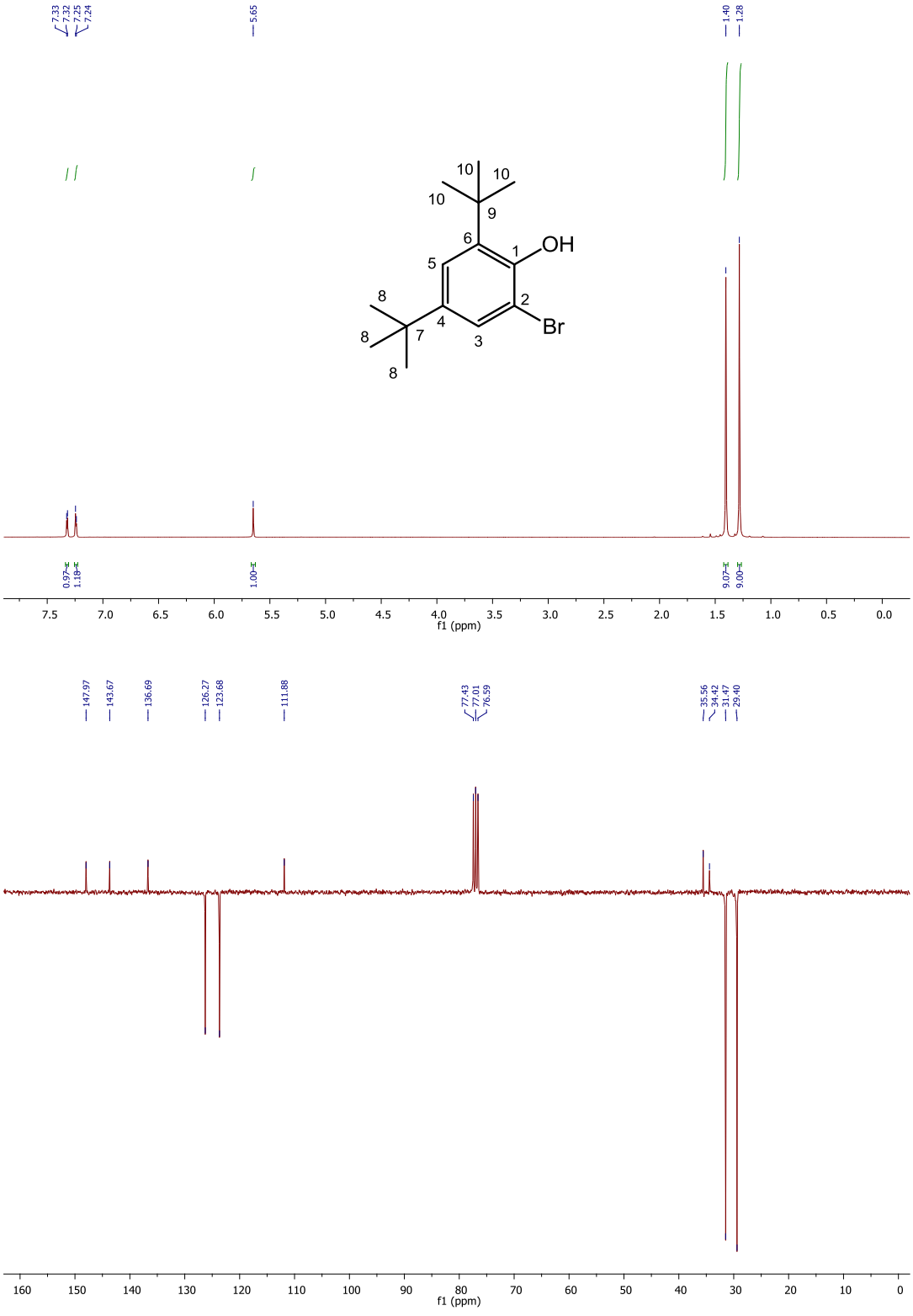

Figure 5.3. ^{1}H-NMR and ^{13}C-NMR of Molecule 40a

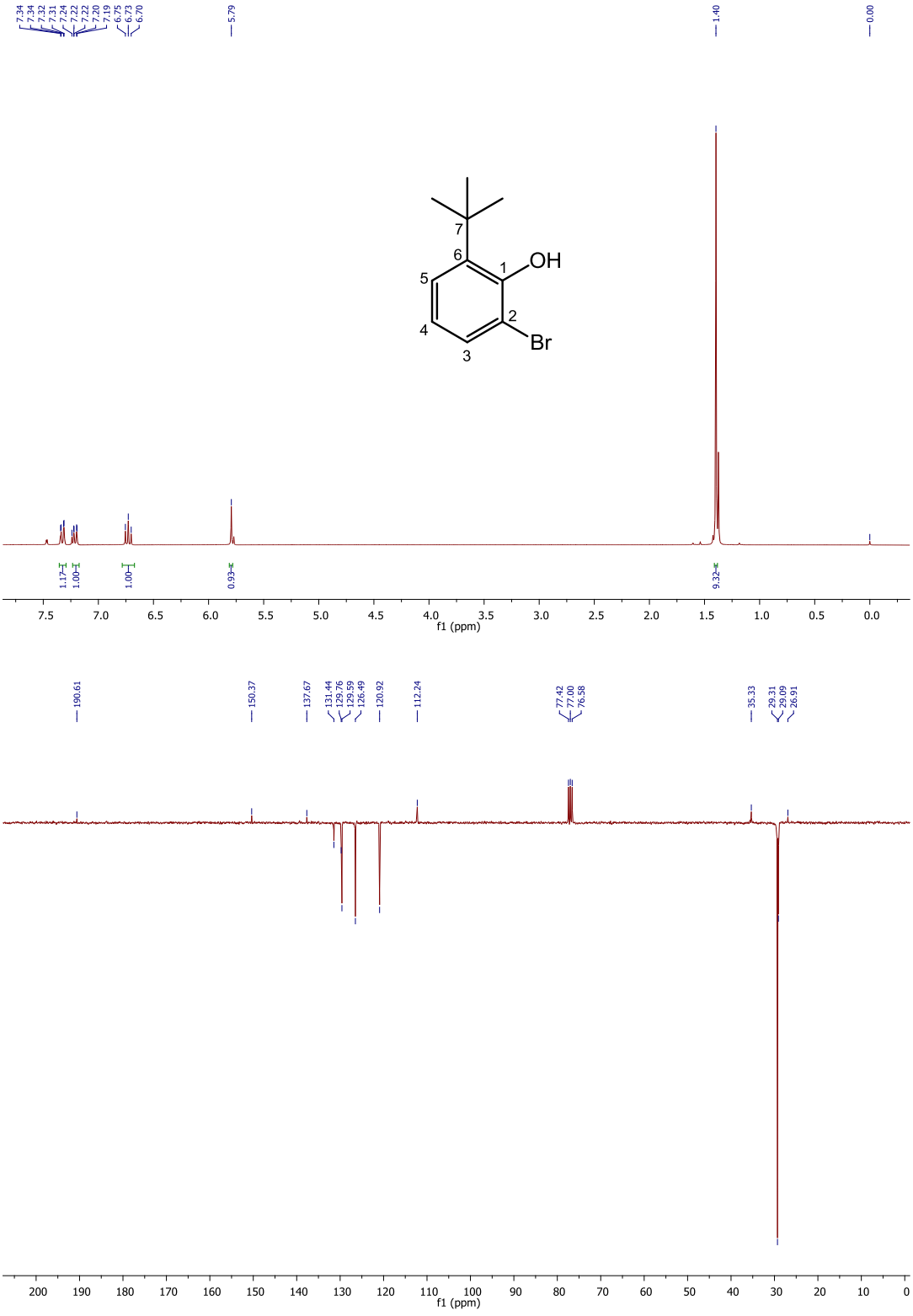

Figure 5.4. ^{1}H-NMR and ^{13}C-NMR of Molecule 40b

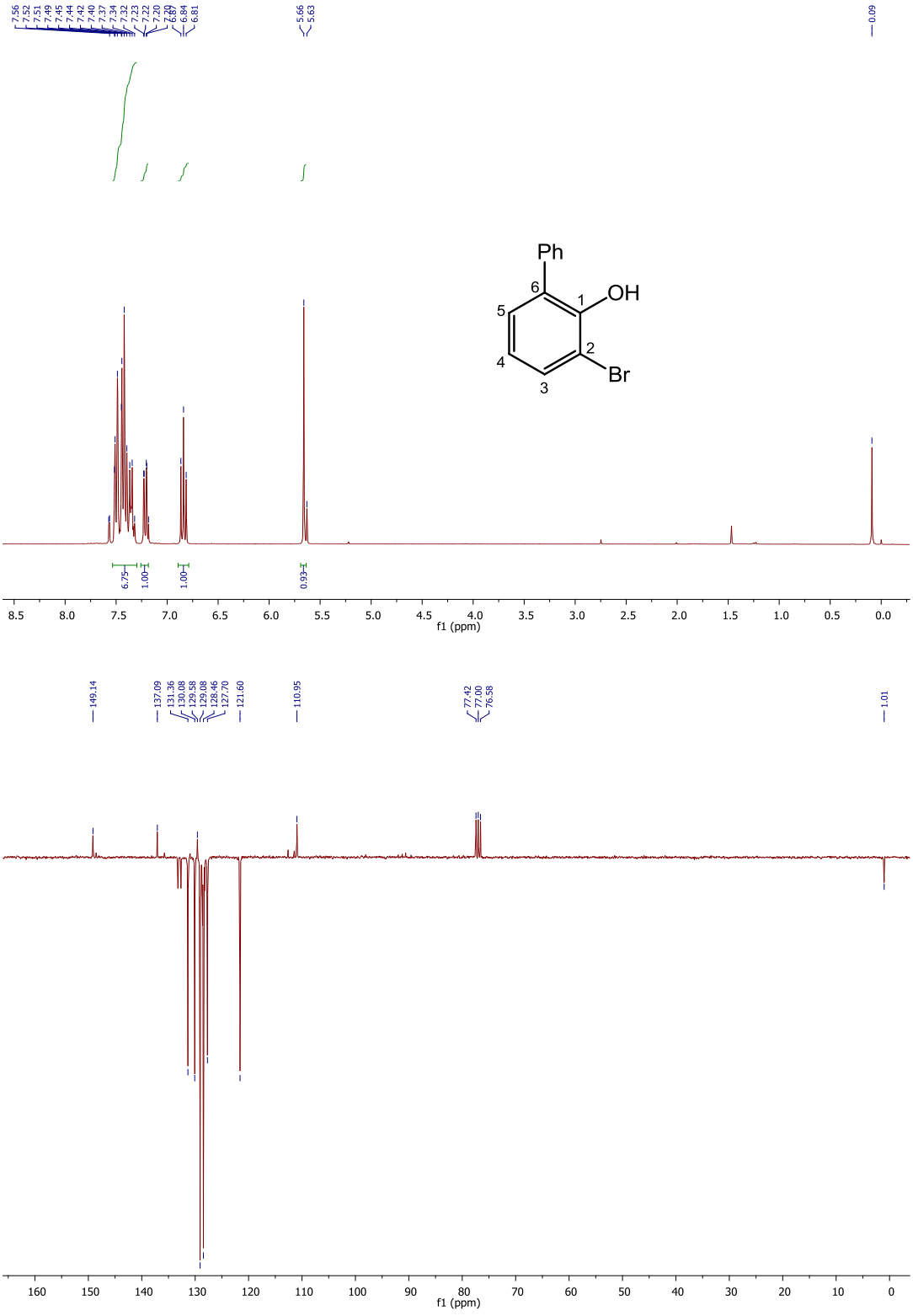

