Synthesis and Application of Chiral Novel Bis(isonitrile) Ligands in Catalysis

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Herrn Prof. Dr. Oliver Reiser möchte ich herzlich für die Überlassung des äußerst interessanten Themas, die anregenden Diskussionen und seine stete Unterstützung während der Durchführung dieser Arbeit danken.

To my Family

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Abbreviations

Atm.	atmosphere
BArF	tetrakis(3,5-trifluoromethyl-phenyl) borate
BINAM	1,1'-bi-2-naphthylamine
H_8-BINAM	5,5',6,6',7,7',8,8'-octahydro- 1,1'- binaphthyl-2,2'-diamine
Bn	benzyl
COD	1,5-cyclooctadiene
DABCO	1,4-diazabicyclo[2.2.2]octane
DBU	1,8-Diazabicyclo[5.4.0]undec-7-ene
DDQ	2,3-Dichloro-5,6-dicyanobenzoquinone
DMF-DMA	N,N-dimethylformamide dimethylacetal
dppf	diphenylphosphino ferrocene
ee	enantioselectivity
GC	gas chromatography
h	hour
HMDS	1,1,1,3,3,3-Hexamethyldisilazan
HPLC	high performance liquid chromatography
IR	infrared spectroscopy
LDA	lithium diisopropylamide
LHDMS	lithium-bis(trimethylsilyl)amide
m-	*meta*
MCR	multicomponent reaction
min.	minute
MS	molecular sieves, mass spectroscopy
*m*CPBA	3-chloroperoxybenzoic acid

MPV	Meerwein- Ponndorf-Verley
NADH	Nicotinamide adenine dinucleotide
NADPH	Nicotinamide adenine dinucleotide phosphate
NBS	*N*-bromosuccinimide
n.d.	not determined
NHC	N-heterocyclic carbene
NMR	nuclear magnetic resonance
n.r.	no reaction
o-	*ortho*
p-	*para*
quant.	quantitative
rt	room temperature
sat.	saturated
temp.	temperature
TOF	turnover frequency
THP	tetrahydropyran
TBHP	*tert*-butylhydroperoxide
TLC	thin layer chromatography
U-4CR	Ugi-four component reaction

A. Introduction

1. Organometallic Chemistry

Metal complexes are essential instruments in the toolbox of organic chemists, which are studied under the roof of organometallic chemistry. Organometallic chemistry lies at the interface between organic and inorganic chemistry because it deals with the interaction between inorganic metal ions and organic molecules.[1] This field has provided some powerful new synthetic methods in organic chemistry. The fastest growing area of organic chemistry is the application of organometallic reagents and catalysts to synthetic problems. Organometallic catalysts have long been used in industrial processes but are now being routinely applied in organic synthetic problems as well. With the continuing rise in environmental concerns and green chemistry, pressure has grown to maximize the ratio of product to waste. This has, in turn, led to an increasing interest in catalytic reactions, where the metal catalyst is present in minimal quantity and the selectivity of the reaction is enhanced, so the waste product is minimized. Much of the interests in organometallic compounds have been due to their efficiency as catalysts for organic synthesis.

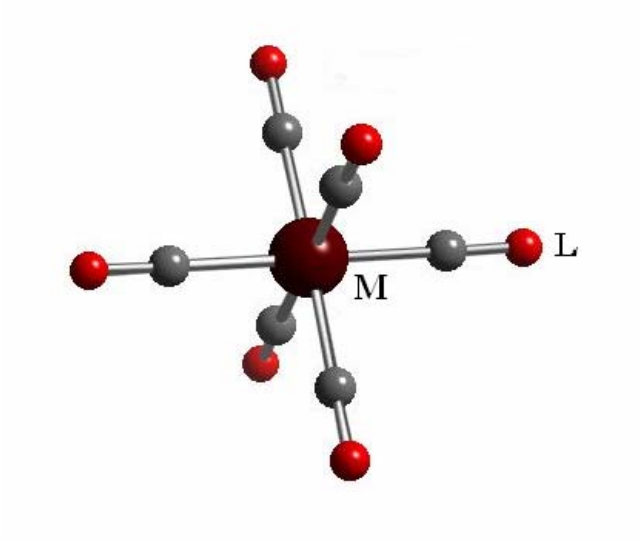


Figure 1: Basic structure of an organometallic compound

In turn, this efficacy originates from infinite number of derivatives, which can be obtained by varying the ligands and metals of organometallic complexes. A transition metal organometallic compound is composed of one or more metal centers surrounded by a set of ligands (Figure 1). In simple terms, the ligand (L) may act as a Lewis base that donates pair of electrons to the central metal atom (M), which acts as a Lewis acid.

Compounds of metal ions coordinated by ligands are referred to as metal complexes.[1] Most ligands are neutral or anionic substances but cationic species, such as the tropylium cation, are also known. Neutral ligands, such as ammonia (NH_3) or carbon monoxide (CO) are independently stable molecules in their free states, whereas anionic ligands, such as Cl^- or $C_5H_5^-$, are stabilized only when they are coordinated to central metals. Representative ligands are listed in Table 1 according to the ligating elements. Ligands with a single ligating atom are called monodentate ligands, and those with more than one ligating atoms are referred to as polydentate ligands, which are also called chelate ligands. The number of atoms bonded to a central metal is the coordination number.

Table 1: Representative ligands[1]

Name	Abbreviation	Formula
hydrido		H^-
carbonyl		CO
cyano		CN^-
cyclopentadiene	Cp	$C_5H_5^-$
carbonato		CO_3^{2-}
amine		NH_3
pyridine	py	C_5H_5N
triphenylphosphine	PPh_3	$P(C_6H_5)_3$
aqua	aq	H_2O
acetylacetonato	acac	$CH_3C(O)CH_2C(O)CH_3^-$
thiocyanato		SCN^-
chloro		Cl^-
ethylenediaminetetraacetato	edta	$(OOCCH_2)_2NCH_2CH_2N(CH_2COO)_2^{4-}$

Common ligands or those with complicated chemical formula are expressed in abbreviated forms

The relative stability of each complex is directly proportional to the valence electron count of the metal. Thus, the 18-electron rule predicts that a complex will be relatively stable if it has eighteen valence electrons associated with each metal center (i.e., in the non bonding orbitals of the metal and in the metal-ligand bonds). There are some exceptions to the rule, but metals in the middle of the transition series in low formal oxidation states generally obey the rule.

Isonitrile ligands are perhaps not the most common ligands in transition metal organometallic chemistry. Their bonding in linear geometry is typical of other linear π-acidic ligands such as N_2^+, NO^+, and CO.

Being similar to carbon monoxide as a ligand, isonitriles are more versatile as they tend to stabilize metals in both high and low oxidation states.[2, 3] The electronic and steric properties of isonitriles (CN**R**) are tunable by means of varying the substituent **R** at nitrogen. However, isonitriles are less electronegative than CO and the lobes of the π*-antibonding orbitals on N≡C are less polarized towards carbon. Thus, isonitriles are generally better net electron donors than carbonyls. In terms of Dewar-Chatt-Duncanson model (Figure 2), there is σ-donation from the lone pair of electrons on the carbon (i.e., the sp hybrid orbital) to an empty σ-symmetry orbital of the metal (i.e. d^2sp^3 in octahedral complexes). There is also π-back donation from a pair of filled orbital of π-symmetry on the metal (i.e. d_{xy}, d_{xz} or d_{yz} orbitals in octahedral metals) to a pair of empty π-symmetry orbitals on the isonitrile ligands (i.e. π* orbitals localized on N≡C).

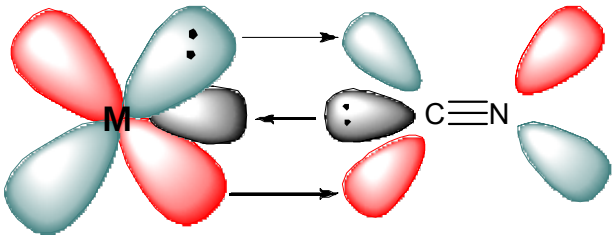


Figure 2: Representation of bonding interactions of organic isonitriles and transition metal ions

Valence Bond Theory (Figure 3) provides an alternative and complementary explanation of the bonding that occurs during the coordination of an isonitrile to a transition metal. In Valence Bond terms, the coordination is explained via resonance. Thus, greater back bonding results in an increased contribution from the second resonance (**II**) form and hence a decreased CN-R bond angle due to sp^2 hybridization of the nitrogen atom on the latter.[4]

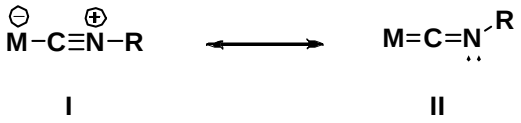


Figure 3: Valence bond theory representation of the bonding of isonitrile ligand

Both the Dewar-Chatt-Duncanson and Valence Bond Theory explanation can be used to rationalize the same experimental observations. The electron richness of the metal centre affects the bond orders for the metal-carbon and carbon-nitrogen bonds as well as the CN-R angles. If the electron richness of the metal is increased, there is more back bonding and the second resonance form is favored. The metal-carbon bond order therefore increases and carbon-nitrogen bond order decreases while the CN-R angle decreases. The electron richness of isonitriles complex can be measured through infrared spectroscopy. The CN stretching frequency for isonitrile complexes is 250-350 wave number (cm^{-1}) lower than the stretching frequency for the free isonitrile, reflecting the weakening of the net N≡C σ and π- bonds upon co-ordination.[5, 6]

Isonitriles play an important role in organic and organometallic synthesis, catalysis, material science, drug discovery and diagnostic medicine. Since 1995, organic isonitriles are widely used in multi-component reactions (MCR) and have become a powerful method for developing new drugs for the pharmaceutical industry.[7-9] For example, the preparation of Crixivan® (Figure 4), an HIV protease inhibitor produced by Merck & Co[8b] via one pot, four component reaction.

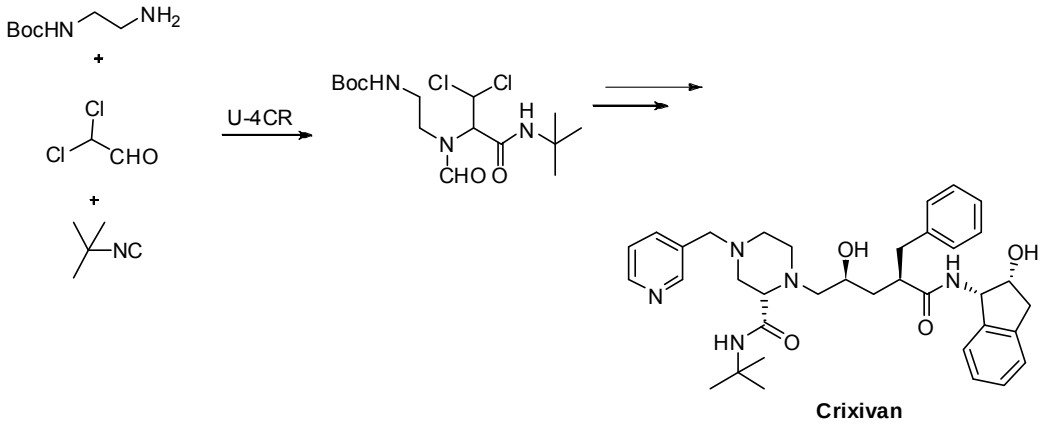


Figure 4: Four component synthesis of Crixivan®

In the field of medicine, isonitrile complexes of 99m-technetium were widely used as radiotracers for diverse diagnostic purposes.[10] $[^{99}Tc(2\text{-methoxyisobutylisocynide})_6]^+$ also known as Tc-99m-MIBI and Cardiolite® is used as a non invasive marker for the diagnosis of P-glycoprotein and related multi drug resistant protein over-expressions in tumors.[11, 12]
The list of applications of isonitriles in organic chemistry is quite extensive and their diverse reactivities can be advantageous in both organic and organometallic applications[13, 14]. Isonitriles are recognized as valuable synthons in organic synthesis, but have been less frequently applied as ligands in metal catalysis, although isonitriles act as unique ligands for a broad variety of transition metal complexes. The development in metal-isonitrile complex catalyzed reactions is undertaken in the next section.

2. Palladium-isonitrile complexes

2.1 Bissilylation of unsaturated C-C bonds

Introduction of silicon into organic molecules is an interesting methodology, which leads to synthetic elaboration of organic molecules via organosilicon compounds and synthesis of new silicon containing materials. Ito and coworkers[15] have reported that *tert*-alkyl isonitriles were effective ligands for a wide range of bissilylation of alkynes and alkenes. Remarkable development has been done in bissilylation of alkenes and alkynes by using combination of commercially available isonitriles (**1a-e**) (Figure 5) and Pd(II).

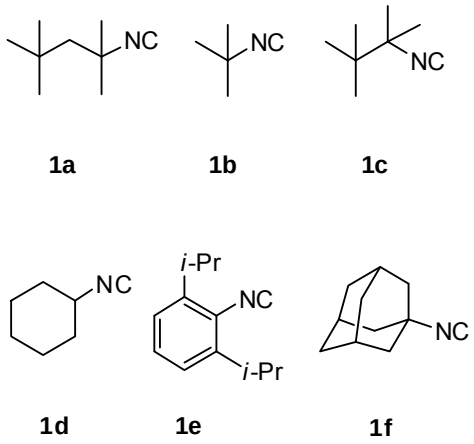
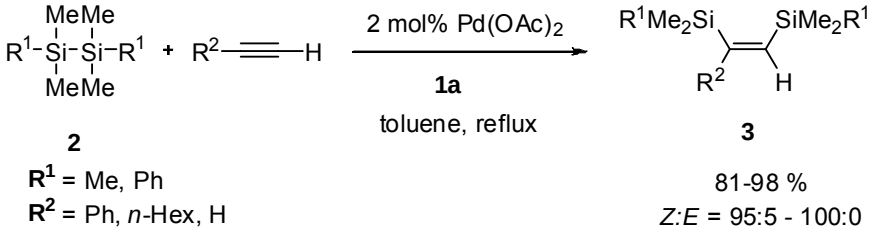


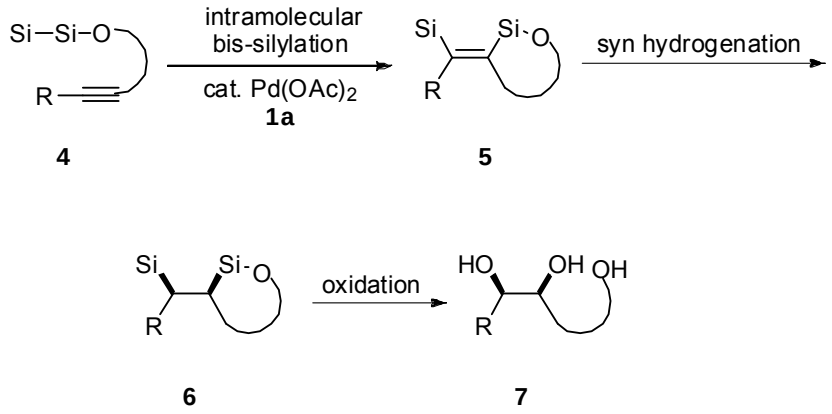
Figure 5: Examples of *tert*-isonitrile ligands

The intermolecular and intramolecular bissilylation of alkynes,[16, 17] catalyzed by palladium-*tert*-alkyl isonitrile catalyst gives bissilylated alkenes and ring closure product in good yields and selectivity. The palladium-*tert*-alkyl isonitrile catalyst is very effective in such reactions, whereas the conventional palladium-phosphine complexes showed only low catalytic activity[18]. Intermolecular bissilylation of phenylacetylene (Scheme 1) was carried out with hexamethyldisilane using palladium (II) acetate-*tert*-octyl-isonitrile catalyst to give bissilylated alkenes (**3**) in yields upto 98% and excellent *Z*:*E* ratio.