Figure 5.5. ^{1}H-NMR and ^{13}C-NMR of Molecule 40c

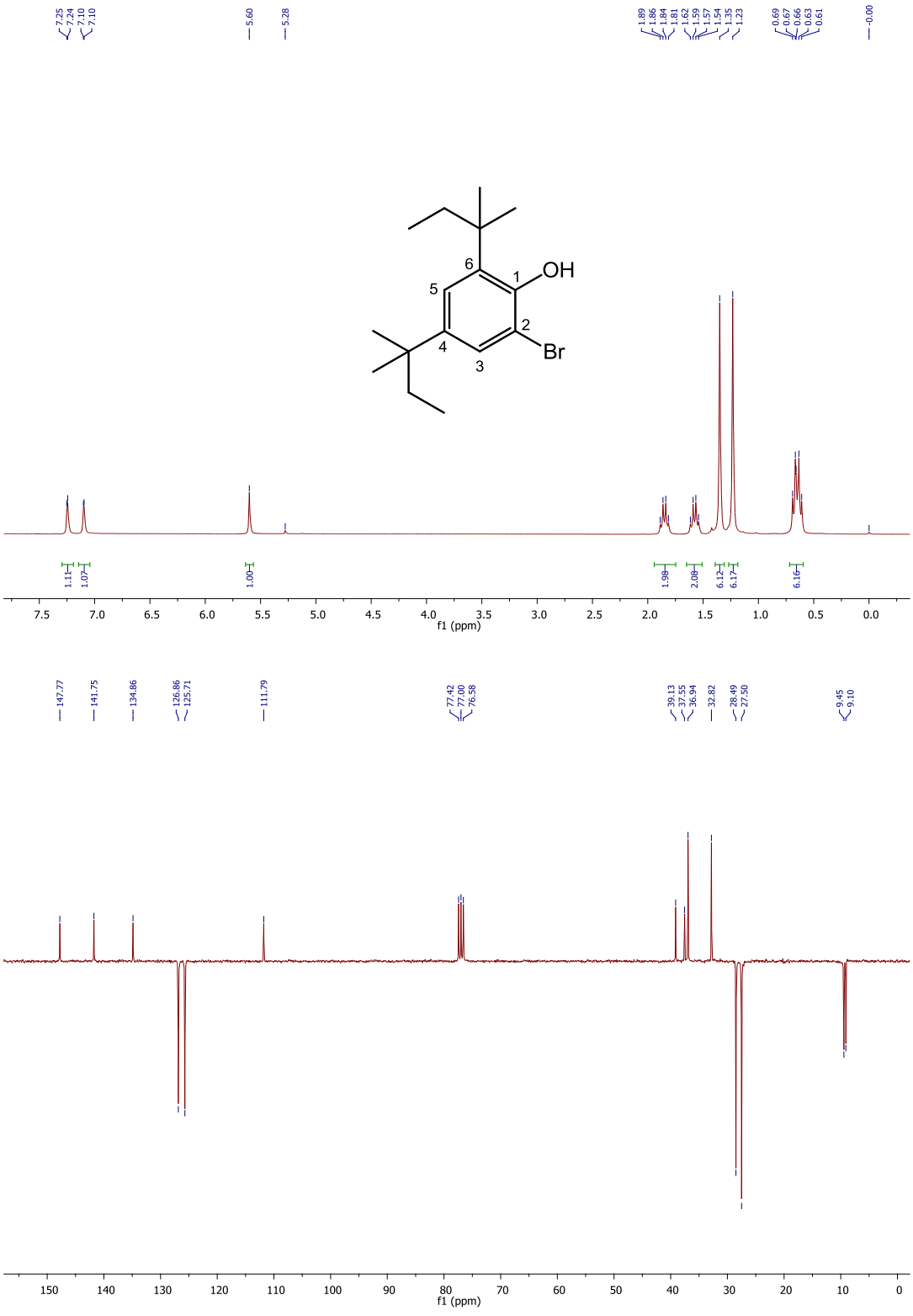

Figure 5.6. ^{1}H-NMR and ^{13}C-NMR of Molecule 40d

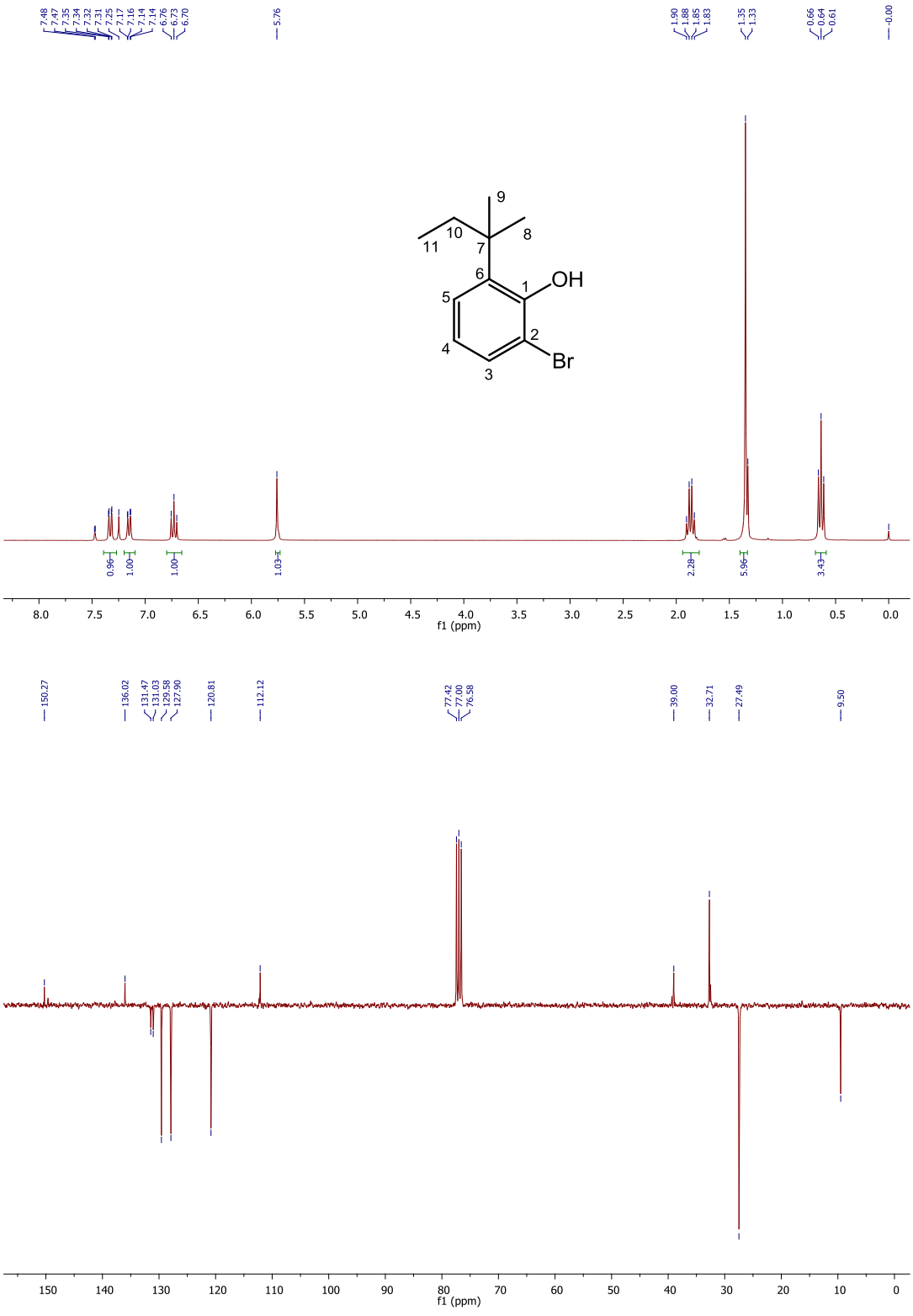

Figure 5.7. ^{1}H-NMR and ^{13}C-NMR of Molecule 40e

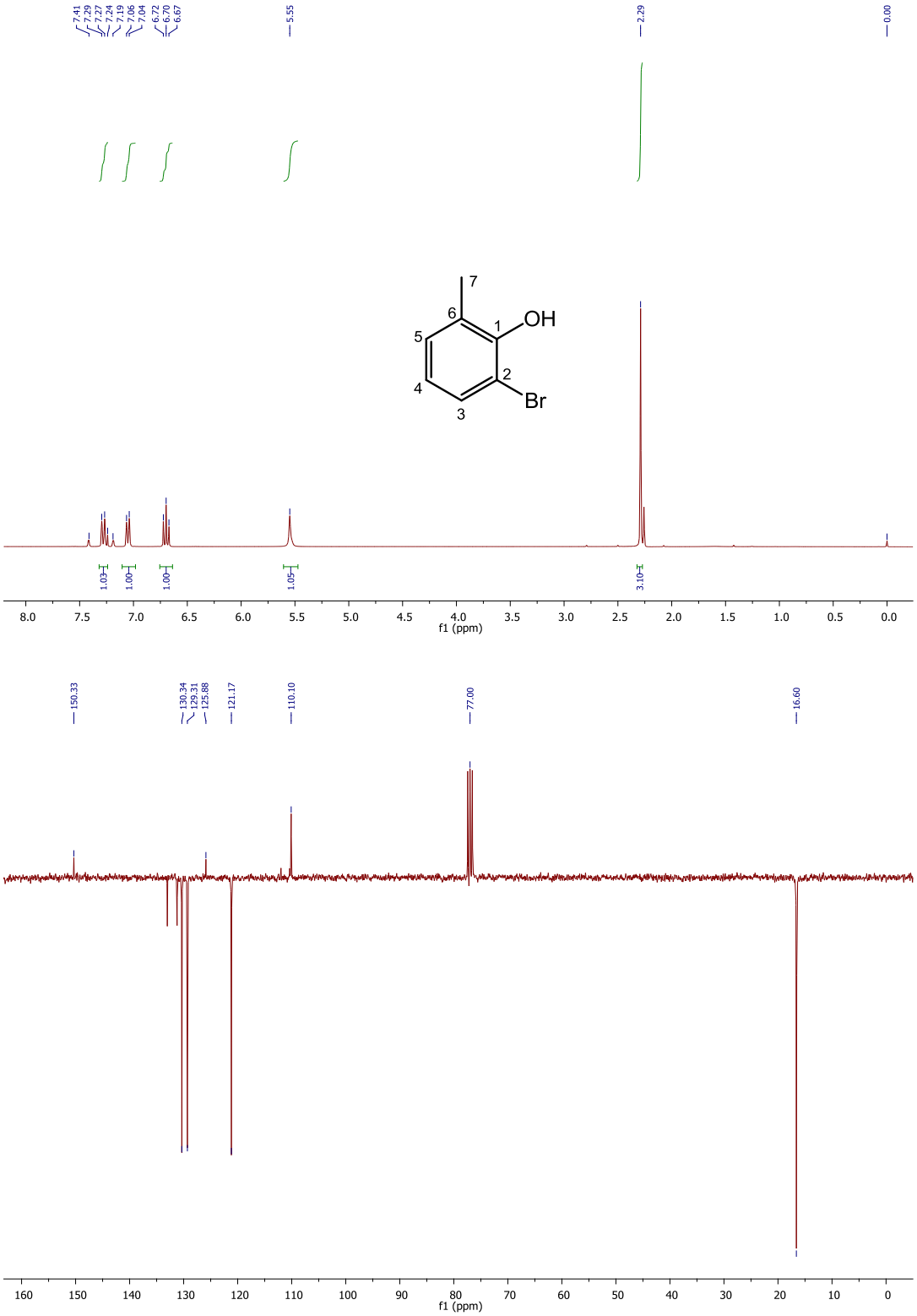

Figure 5.8. ^{1}H-NMR and ^{13}C-NMR of Molecule 40f

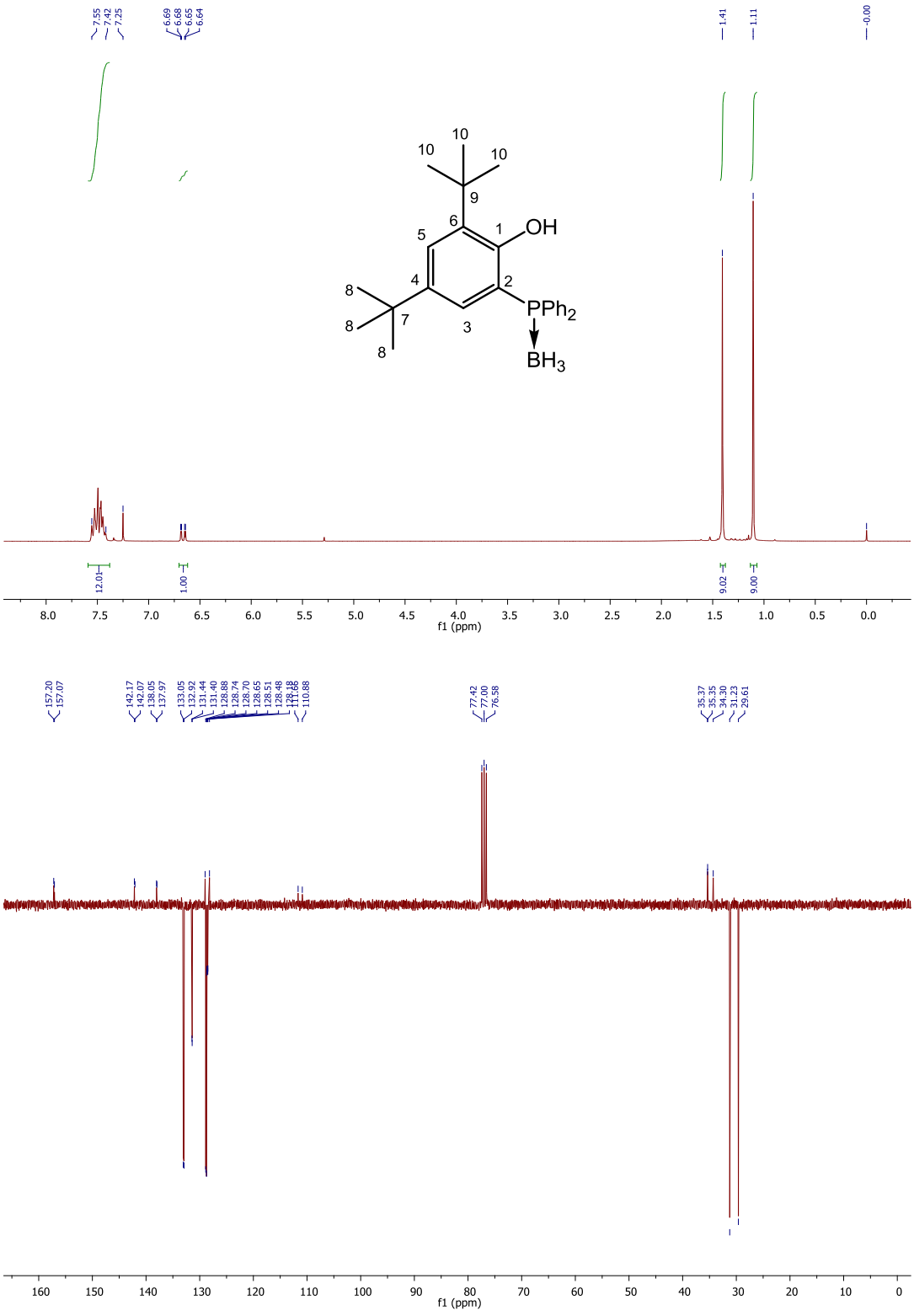

Figure 5.9. ^{1}H-NMR and ^{13}C-NMR of Molecule 42a

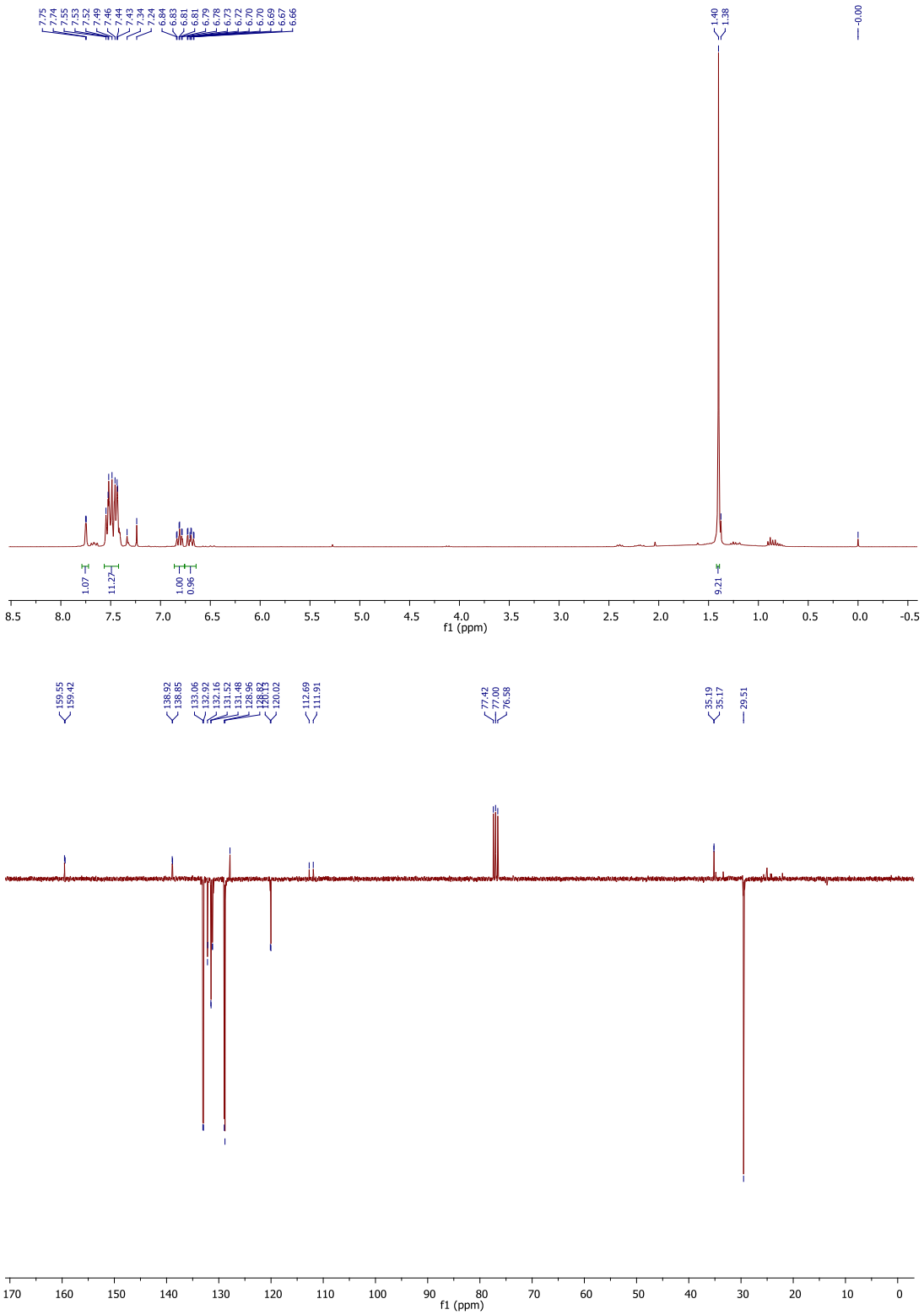

Figure 5.10. ^{1}H-NMR and ^{13}C-NMR of Molecule 42b