Scheme 1: Intermolecular bissilylation of alkynes with disilanes

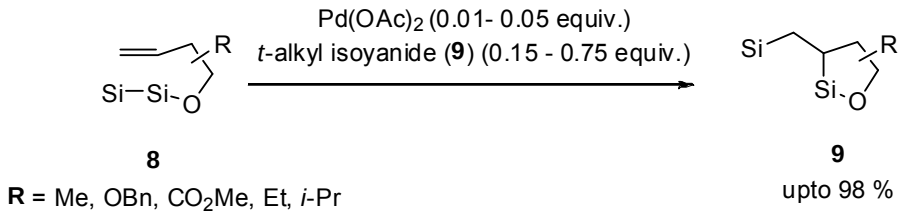
An important feature of this reaction is that excess use of isonitrile ligands such as 1-adamanthyl (**1e**) and *tert*-octyl (**1a**) isonitriles efficiently promotes the catalytic activity of $Pd(OAc)_2$ and hence the reaction rate, while in the absence of isonitrile the reaction fails to occur.



Scheme 2: Intramolecular bissilylation of alkynes

An alkyne tethered to a disilanyl group (**4**), upon treatment with $Pd(OAc)_2$ and *tert*-octyl isonitrile (**1a**), furnished exocyclic bis-silylated olefin[17] (**5**) via intramolecular bissilylation (Scheme 2). Subsequent addition of hydrogen to double bond occurred from the less hindered side of the ring to give *cis*- disubstituted oxasilolanes (**6**) with good diastereoselectivity. Oxidation of the two C-Si bonds of the hydrogenated oxasilolane led to the stereo- and regioselective synthesis of 1,2,4-triols (**7**).

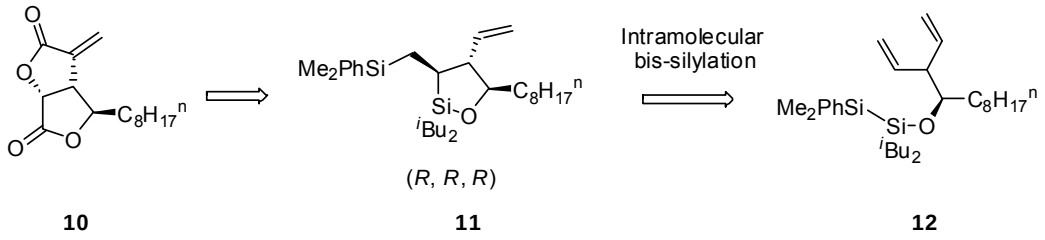
Similarly, stereoselective intramolecular bissilylation of terminal alkenes (**8**) tethered to disilanyl group by chains of two and three atoms promoted by palladium-*tert*-alkyl isonitrile catalyst was studied.[19, 20] However, this catalyst failed to promote the intermolecular bissilylation of alkenes. The bissilylation was carried out in the presence of catalytic amount of $Pd(OAc)_2$ (0.01-0.05 equiv.) and *tert*-alkyl isonitrile (0.15-0.75 equiv.) (**1a-f**) in toluene, under reflux conditions. Intramolecular regioselective addition of the Si-Si linkage to the alkenes took place to furnish an *exo*-ring product, i.e. 1,2-oxasilolane (**9**) (Scheme 3) in excellent chemical yield.



Scheme 3: Intramolecular bissilylation of terminal alkene

The 1,2-oxasilolanes (**8**) thus produced steresoselectively were oxidized to corresponding 1,2,4-triols. Among the *tert*-alkyl isonitriles, 1,1,3,3-tetramethylbutyl isonitrile (**1a**) showed best reaction rate and stereoselectivity. An excess of isonitrile (6–15 times to Pd $(OAc)_2$ was used. Use of less than 6 equiv. of isonitrile to $Pd(OAc)_2$ did not furnish the reaction. Palladium (0) isonitrile complex is the active catalyst species for bissilylation reaction.

In 1995, Ito and coworkers reported an application of distereoselective intramolecular bissilylation of alkene in stereocontrolled synthesis of (-)-avanaciolide (**10**)[21] (Scheme 4).



10 **11** **12**

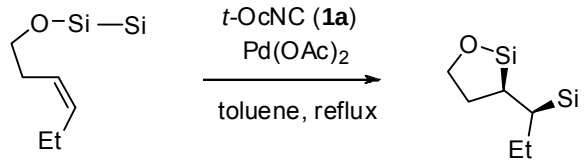
(-) Avanaciolide

Scheme 4: Reterosynthetic analysis of (-)-avanaciolide (**10**)

The intramolecular bissilylation of enatiomerically rich **12** proceeded with high diasteroselectivity in the presence of 0.02 equiv of $Pd(OAc)_2$ and 0.3 equiv of 1,1,3,3-tetramethylbutyl isonitrile (**1a**) in toluene to furnish a five membered cyclic product (**11**) with highly controlled stereogenic centers. The presence of ^{i}Bu group in disilanyl ether was preferable to obtain high chemical yield (92%) and diastereoselectivity (90:10). The major isomer was separated and used for further steps towards the synthesis of (-)-avanaciolide (**10**).

Intramolecular bissilylation of (*Z*)- and (*E*)- disilanyl alkenes (Table 2) tethered to disilanyl group was also carried out in the presence of 1,1,3,3-tetramethylbutyl isonitrile (**1a**, 0.45 equiv.) and $Pd(OAc)_2$ (0.03 equiv.) in refluxing toluene, which proceeded with stereospecific *cis*- addition to give 5-exo ring closure product[22] (**14**). The choice of appropriate disilanyl group is essential to obtain high yields such as the presence of phenyl substituents at the silicon atom proximal to the ether oxygen in the bissilylation of (**Z**)-**13**, which led to enhanced yield and reaction rate (Table 2, entry 5).

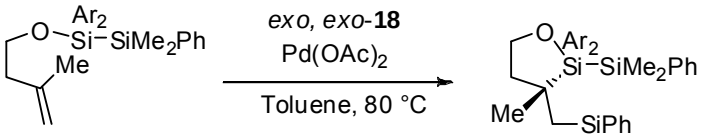
Table 2: Bissilylation of vicinally disubstituted internal alkenes



(*Z*)-**13** **14**

entry	disilanyl group	yield %
1	-$SiMe_2SiMe_3$	no reaction
2	-$SiMe_2SiMe_2Ph$	56
3	-$SiMe_2SiPh_3$	66
4	-$SiMePhSiMe_2Ph$	75
5	-$SiPh_2SiMe_2Ph$	91
6	-$SiPh_2SiMe_3$	56

For the first time optically active chiral isonitriles were employed by the same group in the enantioselective intramolecular bissilylation of alkenes (**15**)[23] (Scheme 5).

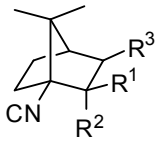


15
Ar = *o*-Tol

16
78% ee (59%)

Scheme 5: Stereoselctive bissilylation of alkenes

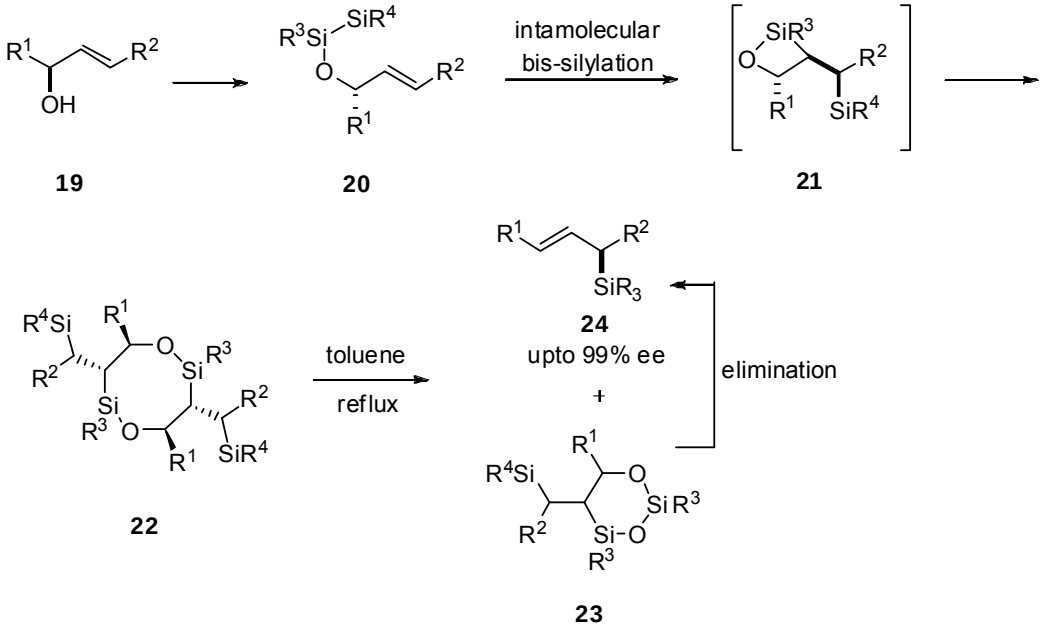
Chiral *tert*-alkyl isonitriles **17** and **15** (Figure 6) with the rigid skeleton derived from D-camphor provides moderate enantioselectivities for the intramolecular bissilylation. However, the isonitrile exo-**17,** bearing exo-siloxy group provided higher enantioselectivity than endo-**17,** bearing an endo-siloxy group, which showed opposite enantioselection. The best *ee* was achieved by ligand **18** with two exo-siloxy groups.



exo-**17** (R^1 = OSiMe3, R^2 = R^3 = H)
endo-**17** (R^1 = OSiMe3, R^2 = R^3 = H)
exo,exo-**18** (R^1 = R^2 = OSiMe3, R^3 = H)

Figure 6: Chiral *tert*-alkyl isonitriles

The stereoselective synthesis of allylsilanes (**24**) was achieved via intramolecular bissilylation of enantiomerically pure allylic alcohol (**19**) [24, 25] (Scheme 6). Palladium (II) *tert*-octyl isonitrile catalyzed intramolecular bis-silylation furnished two new Si-C bonds in regio and stereoselective manner. The intramolecular bissilylation of disilanyl ether initially furnished eight membered ring **22** in refluxing hexanes, which may be obtained from cyclodimerization of oxasiletane **21**. Subsequent heating of **22** under refluxing toluene led to the allylsilane **24** (upto 99% ee) along with the six memebered ring **23**. The **23** was transformed into the allylsilane **24** via Peterson type elimination using *n*BuLi.



Scheme 6: Synthesis of allylsilanes via intramolecular bissilylation

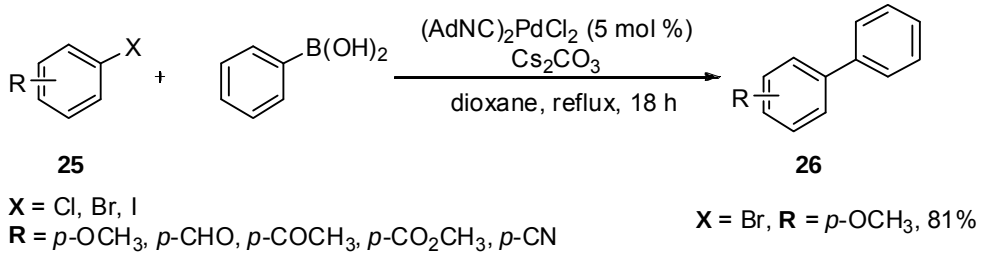
The active specie in the above mentioned reactions is believed to be $(RNC)_nPd(0)$, where the coordination number (n) may vary from 2 to 4. The active species are generated from Pd(II) precursors with *tert*-alkyl isonitriles and $Pd(OAc)_2$, $Pd(acac)_2$ and PdCp(π-allyl) have been

used as palladium precursors. Typically 4–15 equivalents (to Pd) of isonitrile were employed because part of the isonitriles may be consumed for the Pd(II) – Pd(0) reduction. The excess isonitriles do not interfere with the bissilylation reaction. It was explained that $Pd(OAc)_2$ is reduced by isonitriles initially to form Pd(0) species ligated isonitrile. Next the oxidative insertion of Pd(0) species into the Si-Si linkage takes place to give a bis(organisilyl)palladium (II) complex. Insertion of the double bond into Pd-Si bond followed by reductive elimination of the Pd(0) species would complete the catalytic cycle. Excess of isonitrile was required to hinder the palladium(0) isonitrile complex from decomposing during the reaction course.

2.2 Suzuki Miyaura coupling

Isonitrile palladium complexes $[(RNC)_2PdCl_2]$ were also tested by Villemin and co-workers[26] for Suzuki Miyaura reaction of bromoaromatic or heteroaromatic substrates and activated chloroaromatic and *p*-deficient heteroaromatic substrates (Scheme 7). It was explained that isonitriles are isoelectronic with Arduengo's carbenes (NHC) and hence can promote Suzuki coupling reaction. Palladium complexes of hindered isonitriles $[(RNC)_2PdCl_2]$ such as tert-butylisonitrile (^{t}BuNC, **1b**), 1,1,3,3-tetramethylbutylisonotrile (^{t}OcNC, **1a**), cyclohexylisonitrile (CyNC, **1d**), 2,6-didiopropylphenylisonotrile [(^{i}Pr)$_2$PhNC), **1e**] and adamantylisonitrile (AdNC, **1f**) were prepared by the reaction of isonitriles with $PdCl_2$ in DMF at room temperature.

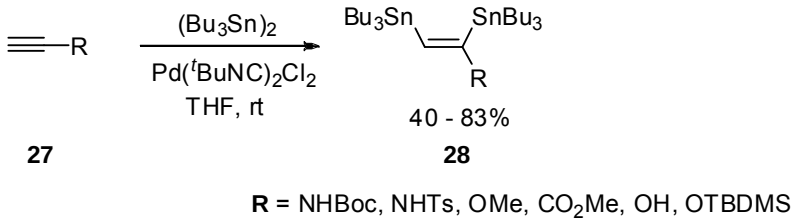
$(AdCN)_2PdCl_2$ complex showed the maximum reactivity in Suzuki Miyaura coupling of 4-halogenanisoles (**25**) in comparison to other palladium-isonitrile complexes. Moderate to excellent yields of isolated phenylated products were obtained by the reaction of phenylboronic acid and aryl halides. Heteroaromatic substrates were also coupled in moderate yield with the same catalyst.



Scheme 7: Suzuki Miyaura coupling employing Pd-isonitrile catalyst

2.3 Bisstannylation of alkynes

Bisstannylation of terminal and internal alkynes (**27**) was also achieved using palladium-isonitrile complex[27] and hexaalkylditin as stannyl source under mild conditions (Scheme 8). Generally, good yields were obtained with different types of alkynes, and functional groups such as amine, carbamate, silyl, ether and ester were tolerated very well. For example, silyl homopropargylic ether showed lower reactivity versus propargylic substrates, giving a modest yield (40%). Sterically bulky alcohol also underwent smooth conversion indicating the catalysts' tolerance towards steric substrates. Terminal alkynes were found to be more reactive than the internal alkynes in bisstannylation, nevertheless, in latter case the reaction is feasible only with activated alkynes.



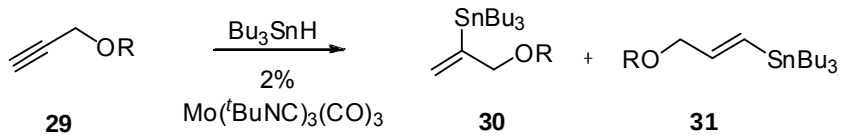
Scheme 8: Bisstannylation of alkynes using Pd-isonitrile complex

3. Low valent transition metal isonitrile complexes (M = W, Mo, Ni)

3.1 Hydrostannylation and bisstannnylation of alkynes

Hydrometalation is an important category of reactions catalyzed by transition metals such as hydrostannation of alkynes, used for the synthesis of vinylstannanes, which can be subjected to Stille coupling for further reactions. Regioselective hydrostannation of alkynes catalyzed by $Mo(^tBuNC)_3(CO)_3$ was reported by Kazmaier et. al (Scheme 9).[28] Substitution of three CO ligands in $Mo(CO)_6$ by isonitrile ligands resulted in $Mo(^tBuNC)_3(CO)_3$, which catalyzed hydrostannylation of propargylic alcohol derivatives (**29**) with excellent yield and regioselectivity to afforded α-stannylated allylic alcohols or their derivatives as a major product (**30**). MoBr-(allyl)$(CO)_2(CH_3CN)_2$ and $Mo(CO)_6$ (Table 3) were also found to be

suitable for the hydrostannation of propargylic alcohol derivatives, but without significant regioselectivity (Table 3).



Scheme 9: Hydrostannylation of unsymmetric alkynes

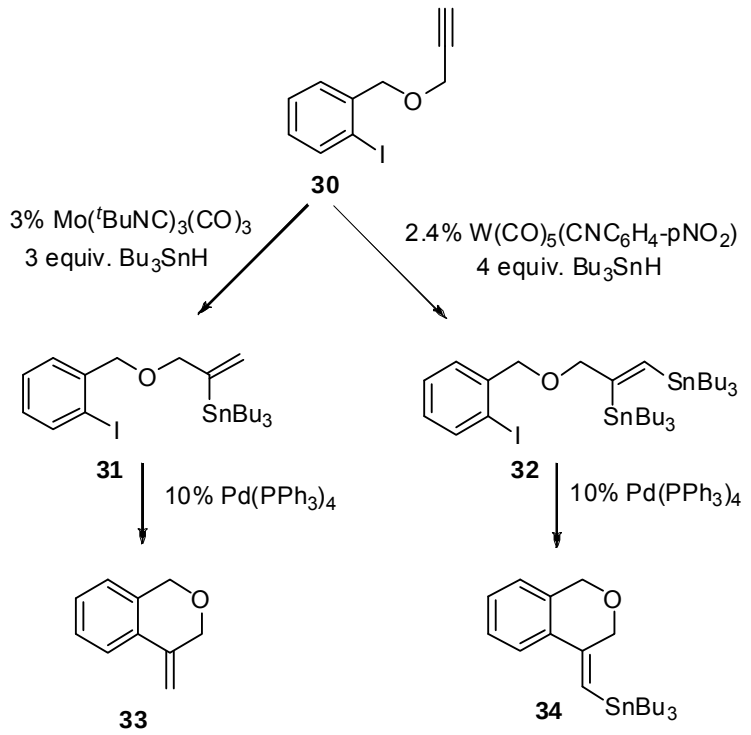
^{t}BuNC was chosen as the best ligand because of the sterically demanding *t*-butyl group, which may have an influence on the regioselectivity of the reaction. Indeed, $Mo(^t BuNC)_3(CO)_3$ transfers the stanne to the sterically more hindered position of the triple bond. An additional isonitrile ligand $Mo(^t BuNC)_4(CO)_2$, has no significant effect on the reaction. The lower yield might have resulted from the lower stability of $Mo(^t BuNC)_4(CO)_2$ in comparison to that of $Mo(^t BuNC)_3(CO)_3$ (Table 3). Hydrostannation of terminal alkynes proceeded very well at room temperature, whereas high temperature (50-70 °C) was required for sterically hindered alkynes.

Table 3: Hydrostannylation of alkynes **29**

Catalyst	yield %	selectivity
$PdCl_2(PPh_3)_2$	68	67:33
$MoBr(allyl)(CO)_2(MeCN)_2$	nr	64:36
$Mo(CO)_3(^t BuNC)_3$	98	98:2

Kazmaier has also shown that tungsten based isonitrile complex $W(CO)_5(CNC_6H_4$-*p*$NO_2)$ can achieve the same bisstannylation reaction using Bu_3SnH,[29] whereas $Mo(^t BuNC)_3(CO)_3$ allows regioselective hydrostannation of terminal alkynes (**30**) with Bu_3SnH[28] (Scheme 10). Both hydrostannylation product (**31**) and bisstannnylation product (**32**) further underwent intramolecular Stille coupling to afford compound **33** and **34,** respectively. Hydrostannylation

of alkynes catalyzed by $Mo(^tBuNC)_3(CO)_3$ can be used for the construction of a heterocyclic system[30] via subsequent intramolecular Stille coupling.

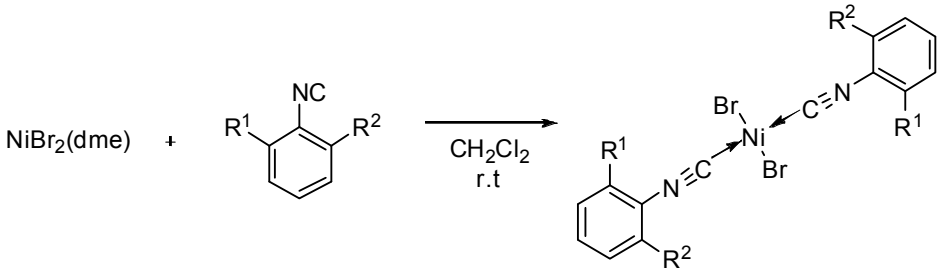


Scheme 10: Hydro- and Bisstannylation of propargylic ethers **30**

3.2 Polymerization reactions

Low valent transition metal isonitrile complexes can function as catalysts in certain polymerization processes.[31-34] For example, polymerization of butadiene by $M(CNAr)_6$ (M = Cr, Mo, W) which produces either isotactic or syndiotactic polybutadienes. The nature of the polybutadiene is determined by the nature of the metal center and the aryl group of the isonitrile.[33] Moreover, Ni isonitriles $Ni_4(^tBuNC)_7$ have been shown to effect efficient dimerization of butadiene to form cyclooctadiene, as well as trimerization of substituted acetylenes to give highly functionalized benzenes.[34] Isonitrile complexes of Ni, $NiBr_2(ArNC)_2$ **(35)** (Scheme 11) were reported by Nagashima and co-workers[35] and employed as catalysts for ethylene polymerization in the presence of methylaluinoxane (MAO). Substituents on the aryl group of isonitriles especially at the 2- or 2, 6-positions

affect the catalytic activity, molecular weight and number of methyl branches of the formed polymer. The nickel-isonitrile complexes having 2,6-diphenylphenylisonitrile and its analogues showed moderate activity and furnished high molecular weight polyethylene ($M_v > 10^6$), whereas isonitrile bearing 2-phenylphenylisonitrile and its analogue gave polyethylene with $M_w = 10^3 - 10^4$.



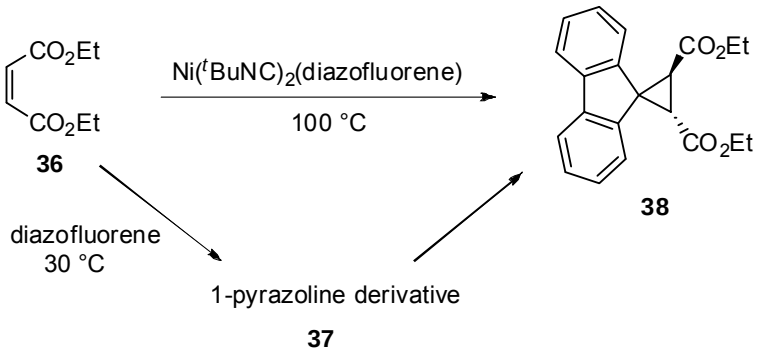
35

R¹ = R² = Me, Et, ^{i}Pr, Ph, 4-^{t}BuC$_6$H$_4$, 2-MeC$_6$H$_4$, 2,6-Me$_2$C$_6$H$_3$

Scheme 11: Synthesis of $NiBr_2(ArNC)_2$ complex **35**

3.3 Cyclopropanation of olefins

Ibers *et. al*[36] reported the structure and catalytical activity of (Diazofluorene)bis(*tert*-butyl isonitrile)nickel(0) complex, which was prepared by the low temperature reaction of Ni(^{t}BuNC)$_2$ and diazofluorene. This kind of complex was used for cyclopropanation of substituted olefins (methyl acrylate or diethyl maleate, **36**) at 100 °C (Scheme 12). Although good yield of cyclopropanation product was obtained with methyl acrylate and ethyl acrylate, but only trace yield was obtained with alkyl or arylethylenes. The absence of Ni-isonitrile catalyst in the thermal reaction of free diazofluorene with diethyl maleate readily gives 1-pyrazoline derivative (**37**) at room temperature, which subsequently undergoes nitrogen elimination at 30 °C to give trans-cyclopropane derivative (**38**). Therefore, the trans-cyclopropane derivative obtained from the nickel complex may result from the thermal reaction of free diazofluorene with diethyl maleate.

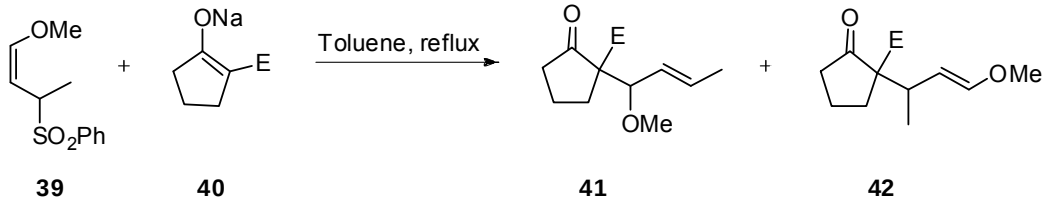


Scheme 12: Ni(^{t}BuNC)$_2$(diazofluorene) catalyzed cyclopropanation of olefins

In the case of diazomethane, rapid reaction of diazomethane with Ni-isonitrile catalyst produces the carbene, which further reacts with the ethylacrylate, and hence no formation of 2-pyrazoline. However, 2-pyrazoline derivatives are formed in the absence of nickel isonitrile complex but it does not undergo ring contraction to yield the cyclopropane derivatives. Thus, the presence of Ni-isonitrile complex hinders the formation of the pyrazoline derivatives of both diazomethane and diazofluorene.

3.4 Allylic allylation

Highly reactive Molybdenum-isonitrile complexes were prepared by Trost and co-workers[37] for the allylic alkylation reaction (Scheme 13). Mo(^{t}BuNC)$_4$(CO)$_2$ was proven to be a superior catalyst in comparison to Mo(CO)$_6$ and also furnished enhanced reactivity as well as chemo-, region-, and stereoselectivity in allyl alkylation reaction. Alkylation at the less substituted allylic carbon (**41**) with net retention stereochemistry was observed.



Mo(^{t}BuNC)$_4$(CO)$_2$	(40%)	93	:	7
Mo(CO)$_6$	(68%)	60	:	40

Scheme 13: Allylic allylation catalyzed by Mo(^{t}BuNC)$_4$(CO)$_2$ complex

4. Rhodium, Ruthenium and Rhenium isonitrile complexes

4.1 Hydrogenation

Efraty *et. al*[38] prepared an insoluble matrix of $[RhCl(CO)(1,4\text{-}(CN)_2C_6H_4)]_n$ using $[Rh(CO)_2Cl]_2$ and an equimolar amount of 1,4-diisocyanobenzene and its activity was investigated with respect to 1-hexene hydrogenation and isomerization in dark conditions as well as under irradiation. The insoluble matrix may exist as a linear polymer, non linear polymer, or a tetranuclear cyclic oligomer (Figure 7).

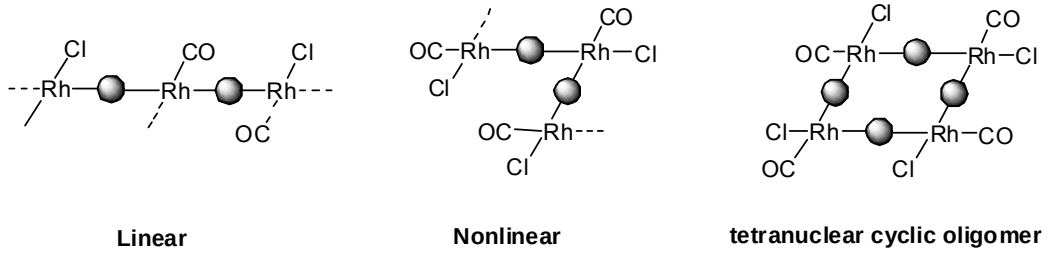


Figure 7: Types of insoluble matrix of $[RhCl(CO)(1,4\text{-}(CN)_2C_6H_4)]_n$

The hydrogenation and isomerization of 1-hexene was carried out using the insoluble catalyst under hydrogen pressure of 0.5 atm at 25 °C. Under dark conditions, hydrogenation of 1-hexene to n-hexane also involves isomerization to *trans*- and *cis*- hexenes which subsequently hydrogenated to n-hexane. While in the presence of UV radiation, the formation of n-hexane slowed down. Isomerization was observed at an early stage in the presence of light but no hydrogenation of isomers was observed.