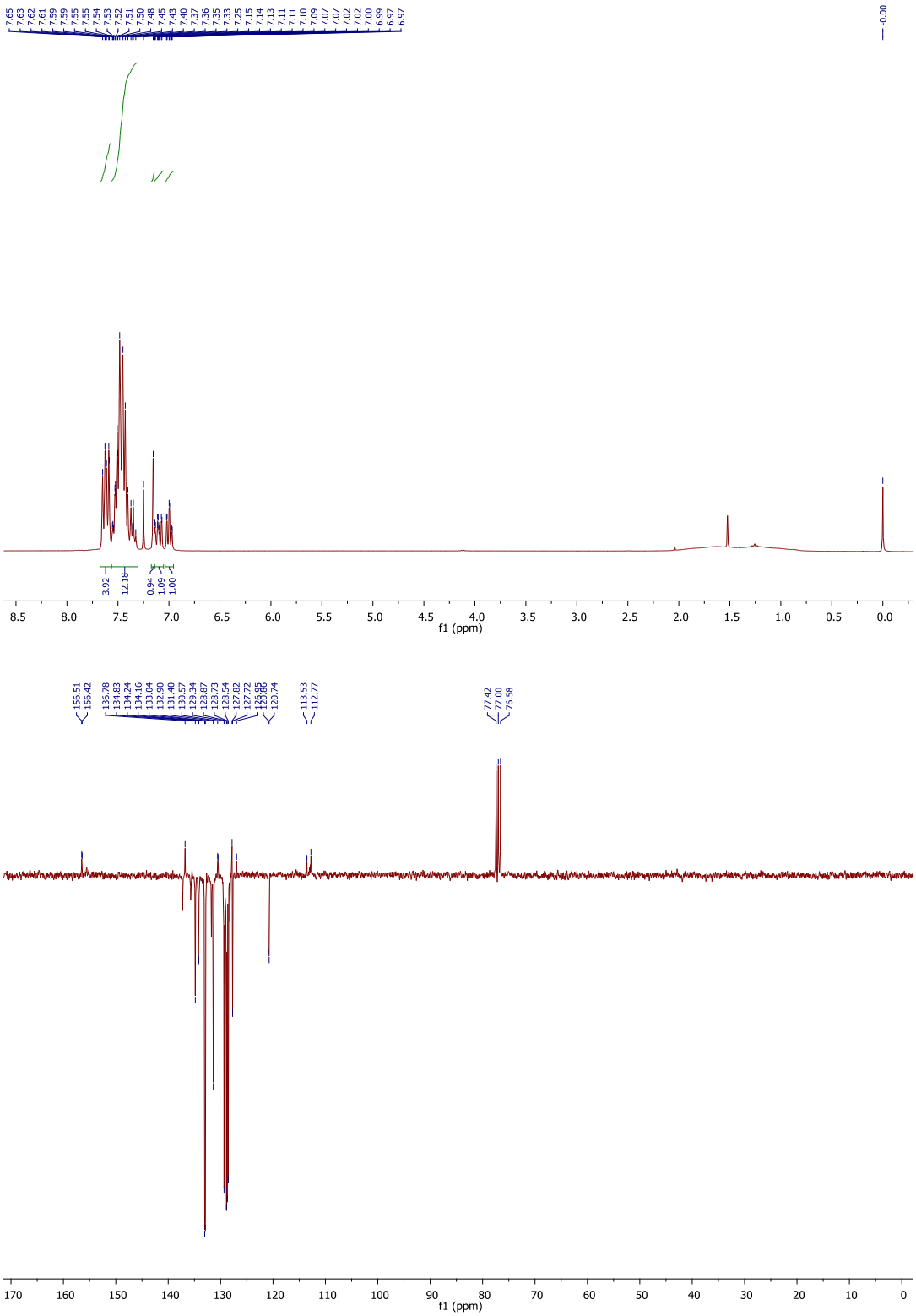

Figure 5.11. ^{1}H-NMR and ^{13}C-NMR of Molecule 42c

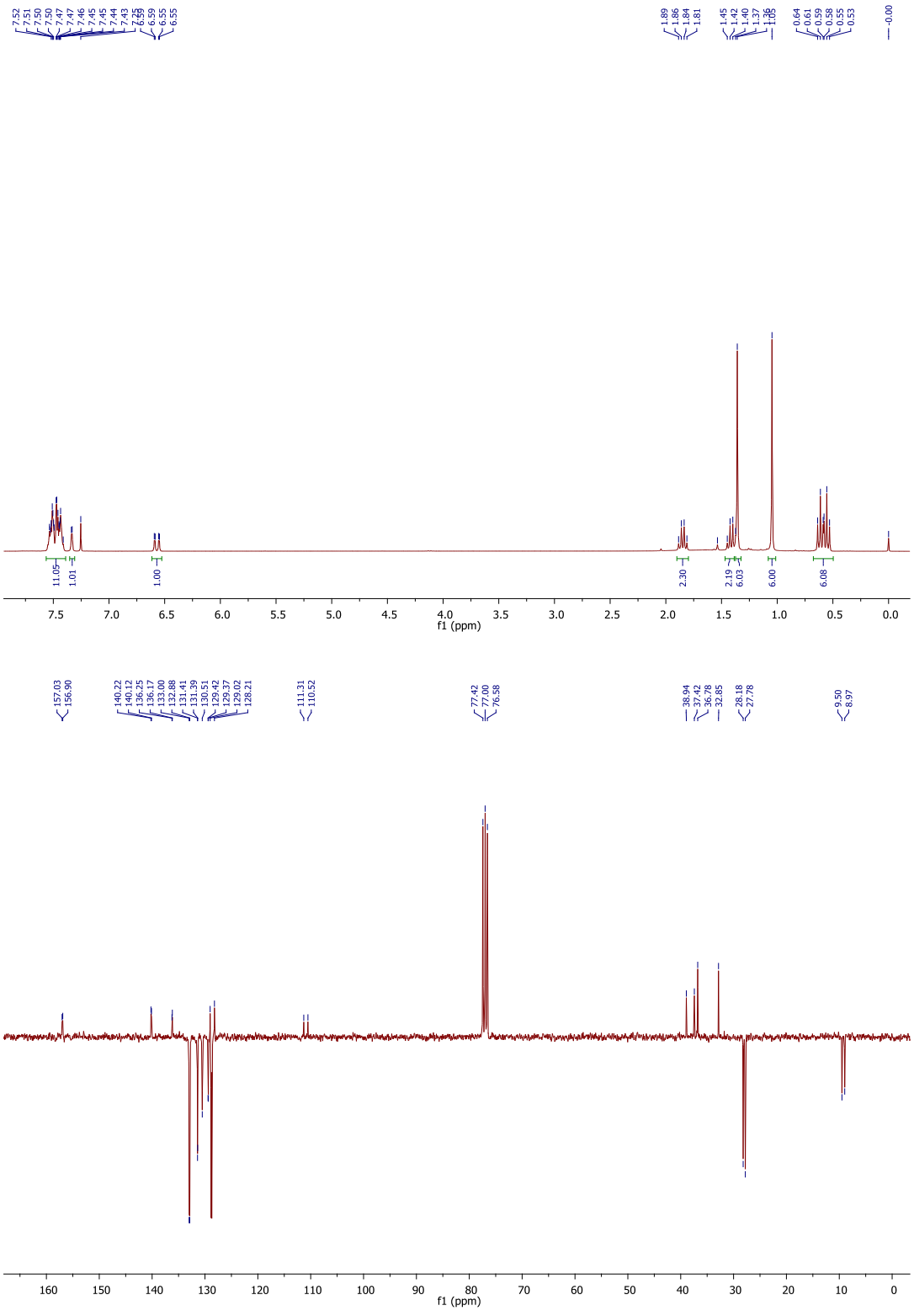

Figure 5.12. ^{1}H-NMR and ^{13}C-NMR of Molecule 42d

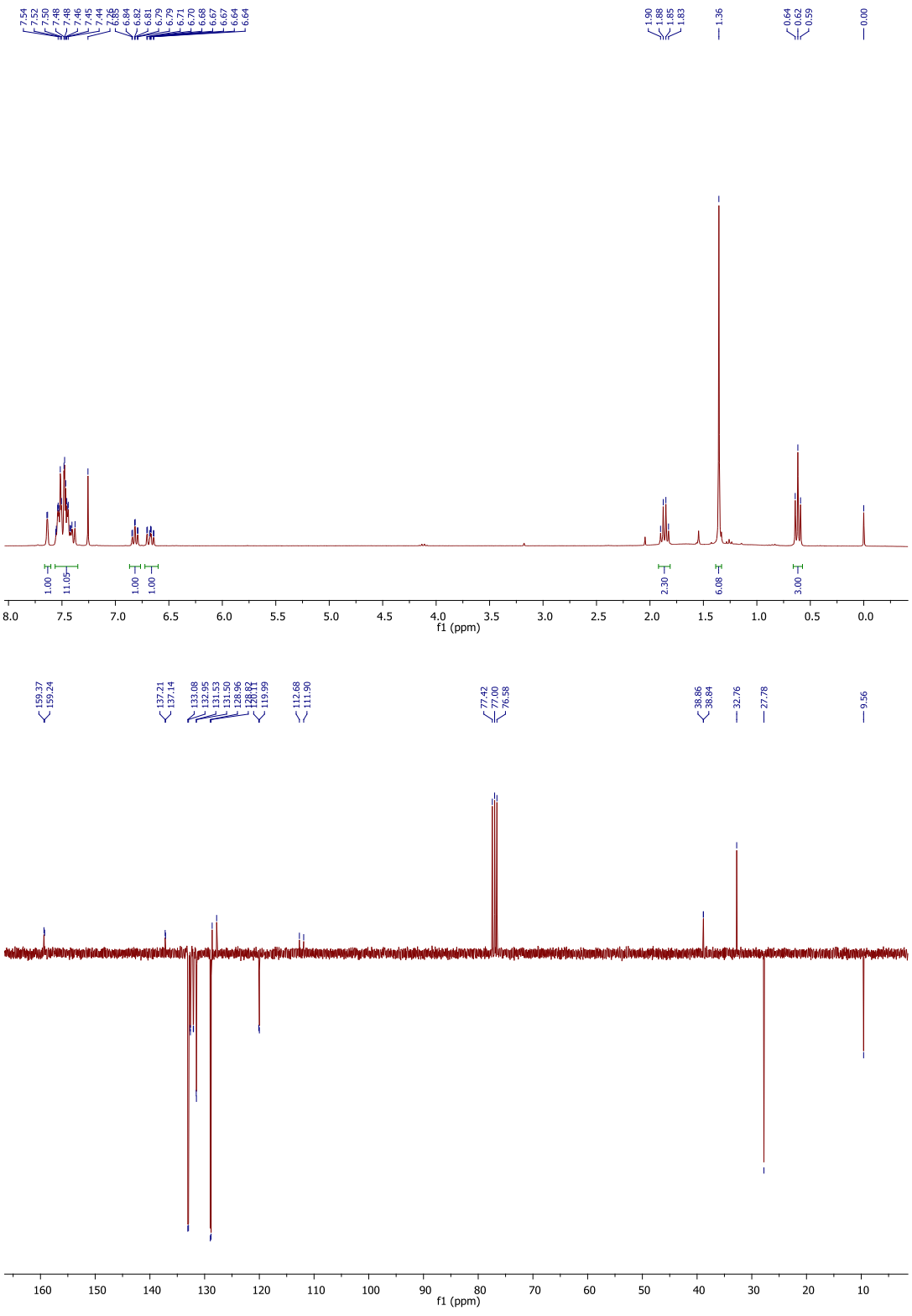