The TCSM (tethered complexes on supported metal) (Figure 8) catalysts Rh-CNR_2/Pd-SiO_2, Rh-CNR_3/M-SiO_2(M) Pd, Pt, Ru) and Pt-CNR_2/Pd-SiO_2 were synthesized by Angelici *et al*.[39] to catalyze hydrogenation of arenes and cyclohexanone under mild conditions. These TCSM were prepared using rhodium and platinum complexes $RhCl(CO)[CN(CH_2)_3Si(OC_2H_5)_3]_2$ (Rh-CNR_2), $RhCl[CN(CH_2)_3Si(OC_2H_5)_3]_3$ (Rh-CNR_3), and $PtCl_2[CN(CH_2)_3Si(OC_2H_5)_3]_2$ (Pt-CNR_2) tethered to the silica supported metal heterogeneous catalysts M-SiO_2 (M) Pd, Pt, Ru). Rhodium complex Rh-CNR_3/Pd-SiO_2 exhibits highest activity for the toluene hydrogenation (TOF 5.5 mol H_2/mol Rh min and TO 2420 mol H_2/mol Rh during 8.5 h) as

compared to Rh-CNR_3/M-SiO_2(M) Pt, Ru). The catalytic activity of TCSM are higher than those of the separate homogenous Rh or Pt isonitrile complex, the separate silica supported metal heterogeneous catalyst or the Rh or Pt complex catalyst tethered on just SiO_2. IR (DRIFT) spectral studies of the TCSM catalysts showed that the isonitrile ligands remain coordinated to the rhodium (or platinum) center even after catalysis. Atomic emission spectroscopic analysis of hydrogenation solutions shows that there is no rhodium (or platinum) leaching into the solutions.

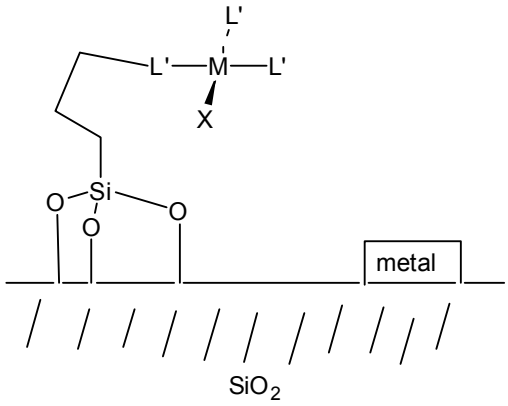
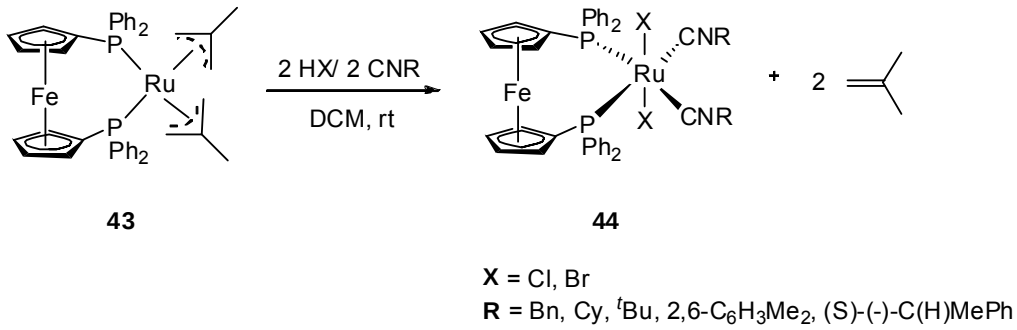


Figure 8: TCSM catalyst consisting of homogenous catalyst tethered to silica supported heterogeneous catalyst

The bis(isonitrile)-ruthenium(II) complexes[40] *trans,cis,cis*-[$RuX_2(CNR)_2$(dppf)] (**44**) have been synthesized by reaction of bis(allyl)-ruthenium(II) derivative [Ru($\eta^3C_3H_4Me)_2$(dppf)] (**43**) with the appropriate isonitrile ligand, in dichloromethane at room temperature and in the presence of the corresponding hydrogen halide HX (Scheme 14). Among these bis(isonitrile)-ruthenium(II) complexes, *trans,cis,cis*-[$RuCl_2(CNCH_2Ph)_2$(dppf)] was found to be the most active catalyst and used as catalyst in the transfer hydrogenation of a large variety of ketones in basic propan-2-ol. It has been shown to be particularly efficient in the reduction of dialkyl ketones (TOF upto 1500 h^{-1}) in comparison to arylalkyl ketones (TOF upto 500 h^{-1}).

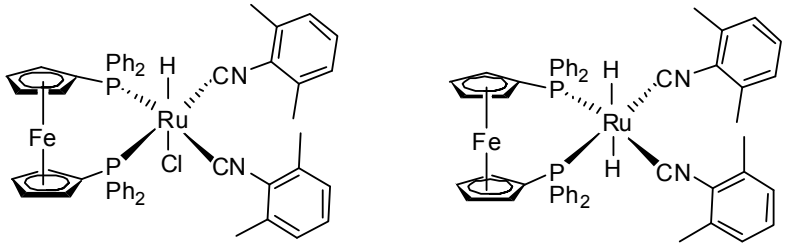


43 **44**

X = Cl, Br
R = Bn, Cy, ^{t}Bu, 2,6-$C_6H_3Me_2$, (S)-(-)-C(H)MePh

Scheme 14: Synthesis of *trans,cis,cis*-[$RuX_2(CNR)_2$(dppf)] (**44**)

In addition, the monohydride derivative *cis,cis*-[RuHCl(CN-2,6-$C_6H_3Me_2)_2$(dppf)] (**45**) and dihydride derivative *cis,cis,cis*-[RuH_2(CN-2,6-$C_6H_3Me_2)_2$(dppf)] (**46**) (Figure 9) have been isolated and characterized. Both hydride complexes catalyze the transfer hydrogenation of acetophenone in the absence of base. The catalytic activity of dihydride species is much more than monohydride as well as dichloride species, indicating that the real active species are dihydride-ruthenium complexes.



45 **46**
Monohydride Dihydride

Figure 9: Monohydride (**45**) and Dihydride (**46**) derivatives of *trans,cis,cis*-[$RuX_2(CNR)_2$(dppf)]

4.2 Hydrosilylation

Rhodium and platinum complexes of sterically hindered 2,6-disubstituted phenylisonitriles were reported by Nile *et al.*[41] for hydrosilylation reaction. The optimum yield of 1-octyltriethylsilane from 1-octene and triethylsilane was obtained at XNC/Rh ratio of 2:1 (Yields. 1:1, 69%. 2:1, 82%, 3:1, 61%, 4:1, 0%), while with the bulky ArNC, the catalyst

remained active even at a higher ratio of 10:1. The Rh-isonitrile complexes showed higher reactivity towards alkylsilanes as compared to alkoxysilanes such as the yield of 1-octylsilane follows the trend $HSiMe_2Ph$ (81%) > $HSiEt_3$ (66%) > $HSi(OEt)_3$ (40%) (Ta
ble 4).

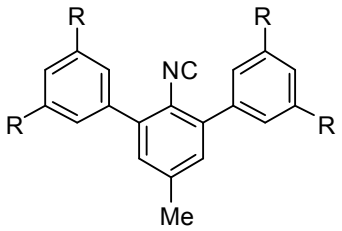
Table 4: Hydrosilylation of 1-octene catalyzed by Rh-isonitrile complexes

isocyanide	silane	isocyanide/Rh	temp. °C	1-octylsilane yield %
XNC	$HSiEt_3$	1:1	100	69
XNC	$HSiEt_3$	2:1	100	82
XNC	$HSiEt_3$	3:1	100	61
XNC	$HSiEt_3$	4:1	100	0
ArNC	$HSiEt_3$	2:1	20	66
ArNC	$HSi(OEt)_3$	2:1	20	40
ArNC	$HSiPhMe_2$	2:1	20	81
ArNC	$HSiEt_3$	10:1	20	53

XNC = 2,6-dimethylphenyisocyanide; ArNC = 2,6-diisopropylphenylisocyanide

Hydrosilylation of acetophenone with dimethylphenylsilane was also achieved using $PtCl_2(2,6\text{-}Me_2C_6H_3NC)_2$ at room temperature[42]. The catalytic activity of the platinum isonitrile complexes was higher than the phosphines.

The rhodium complexes of bulky isonitrile ligands having a meta-terphenyl backbone (Figure 10) were synthesized by Sawamura *et al.*[43] and their catalytic activity was examined in hydrosilylation of cyclohexanone with dimethylphenyl silane in benzene at room temperature (Table 5).



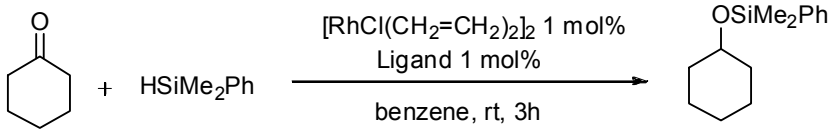
R = H, Me, Me_3Si, $^tBuMe_2Si$

47

Figure 10: Bulky isonitrile ligands with meta-terphenyl backbone

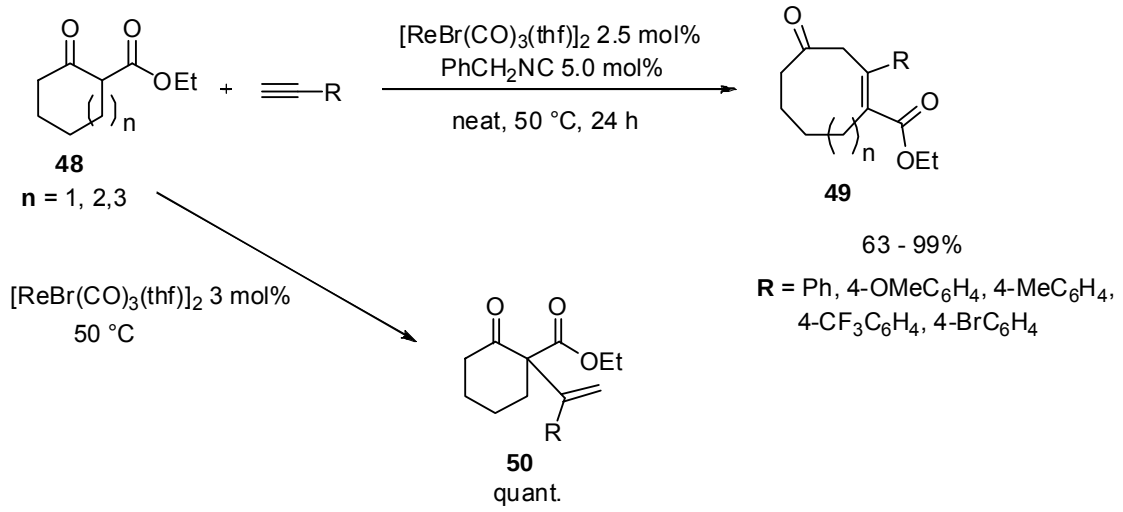
The highest activity was obtained with Rh/L ratio 1:1. The acceleration effect on hydrosilylation reaction which varied with bulkiness of ligands was evaluated with each ligand. Sterically less demanding isonitriles (**47**) (**R** = H, Me, 2,6-diisopropylphenylisonitrile) exhibited less acceleration effect compared to sterically more demanding ligands (**47**) (**R** = Me_3Si, $^tBuMe_2Si$) due to their concave steric features.

Table 5: Hydrosilylation of cyclohexanone using Rh-isonitrile complex



ligands (**R**)	yield %
-	15
H	48
Me_3Si	97
2,6-diisopropylphenylisocyanide	63
PPh_3	24

Very recently, insertion of acetylene into C-C single bond next to carbonyl group of nonstrained cyclic compounds was achieved by Takai and coworkers[44] using rhenium-isonitrile complex (Scheme 15). The reaction of cyclohexanone-2-carboxylic acid ethyl ester (**48**) with phenylacetylene in the presence of rhenium complex $[(ReBr(CO)_3(thf)]_2$ and benzylisonitrile at 50 °C under solvent free conditions gave an eight membered ring product (**49**). In the absence of isonitrile, rhenium catalyzed reaction of a ß-keto ester with phenylacetylene afforded compound **50** in quantitative yield.

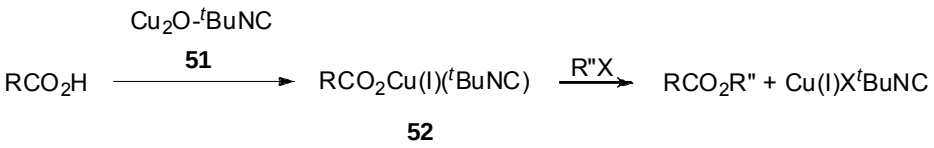


Scheme 15: Re-isonitrile complex catalyzed synthesis of eight membered rings **50**

5. Copper isonitrile complexes

5.1 Esterification of carboxylic acid and cyclopropanation

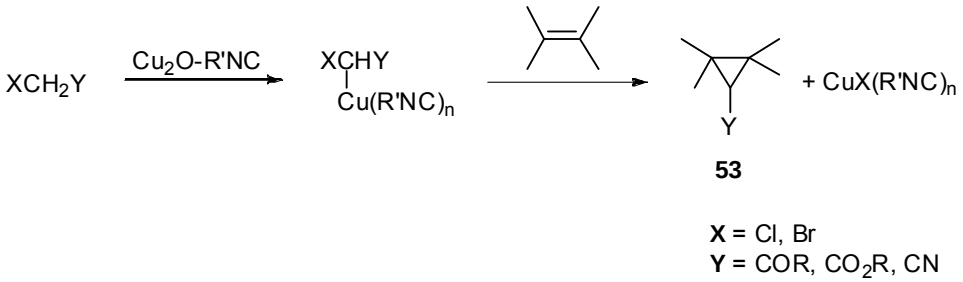
Ito and co-workers[45-47] have reported a number of reactions catalyzed by Cu-isonitrile complexes. For example, esterification of carboxylic acid[45] was performed in the presence of Cu_2O-isonitrile complex (**51**) (Scheme 16).



Scheme 16: Esterification of carboxylic acid

Cu(I) carboxylate-isonitrile complex (**52**) was generated from Cu_2O-isonitrile complex and carboxylic acid, which on reaction with alkyl halide produced the corresponding carboxylic ester. The reaction of α-halocarbonyl or α-halonitrile[46] was performed with α, ß-unsaturated carbonyl or nitrile in the presence of Cu_2O-isonitrile complex to produce cyclopropane derivatives (**53**) (Scheme 17). The key intermediate of this reaction was assumed to be a Cu-

carbenoid which may be formed via an oxidative addition of the C-Cl bond to the Cu_2O-isonitirle complex.

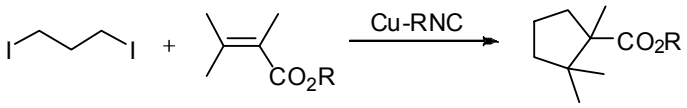


53

X = Cl, Br
Y = COR, CO_2R, CN

Scheme 17: Cyclopropanation of alkenes using Cu_2O-isonitirle complex

Similarly, the reaction of 1,3-diiodopropane with methylacrylate afforded cyclopentanecarboxylic acid methyl ester[47] (**54**) (Scheme 18). In this reaction the formation of 3-iodopropylcopper-isonitirle complex was proposed, which was followed by the subsequent addition to an, α, ß-unsaturated carbo ester and the final cyclization via the intramolecular elimination of the copper halogen-isonitrile complex.



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Scheme 18: Cu_2O-isonitirle complex catalyzed preparation of cyclopentanecarboxylic acid methyl ester (**54**)

6. Conclusion

Till now, the development mainly has been done on metal complexes of monodentate isonitriles and their chemistry, where they have been widely used in catalysis. Multidentate ligands being a sibling of their monodentate analogs have special properties in terms of steric and electronic properties, which make them an attractive candidate for further exploration in catalysis. Nevertheless, chelated complexes are more stable than similar complexes with unidentate ligands, as dissociation of the complex involves breaking two bonds rather than one. The goal of this research work was to synthesize chiral bis(isonitrile) ligands and employ them in catalysis.

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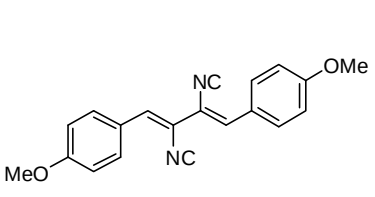
B. Synthesis of Bis-(isonitrile) (BINC) Ligands

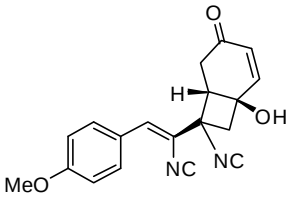
1. Introduction

Isonitriles are extraordinary functional groups which can act as nucleophiles as well as electrophiles in the course of a reaction. The chemistry of isonitriles is fundamentally different from the rest of organic chemistry, since they are one of the chemical compounds with divalent carbon atoms C^{II}, and all of their chemical reactions correspond to conversions of the divalent carbon atoms C^{II} into the tetravalent carbon atoms C^{IV}.

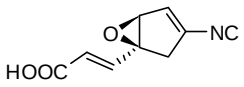
Isonitriles play a vital role in radical reactions and in several total and combinatorial synthesis.[1] Since they are isoelectronic with carbon monoxide, they can substitute the gaseous and poisonous carbon monoxide in organometallic reactions.[2] Isonitriles polymerize under Lewis acid catalysis to form polyiminomethylenes having cylindrical helical structure.[3] Hundreds of isonitrile groups containing natural products were isolated, especially from marine species (Figure 11).[4] Many natural isonitriles show strong antibiotic, fungicidal, or antineoplastic effects.[5] Isonitriles are also used as versatile building blocks for the synthesis of heterocyclic systems.[6]



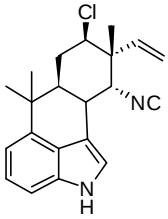
Antibiotic xanthocillin



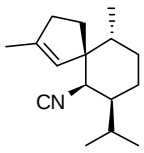
leptocillin



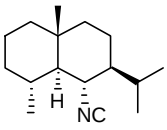
4-((E)-2-carboxyvinyl)-3,4-epoxy-1-cyclopentenyl isocynide



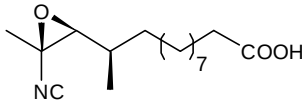
hepalindole A



axisonitrile-3



acenthellin-1



aerocyanidine

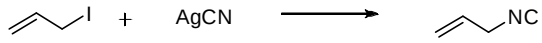
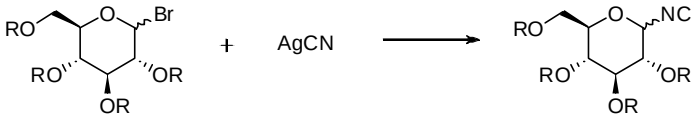
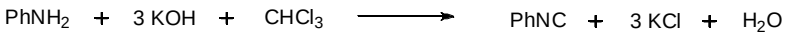
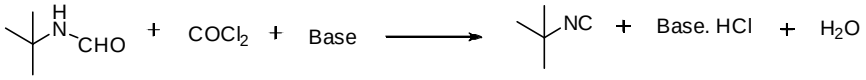
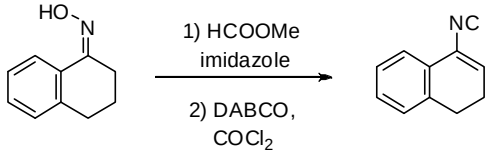
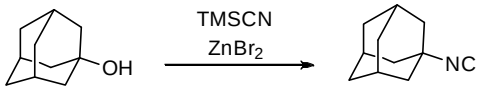
Figure 11: Selective bioactive natural products with isonitrile functionality

Isonitriles were first synthesized in 1859 by Lieke[7] (Table 6) employing a substitution reaction of reactive alkyl halides with silver cyanide, which was further developed by Gautier[8] in 1867. At the same time Hoffmann[9] found a new approach towards isonitriles with the reaction of primary amines with potash and chloroform. During this period, the methods for preparation of isonitriles were facing a number of problems such as their cumbersome preparation, poor substrate tolerance and low yields of products.

In 1921, Passerini[10, 11] introduced the first MCRs (multi component reactions) of isonitriles. Isonitriles reacted with carboxylic acids and carbonyl compounds into the acyloxy-carbonamides. In 1958, isonitriles became generally well available[12, 13], and shortly after, Ugi *et al*.[14] introduced a four-component reaction of isonitriles, which is referred to as the Ugi reaction (U-4CR). The U-4CRs are one-pot reactions of amines, carbonyl compounds, acids, and isonitriles. Many natural products have been formed by the U-4CR, for example a great variety of ®-lactam antibiotics and related compounds has been produced by the U-4CR[15].

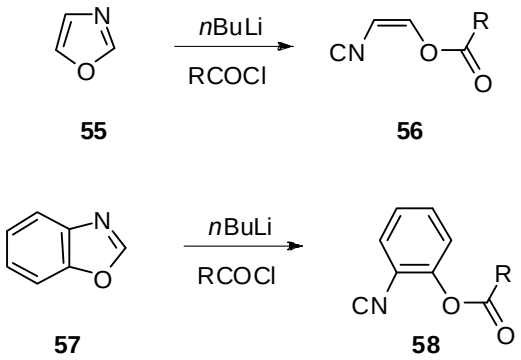
Although several methods have been reported for the synthesis of isonitriles[16], the reaction of N-formamides with phosgene or its synthetic equivalents such as diphosgene and triphosgene is the method of choice considering cost, yield, and implementation.[10a, b] Dehydration of N-formamides was also achieved using $POCl_3$,[10c] chlorodimethylformiminium chloride,[17] DABCO,[18] aryl chlororthionformate,[19] supported sulfonyl chlorides under microwave irradiation,[20] and 2,4,6-trichloro[1,3,5]triazine (cyanuric chloride, TCT).[21] Unfortunately, most of these methods have limited utility and applicability due to extreme toxicity, unmanageable handling, and high costs in the availability of the reagents. Purification of the reaction product can be problematic due to the reactivity of the isonitriles.

Table 6: Methods for Isonitrile preparation

Examples	Methods
	**Lieke, 1859**
	**Meyer, 1866**
	**Hoffmann, 1867**
	**Ugi, 1958**
	**Barton, 1988**
	**Kitano, 1998**

Another barrier to the use of isonitriles is their piercing and well known odor. Almost all commercially available isonitriles are volatile and carry repulsive odor. Ugi states "*The development of the chemistry of isonitriles has probably suffered ... through the characteristic odor of volatile isonitriles, which has been described by Hofmann and Gautier as highly specific, almost overpowering', 'horrible', and 'extremely distressing'. It is true that many potential workers in this field have been turned away by the odor.*" They are sufficiently intolerable to have been included in nonlethal weapons.[22]

Pirrung and coworkers[23d] developed a new family of fragrant isonitriles by treating oxazole (**55**) or benzoxazole (**57**) with n-butyllithium and various acyl chlorides to generate a series of (Z)-isocyanovinyl esters (**56**) (Scheme 19) and 2-isocyanylphenyl esters (**58**), which smell of mild isonitrile at their worst and like taffy or cherry at their best. The sweet-smelling compounds are easy to make and react just like their fragrant cousins.

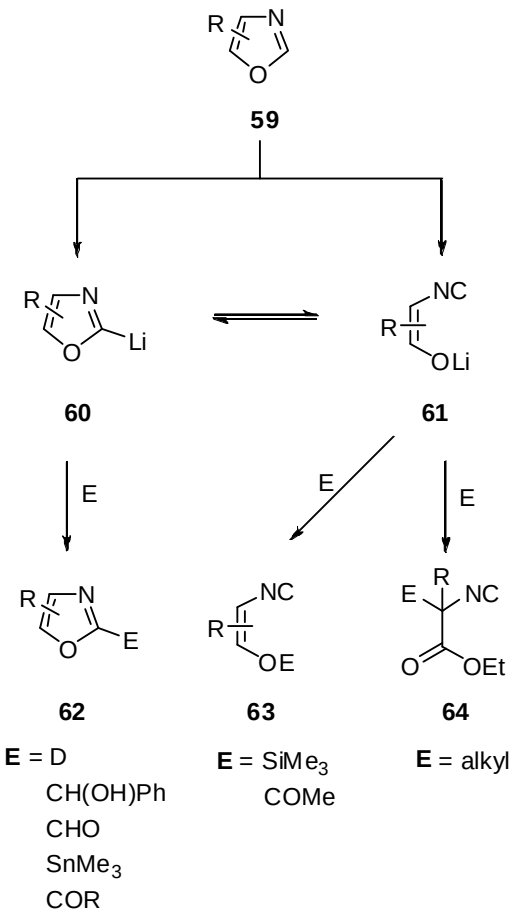


R = Me, ^{t}Bu, O-^{t}Bu, Ph, C_6H_4CN

Scheme 19: Synthesis of fragrant isonitriles from oxazoles

The approach towards the preparation of chiral bis(isonitrile) ligands is inspired from the synthesis of monoisonitriles via metallation of oxazoles (**59**).[23] The three C-H groups in oxazole exhibit different acidity. The 2-H is the most acidic with pKa = 20 ± 2. An equilibrium mixture of C-2 anion (**60**) and the open chain isomer, α-isocyano enolate (**61**) was achieved via lithiation of oxazoles (Scheme 20). The existence of facile ring chain tautomerism of 2-lithiooxazoles was first proposed by Schoellkopf and co-workers.[24] Oxazoles can be converted into isonitriles upon metalation followed by trapping of the resulting anion with hard electrophiles such as acetyl chloride or trimethylsilyl chloride.

Selective trapping of this equilibrium anion (**60**, **61**) is electrophile dependent, for example, treatment of lithiated 2-H oxazoles with D_2O[25, 26] or carbonyl electrophiles[23a, 24] leads to the corresponding 2-substituted oxazoles **62** whereas quenching with chlorotrimethylsilane,[24] acyl halides[23c] or alkyl halides[26] affords the open chain products **63** and **64**.

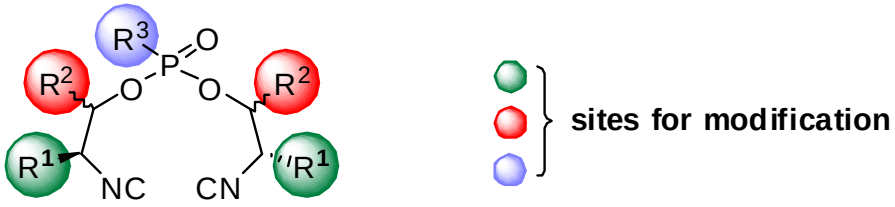


Scheme 20: Chemistry of metallated oxazoles

2. Synthesis of Bis(isonitrile) Ligands

2.1 Bis(isonitrile) Ligands derived from amino alcohol

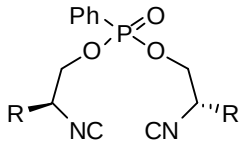
A broad variety of sterically and electronically different bis(isonitrile) ligands (**65**) were prepared by structural variations at R^1, R^2 and R^3. Substituted phosphorus oxide acted as a linker between two isonitrile arms (Figure 12). By fixing the stereochemistry at R^1, which arrives from natural amino acid such as valine and *tert*-leucine, stereochemistry at R^2 can be adjusted using synthetic methods.



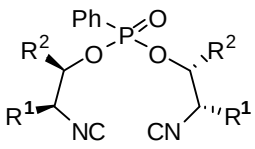
65

Figure 12: Representative structure of Bis(isonitrile) ligands

We envisioned to develop a synthetic protocol that would provide an easy and short access to a wide array of ligands **66-69** (Figure 13). Our synthetic plan called for 2-oxazolines **71a-e** as common intermediates, which are among the most ubiquitous motifs in ligand design.[27] This strategy, which differs from known synthetic approaches to isonitriles, is attractive because simple and readily accessible oxazolines **71** can be used as precursors. A wide variety of sterically and electronically different bis(isonitrile) ligands can be prepared by structural variations of the oxazolines **71** and phosphorus chloride.



66



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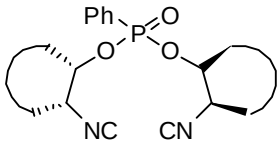

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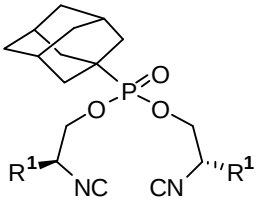
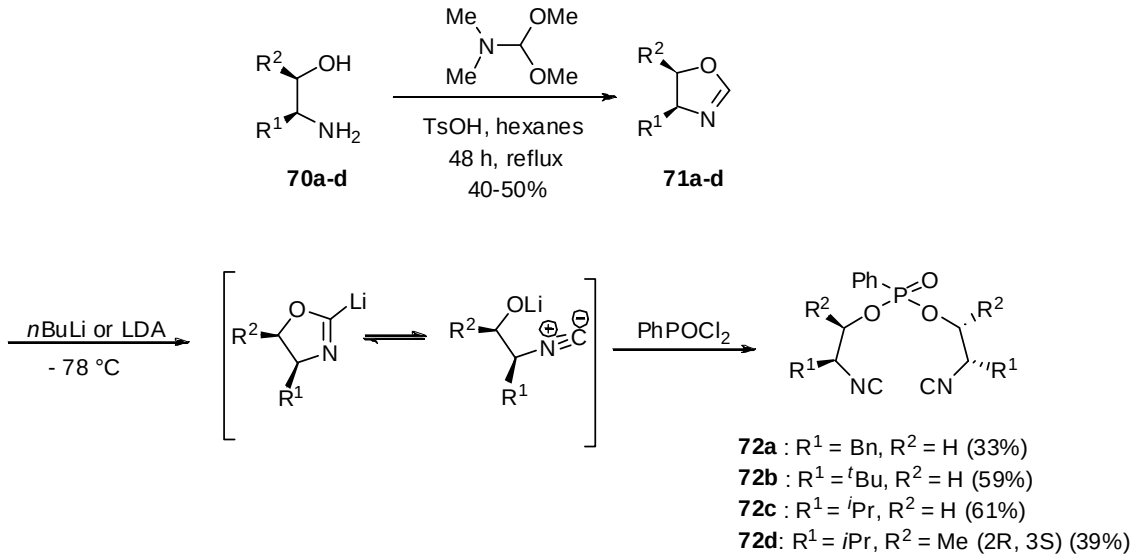


69

Figure 13: Structural variation of bis(isonitrile) ligands

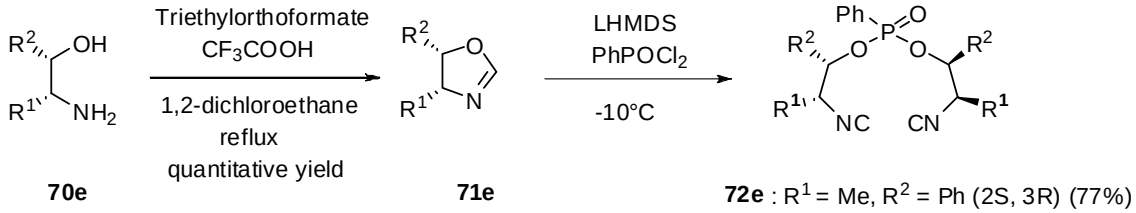
In the forward sense, the synthesis commenced with a two step conversion of the commercially available and inexpensive amino alcohols **70a-d, f** and **70e** (Scheme 25 and 26) into substituted bis(isonitriles) **72** via oxazoline lithiation as outlined in scheme 21-24. When

treated with DFM-DMA (N,N-dimethylformamide dimethylactal) under reflux condition, amino alcohols **70a-d** gave corresponding 2-oxazolines **71a-d** in 40-50% yields[28] whereas the synthesis of 2-oxazoline **71e, f** with additional chiral centre at C-2 was accompanished by refluxing amino alcohols **70e, f** with triethylformate and trifluroacetic acid in 1,2-dichloroethane (Scheme 22 and 23).