Figure 5.13. ^{1}H-NMR and ^{13}C-NMR of Molecule 42e

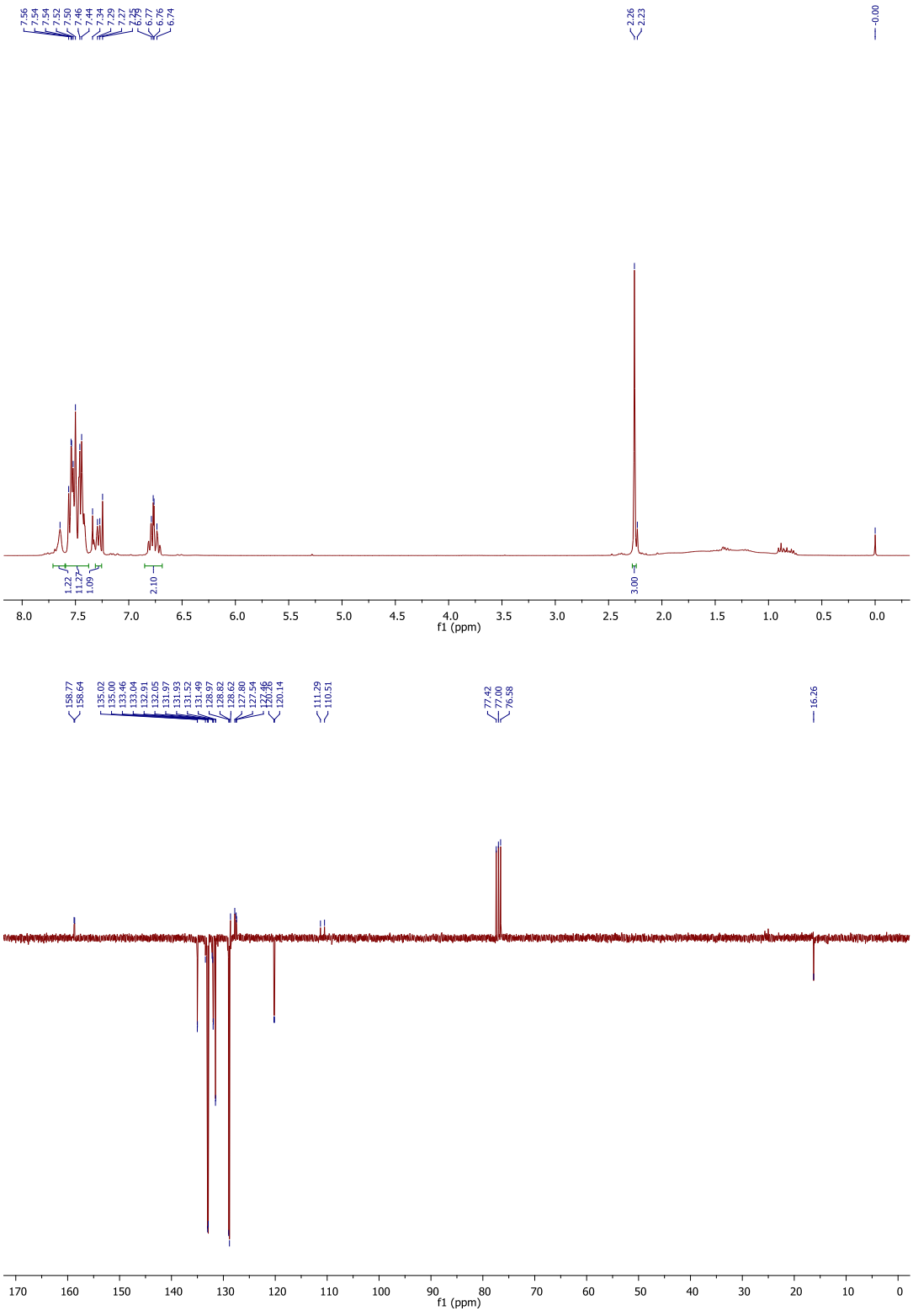

Figure 5.14. ^{1}H-NMR and ^{13}C-NMR of Molecule 42f

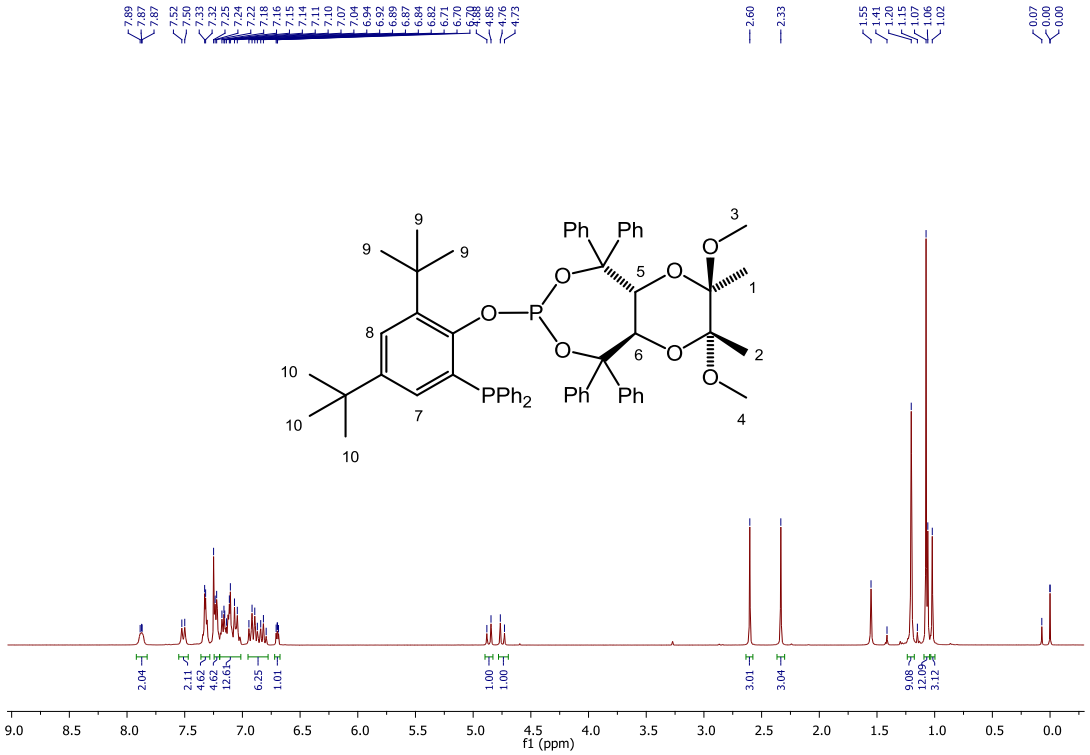

Figure 5.15. ^{1}H-NMR of Molecule 45a

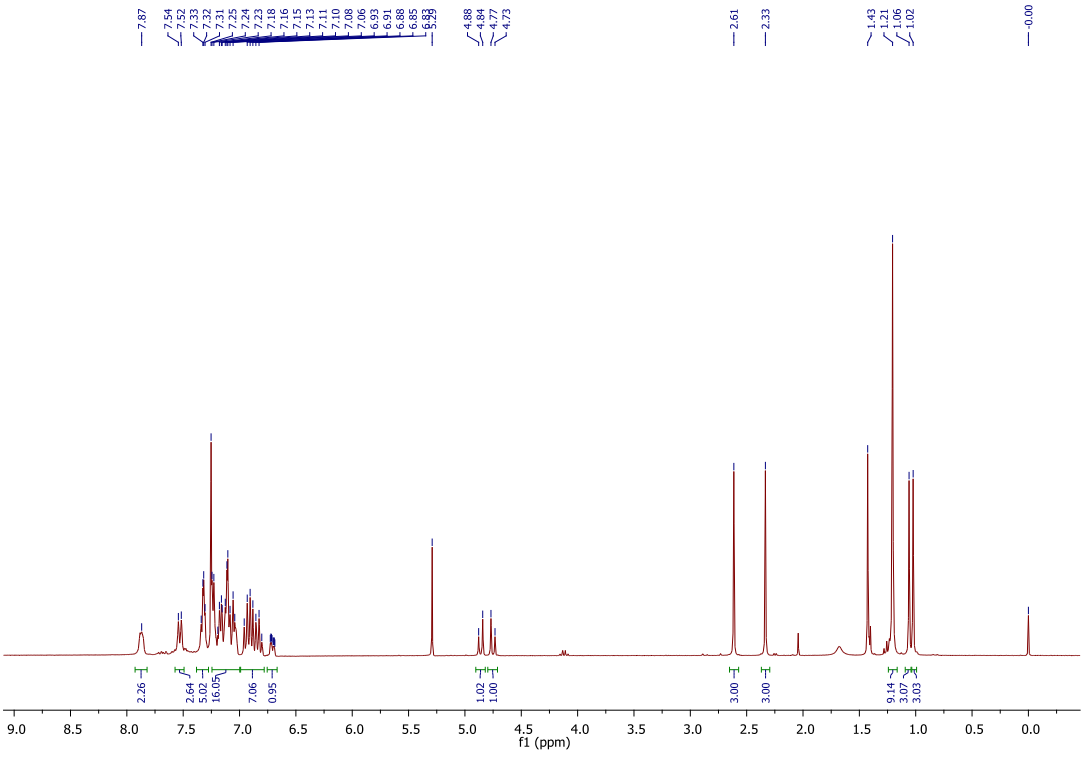