Scheme 21: Synthesis of BINC ligands **72a-d**

With the 2-oxazolines **71** in hand, preparation of the requisite bis(isonitrile) ligands **72** was achieved via lithiation of 2-oxazolines (**71**) following the procedure of Meyers and Novachek[28] and subsequent treatment with 0.6 equivalent of phenylphosphonic dichloride at low temperature (Scheme 21-24). These compounds were isolated in analytically pure form as colorless solids or oils, depending upon the nature of the substituents at C-2 and C-3.



Scheme 22: Synthesis of BINC ligands **72e**

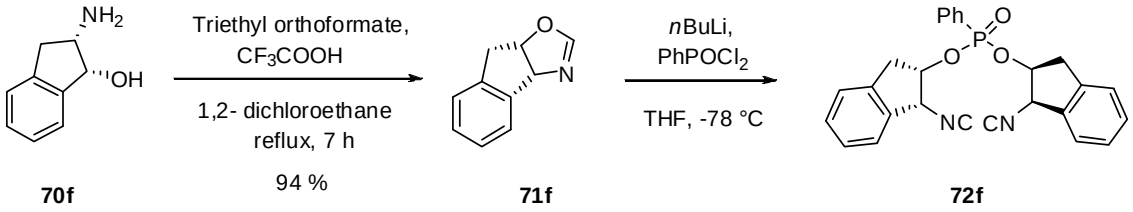
The best results for the valine- and *tert*-leucine-derived ligands **72 b, c** were observed when lithium diisopropylamide (LDA) was used as a base (Table 7, entry 3, 5), while **72a** could only be obtained in lower yield by applying *n*BuLi for deprotonating **71a** at -78 °C (Table 7, entry 2). It was observed that the synthesis of bis(isonitrile) ligands **72d** and **72e** was achieved at -10 °C using LHMDS and LDA as bases, respectively (Table 7, entry 12, 13), whereas all attempts of performing the reaction at -78 °C were unsuccessful (Table 7, entry 9-11).

Table 7: Effect of base on the synthesis of BINC ligands **72a-e**

entry	ligand	base	temp. (°C)	time (h)	yield (%)
1	**72a**	LDA	- 78	12	-
2	**72a**	*n*BuLi	- 78	2	33
3	**72b**	LDA	- 78	2	59
4	**72b**	*n*BuLi	- 78	12	20
5	**72c**	LDA	- 78	2	61
6	**72c**	*n*BuLi	- 78	12	20
7	**72c**	^{t}BuLi	- 78	12	traces
8	**72c**	LHMDS	- 78	12	-
9	**72d**	LDA	- 10	2	70
10	**72e**	LDA	- 78	4	<10
11	**72e**	*n*BuLi	- 78	12	-
12	**72e**	LHMDS	- 78	2	10
13	**72e**	LHMDS	- 10	2	77

Moreover, bis(isonitrile) ligand derived from (1*R*,2*S*)-2-amino-2,3-dihydro-1H-inden-1-ol (**70f**) (Scheme 23) was also prepared using the synthetic route explained in Scheme 21 and 22. Amino alcohol **70f** was transformed into the oxazoline **71f** in excellent yield as described

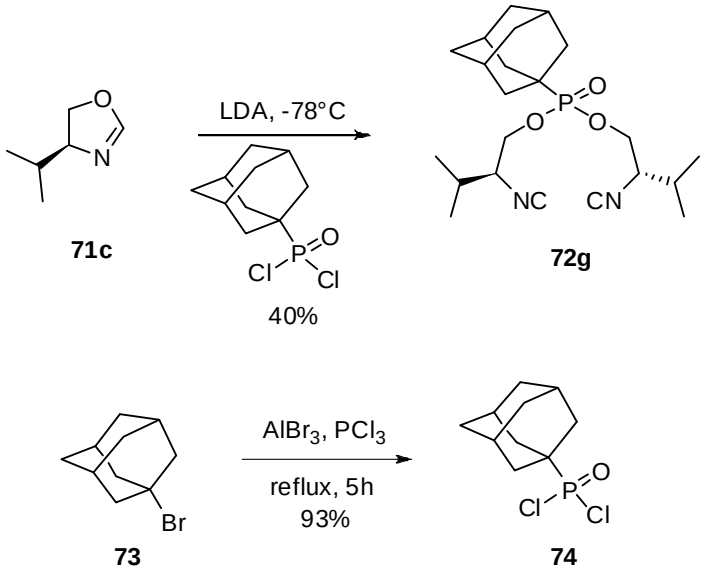
earlier, which was subjected to lithiation with *n*BuLi followed by trapping of lithiated oxazoline with $PhPOCl_2$ to give rise to BINC **72f**. All efforts to purify the ligand **72f** were not fruitful because of its instability on silica, which may arise from the presence of very acidic benzylic proton proximal to isonitrile group. However, a pure sample for NMR studies was obtained by preparative HPLC.



70f **71f** **72f**

Scheme 23: Synthesis of BINC ligand **72f**

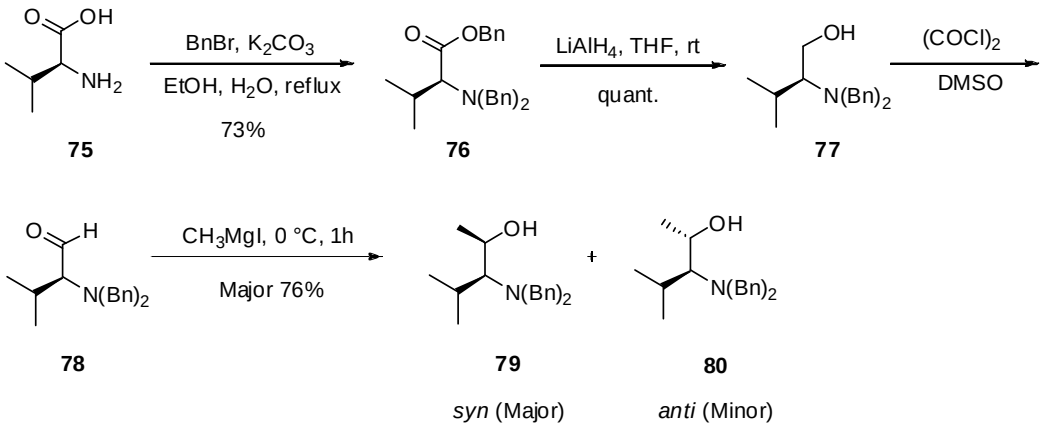
A different bis(isonitrile) ligand **72g** in contrast to other BINC ligand **72a-e** was planned to be prepared by changing the source of phosphorus dichloride. The reaction of admantylbromide (**73**), with aluminiumtribromide in refluxing phosphortrichloride furnished admantylphosphonic dichloride (**74**) in 93% yield (Scheme 24). Lithiation of oxazoline (**71c**) using LDA, followed by treatment with admantylphosphonic dichloride (**74**) afforded the desired BINC ligand (**72g**) in 40% yield.



71c **72g** **73** **74**

Scheme 24: Synthesis of BINC ligands **72g**

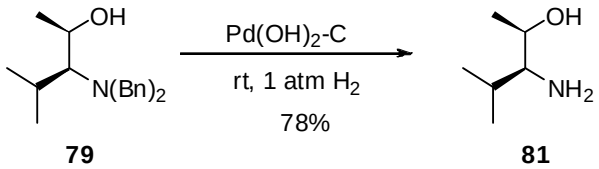
The preparation of ß-amino alcohol **70d**, precursor for BINC **72d** (Scheme 22) synthesis was achieved via well defined Reetz methodology.[29] Valine, after treatment with benzylbromide and potassium carbonate in ethanol/water solvent mixture at reflux was transformed into *N***,** *N*-dibenzylamino benzyl esters (**76**) in 73% yield, subsequently followed by its reduction to optically active alcohol (**77**) in quantitative yield. Aldehyde (**78**) prepared by Swern oxidation of 2-(dibenzylamino) alcohol (**77**) was used without further purification for the next step, as summarized in Scheme 25.



Scheme 25: Synthesis of ß-amino alcohols *syn*-**79** and *anti*-**80**

Treatment of the *N*,*N*-dibenzylamino aldehydes (**78**) with 2 equiv of MeMgCl in ether at 0 °C gave the corresponding *syn* amino alcohols (**79**) in good chemical yields and excellent stereoselectivity (Scheme 25). The degree of stereoselection was moderately affected by the size of the substituent at the stereogenic center in the *R*-amino aldehyde.

After purification by flash chromatography *syn*-**79** was debenzylated to the final *ß*-amino alcohols *syn*-**81** by hydrogenolysis on Pearlman's catalyst in excellent chemical yields (Scheme 26). Assignment of the absolute stereochemistry of amino alcohol (**81**) was done by ^{1}H NMR spectroscopy.



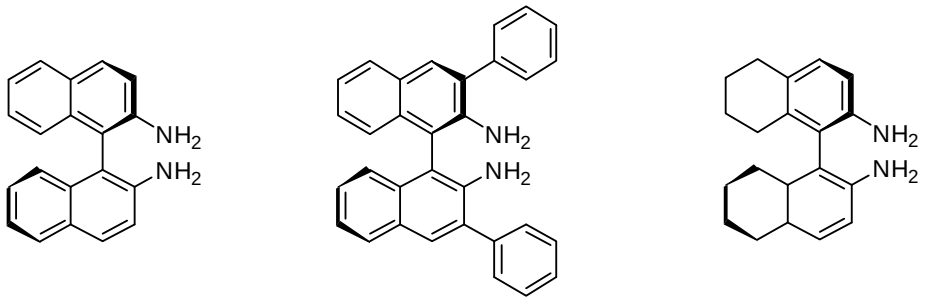
Scheme 26: Debenzylation of ß-amino alcohols *syn*-**79**

No erosion of stereochemistry was observed in the course of the reaction, which gave rise to the new BINC ligands **72** as odorless compounds in enantiomerically pure form. The structure of **72b** was unambiguously established by X-ray analysis (Figure 14), which revealed a dissymmetric arrangement of the two diastereotopic isonitrile arms in the solid state that are also clearly distinguishable, in both the ^{1}H and ^{13}C NMR spectra.

Figure 14: X-ray structure of BINC **72b**

2.2 1,1'-binaphthyls and H_8-1,1'-binaphthyl based bis(isonitrile) ligands

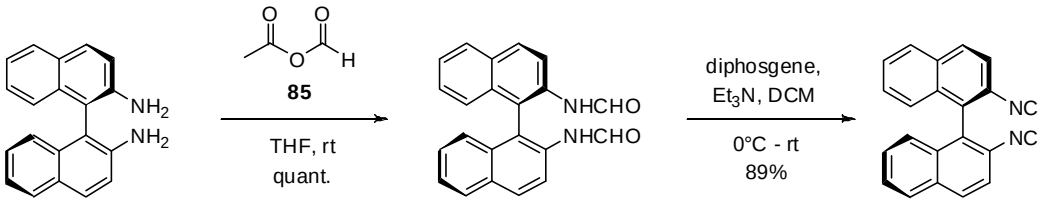
Optically active 1,1'-bi-2-naphthylamine (BINAM) (**82**), and their numerous derivatives (**83**) have established extensive application as chiral ligands for asymmetric catalysis.[30] During the last years, it was found that several ligands based on the H_8- binaphthalene core (**84**) (Figure 15) show higher asymmetric induction than those based on parent 1,1'-binaphthyls in asymmetric hydrogenations, alkylations of aldehydes, hetero-Diels-Alder, and Morita-Baylis-Hillman reactions.[31] Higher efficiency and enantioselectivity was gained by using chiral catalysts derived from optically active H_8-1,1'-bi-2-naphthylamine (H_8-BINAM) (**84**) for asymmetric reactions than those prepared from their parent ligands, (**82**) due to the steric and electronic modulation in the binaphthyl backbone.[32] Therefore, optically active H_8-1,1'-bi-2-naphthylamine (H_8-BINAM) represent extremely useful starting materials for the synthesis of relevant chiral ligands.



82 **83** **84**

Figure 15: BINAM derivatives **82-84**

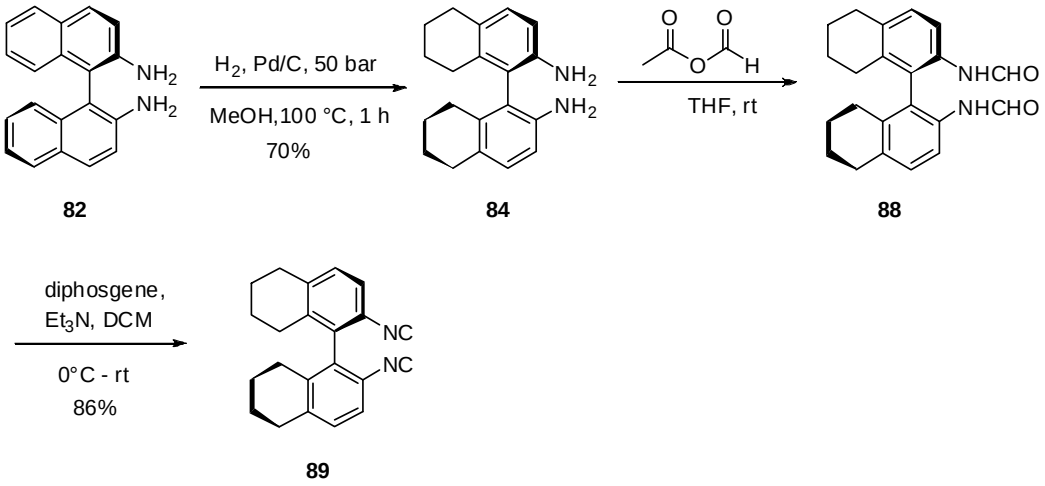
Inspired by the current course of interest in the development of 1,1'-binaphthyls and H_8-1,1'-binaphthyl based ligands, we have prepared structurally related bis(isonitrile) ligands incorporating the parent 1,1'-binaphthyls and H_8-1,1'-binaphthyl core. In this part, the syntheses of isonitriles were achieved by classical method *i.e.* dehydration of N-formamides using diphosgene and triethylamine. Commercially available (*R*)-BINAM (**82**) was chosen as starting material for the synthesis of 1,1'-binaphthyls and H_8-1,1'-binaphthyl based bis(isonitrile) ligands (Scheme 27 and 28). The formylation of enantiopure (*R*)-1,1'-bi-2-naphthylamine (BINAM) (**82**) was carried out with acetic formic anhydride (**85**) in THF at room temperature (Scheme 27). Under these conditions the reaction proceeds very cleanly and furnished (*R*)-N,N'-(1,1'-binaphthyl-2,2'-diyl)diformamide (**86**) products in nearly quantitative yield, which further transformed into (*R*)-2,2'-diisocyano-1,1'-binaphthyl (**87**) with diphosgene under basic conditions in good isolated yields.



82 **86** **87**

Scheme 27: Synthesis of (*R*)-2,2'-diisocyano-1,1'-binaphthyl (**87**)

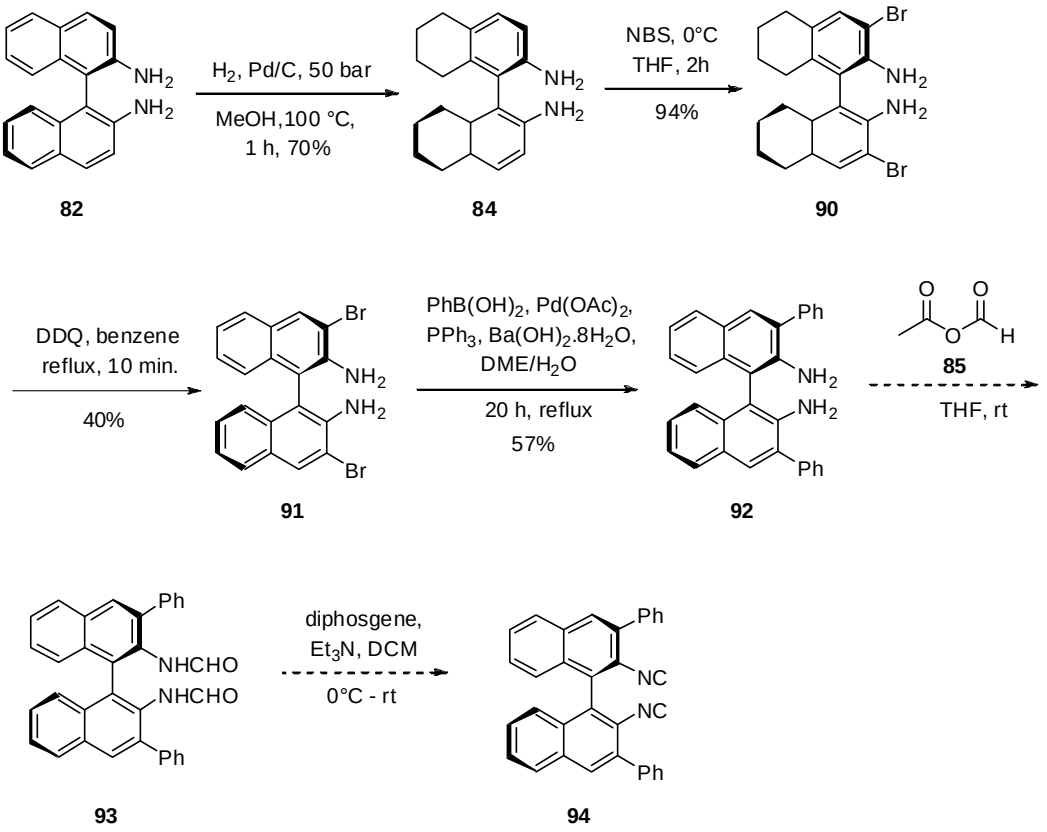
In analogy to synthesis of (*R*)-2,2'-diisocyano-1,1'-binaphthyl (**87**), synthesis of (*R*)-2,2'-diisocyano-H_8-1,1'-binaphthyl (**89**) was undertaken by similar strategy. (*R*)-2,2'-diamino-1,1'-binaphthyl (**82**) was quantitatively reduced to its H_8-derivative (**84**) under 50 bar H_2 at 100 °C with Pd/C (10 mol %) within 60 min (Scheme 28). No traces of the starting material or the opposite enantiomer of **84** could be detected by HPLC. Formylation of (*R*)-2,2'-diamino-H_8-1,1'-binaphthyl (**84**) with acetic formic anhydride (**85**), followed by treatment with diphosgene and triethylamine afforded (*R*)-2,2'-diisocyano-H_8-1,1'-binaphthyl (**89**) in 86% yield.



Scheme 28: Synthesis of (*R*)-2,2'-diisocyano-H_8-1,1'-binaphthyl (**89**)

Following the protocol developed by Maruoka and coworkers,[33] chiral 3,3′-diphenyl derivatives× of (*R*)-2,2'-diisocyano-1,1'-binaphthyl (**94**) was palnned to be synthesized as summarized in scheme 29. 3,3′-dibromo BINAM (**91**) acts as a key intermediate for the derivatization of BINAM (**82**). Dibromination was achieved on partially hydrogenated H_8-BINAMA (**84**) at 3,3' position by treatment with two equivalents of N-bromosuccinimide in THF at 0 °C in excellent yield. Subsequently, **90** was rearomatized with DDQ in benzene under reflux condition to give the desired (R)-3,3'-dibromo-1,1'-binaphthyl-2,2'-diamine (**91**) in good yield. No loss of enatioselectivity was observed, as confirmed by HPLC analysis. Finally, the Suzuki-Miyaura coupling of (R)-3,3'-dibromo-1,1'-binaphthyl-2,2'-diamine (**91**) with phenylborornic acid furnished 3,3′-diphenyl BINAM (**92**) in good chemical yield,

which subsequently could be subjected to formylation followed by dehydration of formamide to yield chiral 3,3′-diphenyl derivatives of (*R*)-2,2'-diisocyano-1,1'-binaphthyl (**94**).

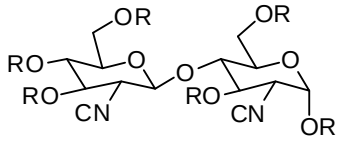


Scheme 29: Synthesis of 3,3'-diphenyl-(*R*)-2,2'-diisocyano-1,1'-binaphthyl (**94**)

2.3 Carbohydrate based bis(isonitrile) ligands

Carbohydrates are the most abundant compounds of the chiral pool, but unlike amino acids, they are far less frequently employed for the preparation of chiral ligands for metal-catalyzed asymmetric synthesis.[34, 35] Carbohydrates have many advantages: they are readily available, are highly functionalized and have several stereogenic centers. This enables series of chiral ligands to be synthesized and screened in the search for high activities and selectivities for each particular reaction. However, the presence of both stereocentres and functional groups in great quantities is regarded rather more of an obstacle than an advantage. In contrast, efficient examples of carbohydrate-based ligands have been reported, many interesting structures have emerged and application of such complex agents has recently met with increasing attention.

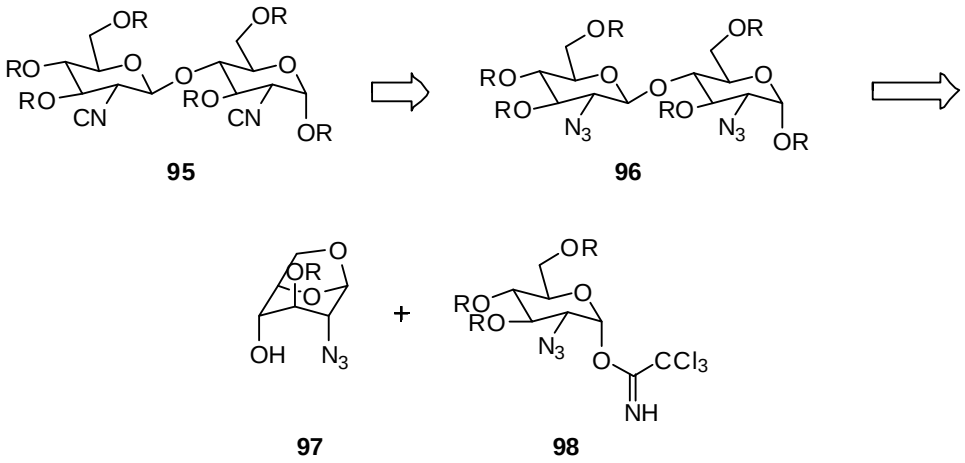
Attracted by the impressive results that have been obtained using carbohydrate derivative ligands in a wide range of catalytic asymmetric reactions, we have also the synthesis of new chiral bis(isonitrile) ligands **95** (Figure 16) with carbohydrate backbone, which are accessible from inexpensive D-glucose.



95

Figure 16: Basic structure of carbohydrate based chiral bis(isonitrile) ligands **95**

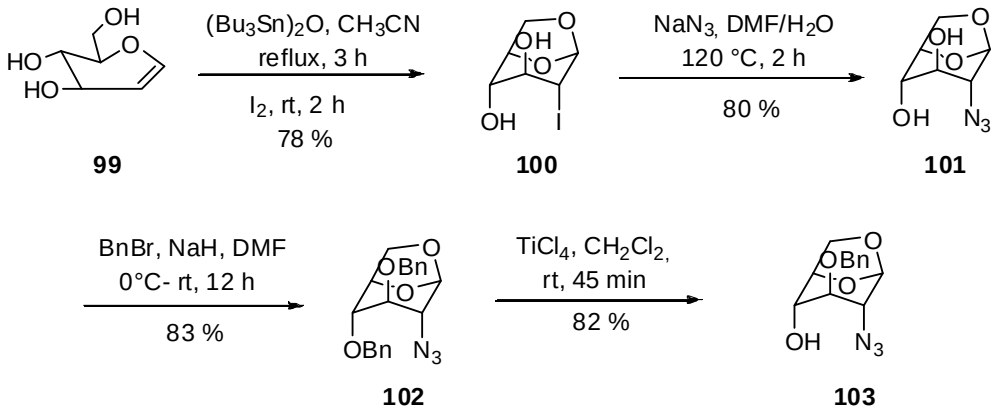
Our reterosynthetic strategy towards the carbohydrate based chiral bis(isonitrile) ligands (**95**) is illustrated in Scheme 30. We envisaged that **96** could be converted into **95** through hydrolysis of azide group followed by amine formylation. Synthesis of **96** was anticipated from the glycosidation of fragments **97** and **98**,[36] which could be easily accessed from D-glucal (**99**).



Scheme 30: Reterosynthetic analysis of **95**

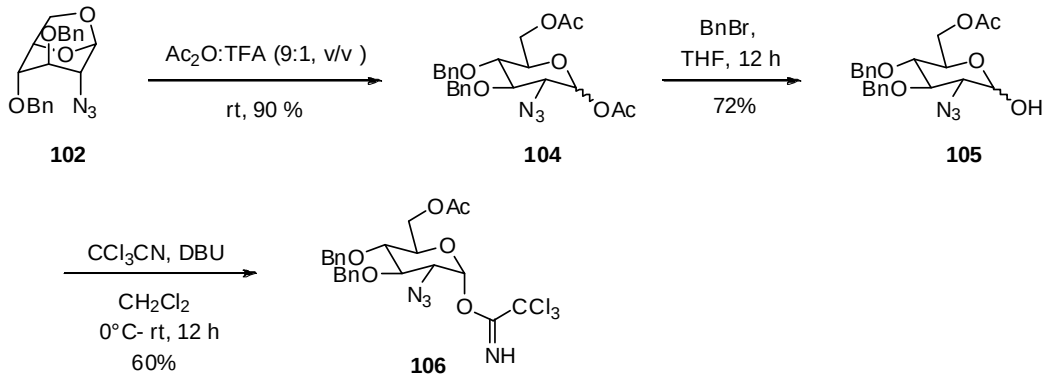
We therefore devised a synthetic route towards carbohydrate based BINC ligands with D-glucal (**99**) as key intermediates. The use of D-glucal has several advantages, as they are easily accessible from D-glucose and highly stable against all conditions.

Starting from glucal, 1,6-anhydro-2-deoxy-2-iodo-ß-D-glucopyranose (**100**) was prepared in good yield by refluxing D-glucal (**99**) with bis(tributylstannyl)oxide in acetonitrile followed by iodine treatment (Scheme 31). Upon treatment with sodium azide in DMF-H_2O at 120 °C, the azide (**101**) was obtained in 80% yield from iodo (**100**). The diol (**101**) was easily transformed into monobenzylated (**103**) via benzylation followed by $TiCl_4$ mediated debenzylation at position 4 of (**102**). By this method, the target, 1, 6-anhydro-2-azido-3-O-benzyl-2-deoxy-ß-D-glucopyranose (**103**) was obtained in 82% yield.



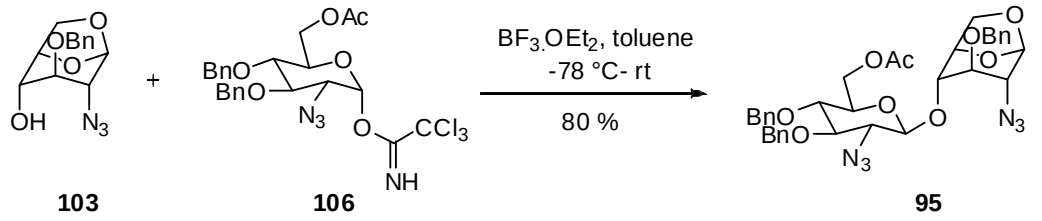
Scheme 31: Synthesis of 1, 6-anhydro-2-azido-3-O-benzyl-2-deoxy-ß-D-glucopyranose (**103)**

Next, the synthesis of fragment **106** was achieved from **102** (Scheme 32). Opening of the anhydro ring in **102** using CF_3COOH-Ac_2O gave the anomeric mixture of the diacetate (**104)** in excellent yield which was converted to the anomeric alcohol (**105)** using benzylbromide in THF. The anomeric mixture of alcohol (**105)** was allowed to react with the trichloroacetonitrile and DBU in dichloromethane to obtain imidate **106** in 60% yields.



Scheme 32: Synthesis of imidate **106**

Towards the end, glycosidation of **103** with **106** using catalytic amount of $BF_3.OEt_2$ as an activator in toluene at -78 °C led to the formation of disaccharide (**107**) (Scheme 33), which can be transformed into bis(isonitrile) ligand (**95**) via three more steps including azide hydrolysis to amine, amine formylation and finally dehydration of foramide.