Figure 5.16. ^{1}H-NMR of Molecule 45b

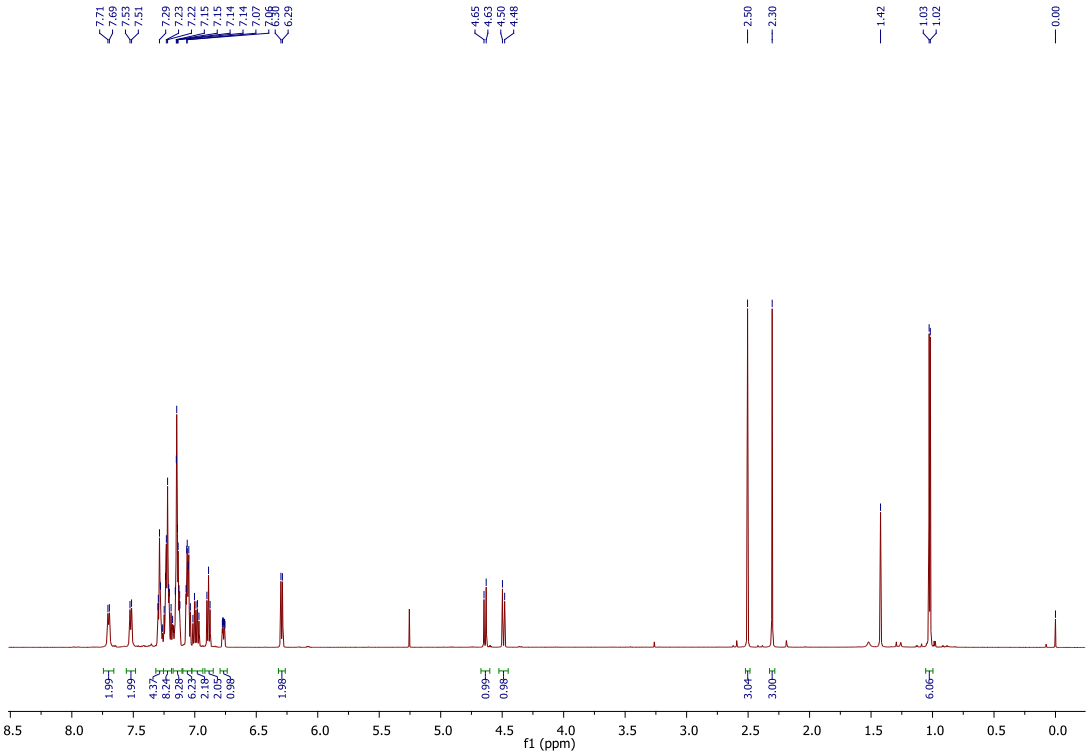

Figure 5.17. ^{1}H-NMR of Molecule 45c

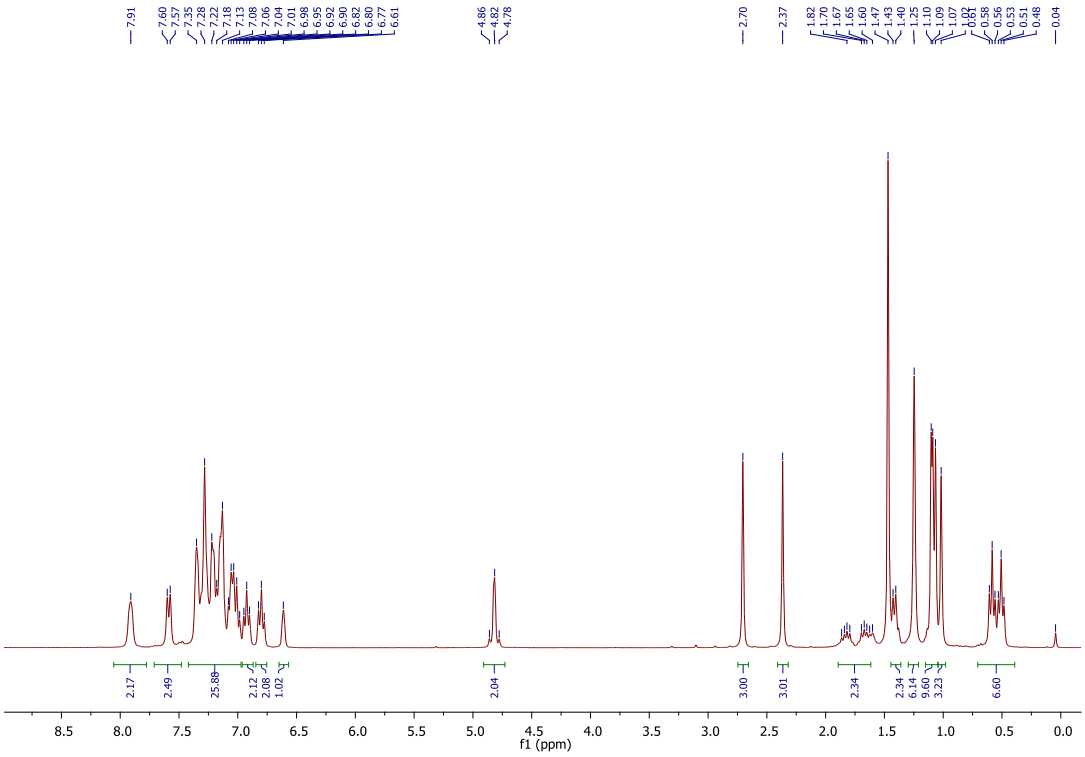

Figure 5.18. ^{1}H-NMR of Molecule 45d

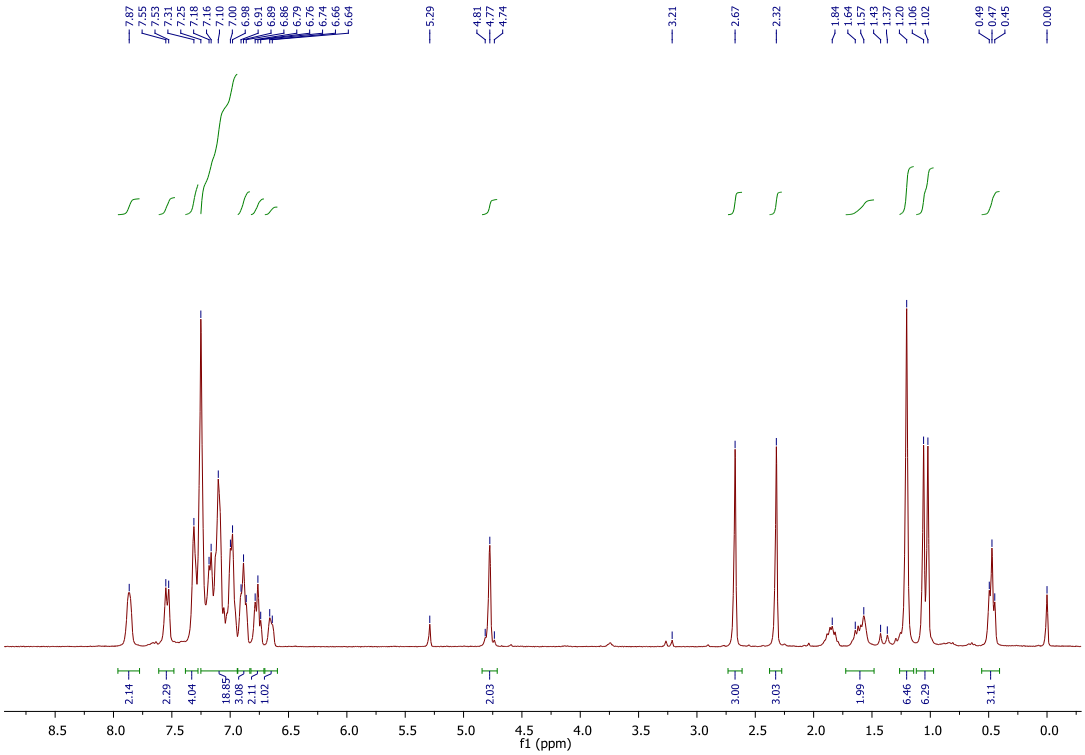

Figure 5.19. ^{1}H-NMR of Molecule 45e

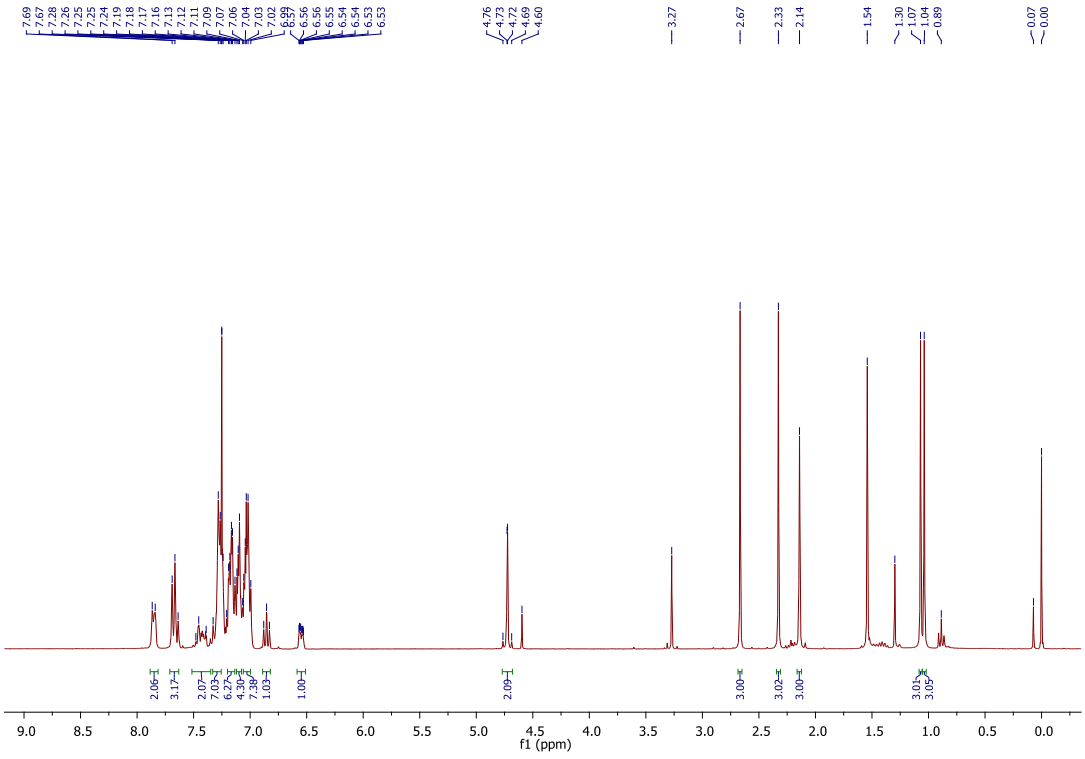

Figure 5.20. ^{1}H-NMR of Molecule 45f

AUTOBIOGRAPHY

Hamza ŞİMŞİR was born in Kocaeli in 1987. He studied primary school and middle school in the same city. He graduated from Gölcük Anatolia High School. He recieved his Diploma in Chemistry from the Sakarya University in 2010. He enrolled the graduate program at department of Chemistry in Karabük University in 2010.

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