Scheme 33: Glycosidation of **103** and **106**

3. Conclusion

In summary, a convenient, short and facile method for synthesis of enantiopure bis(isonitrile) ligands was developed. A wide range of bis(isonitrile) ligands **72** were prepared in moderate to good yields by structural variation of the oxazolines **71** and phosphorus chloride. Further, bis(isonitrile) ligands **87**, **89**, **94** and **95** were also synthesized having binaphthyl and carbohydrate backbone respectively using conventional methods.

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C. Synthesis and Application of Pd-bis(isonitrile) catalysts

1. Introduction

The increasing number of synthetic transformations facilitated by transition metal catalysts shows no sign of abating. Of all the organometallic compounds known, those derived from palladium have become the most important catalysts for an array of synthetic reactions. Generally, palladium has achieved a prominent role in catalysis and synthesis due to its electronegativity ($\chi = 2.2$), which facilitates the formation of relatively strong Pd–H and Pd–C bonds, but also gives rise to polarized Pd–X bonds. It also allows easy access to 0 and +2 oxidative states, where palladium-centered reactions such as oxidative addition, transmetallation and reductive elimination processes occur with dynamic changes in geometry of palladium.[1]

Pd-isonitrile complexes were widely used as catalyst precursors by Ito and co-workers in intra- and intermolecular bissilylation of alkynes and alkenes (Chapter A.2.1). Villemin and co-workers also reported palladium-isonitrile complexes and their use in Suzuki Miyaura coupling (Chapter A.2.2). More interestingly, Kazmaier has reported the $Pd(^tBuNC)_2Cl_2$ catalyzed bisstannylation of asymmetric alkynes (Chapter A.2.3). Owing to their electronic properties, being also strong σ-donor ligands like N-heterocyclic carbenes (NHC) and Arduengo's carbenes (Figure 17), the palladium isonitrile complexes are good candidates for cross-coupling reactions and aerobic Wacker oxidations. Especially, large bite angles of these chelated metal complexes have proven to be beneficial for activity and selectivity in cross-coupling reactions.[2]

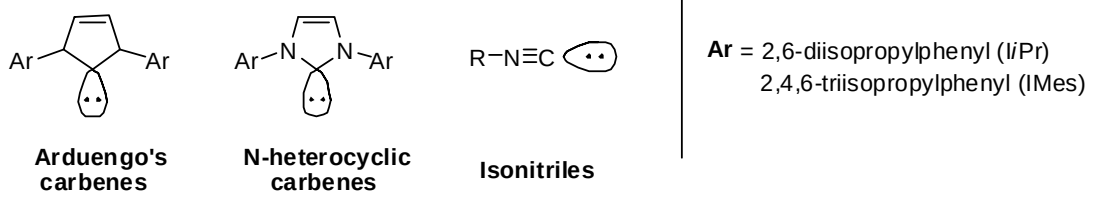
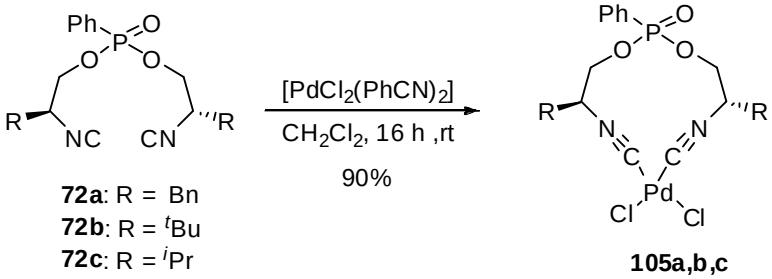


Figure 17: Analogy between carbenes and isonitriles

2. Synthesis of [$PdCl_2$(BINC)] complexes

We prepared [$PdCl_2$(BINC)] complexes to study their catalytic activity in Suzuki-Miyaura coupling as well as in aerobic Wacker oxidation. Complexation of **72a**, **b, c** with [$PdCl_2(PhCN)_2$] in dichloromethane at room temperature gave rise to Pd^{II} complexes **105a**, **b**, **c** in excellent yields, which were characterized by NMR and IR spectroscopy as well as by X-ray structure analysis of **105b** (Scheme 34, figure 18).



72a: R = Bn
72b: R = ^{t}Bu
72c: R = ^{i}Pr

105a,b,c

Scheme 34: Synthesis of **105a, b, c** complexes

The latter revealed that **72b** indeed acts as a bidentate ligand forming a 12-membered ring with palladium. Nevertheless, the bite angle between the isonitrile arms at the palladium center is 88°, quite normal for a square-planar d_8 complex. The two carbons of isonitrile moiety in the complex **105b** are bonded to the Pd center with bond distances of 1.9365 Å (C8) and 1.9435 Å (C1), respectively (Figure 18, table 8), which indicates a dissymmetric arrangement of the two isonitrile moieties around the metal center. This geometry is also reflected in solution, as can be seen from ^{1}H NMR spectrum of **105b**, which displays one set of signals for each isonitrile arm.

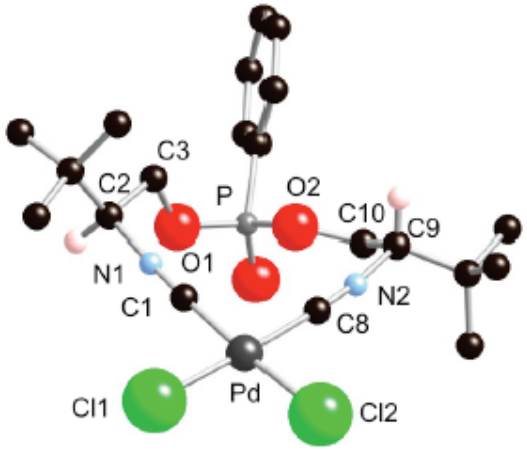


Figure 18: X-ray structure of **105b** complex

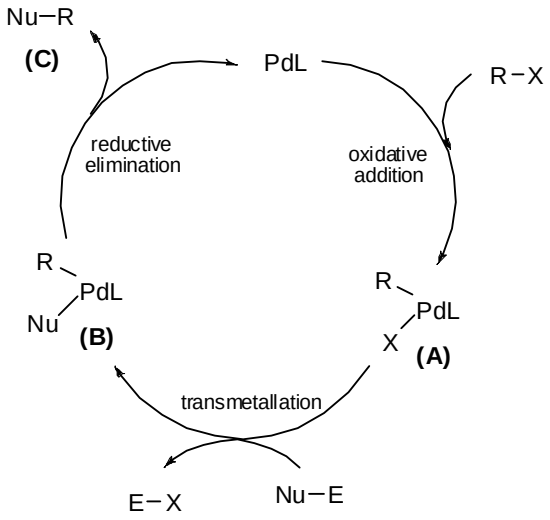
^{1}H NMR studies were also performed to observe any changes in the geometry of complex with respect to temperature. However, no remarkable changes were observed at high as well as at low temperature NMR spectrum. The IR spectrum of [$PdCl_2$(^{t}Bu-BINC)] (**105b**) showed a broad ν(N≡C) absorption at 2237 cm^{-1}. The blue shift of 97cm^{-1} indicated isonitrile complexation with palladium. The two weak Pd-Cl vibrational bands at 343 (w) and 321 (w) cm^{-1} were also observed in IR spectrum which is indicative of a square planar complex with *cis* configuration as confirmed by X-ray analysis.

Table 8: Selected bond lengths [Å] and angles [°] of **105b**.

Bond lengths [A°]		Bond angles [°]	
Pd-Cl1	2.296	C1-Pd-C8	88.2
Pd-Cl2	2.299	C11-Pd-C12	93.7
Pd-C1	1.943	Pd-C1-N1	177.2
Pd-C8	1.935	Pd-C8-N2	174.4
C1-N1	1.128	C1-N1-C2	177.6
C8-N2	1.136	C8-N2-C9	171.8
N1-C2	1.457	C1-N1-C2-C3	62.5
N2-C9	1.453	C8-N2-C9-C10	43.6

3. Suzuki-Miyaura coupling

The palladium-catalyzed Suzuki cross-coupling reaction of aryl bromides, aryl iodides, and pseudohalides (e.g. triflates) is a general method employed for the formation of C-C bonds.[3] The use of aryl chlorides in coupling reactions has proven difficult but would economically benefit a number of industrial processes.[4]



R = aryl or vinyl; **Nu** = aryl; **E** = $B(OH)_2$

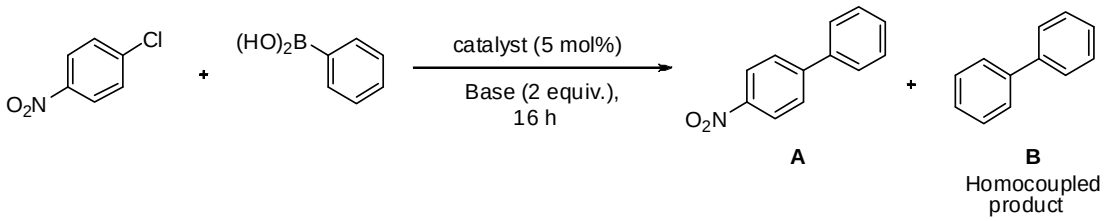
Scheme 35: Reaction mechanism for Suzuki coupling

The first step in the mechanism of Suzuki cross-coupling is oxidative addition (a) of palladium to the halide forming intermediate **(A)**. A transmetallation (b) with boronate forms the organopalladium specie **(B)**. The last step is a reductive elimination (c) which results in the product **(C)** and regeneration of the catalyst (Scheme 35). The mechanism shown above indicates only the main steps proposed for Suzuki coupling, because the details may vary with conditions.[5]

Inspired by the results reported by Villemin and co-workers (Scheme A.2.2), palladium-bis(isonitrile) complexes were tested for Suzuki-Miyaura coupling. An initial screening revealed that **105b** showed best activity in the presence of a solution of K_3PO_4 in DMA at 120°C for 16 h as compared to **106a** and **106b** for Suzuki coupling of activated 4-

chloronitrobenzene with phenylboronic acid (Table 9, entry 4-6). Homocoupled product (**B**) was obtained as a side product on employment of **106a** as catalyst in the presence of toluene and THF (Table 9, entry 1-3), whereas changing the solvent to DMA does not lead to any side products. However, it was found that **106b** was inactive under optimized conditions (Table 9, entry 5). The activity of catalyst **105b** was found to be the best in the presence of two equivalent of K_3PO_4 compared to Cs_2CO_3 and KF (Table 9, entry 6-8). Byproducts resulted from the insertion of isonitriles in the reaction were not observed.

Table 9: Optimization for phenylation of 4-chloronitrobenzene by phenylborornic acid



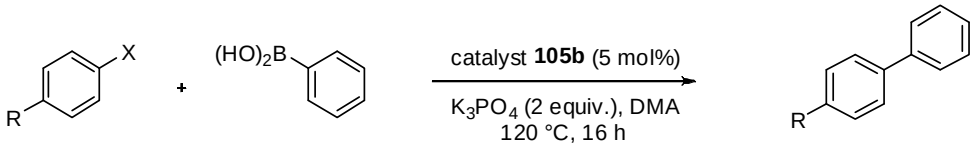
entry	catalyst	base	solvent	temp. (°C)	yield (%) A	yield (%) B
1	[Pd(OAc)$_2$(^{t}*Bu*-BINC)] (**106a**)[a]	K_3PO_4	Toluene	100	20	32
2	(**106a**)	K_3PO_4	THF	70	28	25
3	(**106a**)	KF	THF	70	27	31
4	(**106a**)	K_3PO_4	DMA	120	46	-
5	[Pd(dba)$_2$(^{t}Bu-BINC)] (**106b**)[a]	K_3PO_4	DMA	120	-	-
6	[PdCl$_2$(^{t}Bu-BINC)] (**105b**)	K_3PO_4	DMA	120	94	-
7	(**105b**)	Cs_2CO_3	DMA	120	57	-
8	(**105b**)	KF	DMA	120	51	-

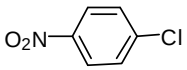
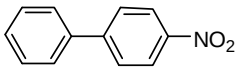
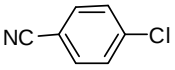
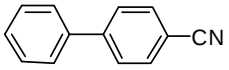
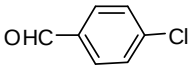
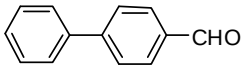
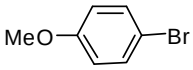
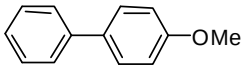
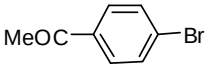
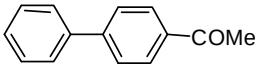
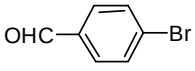
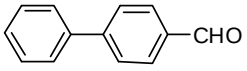
[a] prepared in situ

[PdCl$_2$(^{t}BuNC)] (**105b**) is also considerably more stable to air and moisture than the corresponding **106a** and **106b**. Consequently, catalyst **105b** was used for all subsequent coupling reactions (Table 10). Having obtained the optimized conditions, a variety of substituted aryl chlorides and aryl bromides were investigated for Suzuki coupling reaction catalyzed by **105b** (Table 10). A variety of functional groups on the aryl halides were well tolerated by catalyst **105b**. Electron donating and electron withdrawing substituents were

both well tolerated by the catalytic system and provided the corresponding coupling product in good yields. 4-chlorobenzaldehyde showed diminished reactivity allowing only 10 % yield (Table 10, entry 3). However, activated 4-bromobenzaldehyde afforded a coupled product in good yield (Table 10, entry 6).

Table 10: Complex **105b** catalyzed Suzuki-Miyaura coupling reaction



Entry	Aryl halide	Product	Yield (%)
1			94
2			80
3			10
4			75
5			81
6			87

4. Aerobic Wacker oxidation

The palladium(II)-catalyzed oxidation of alkenes to methyl ketones, known as the Wacker oxidation, is one of the most important catalytic applications in industry.[6]

The first oxidation of alkenes using Pd(II) Chloride solution was discovered in late 19th century by Phillips[7] (1894), where this reaction was used as a test for alkenes (Pd black was the indicator) (Equation 1).

$$C_2H_4 + Pd(II)Cl_2 + H_2O \longrightarrow C_2H_4O + Pd(0) + 2\,HCl \qquad (1)$$

Later, Smidt and co-workers[8] (1962) employed cupric chloride to regenerate the Pd(0) catalyst (Equation 2).

$$\begin{aligned} C_2H_4 + Pd(II)Cl_2 + H_2O &\longrightarrow C_2H_4O + Pd(0) + 2\,HCl \\ Pd(0) + 2\,CuCl_2 &\longrightarrow Pd(II)Cl_2 + 2\,CuCl \end{aligned} \qquad (2)$$

Recycling of CuCl back to $CuCl_2$ by air made this process applicable for large scale production (Equation 3).

$$2\,CuCl + 1/2\,O_2 + 2\,HCl \longrightarrow 2\,CuCl_2 + H_2O \qquad (3)$$

Adding the above three reactions gives Wacker oxidation reaction.

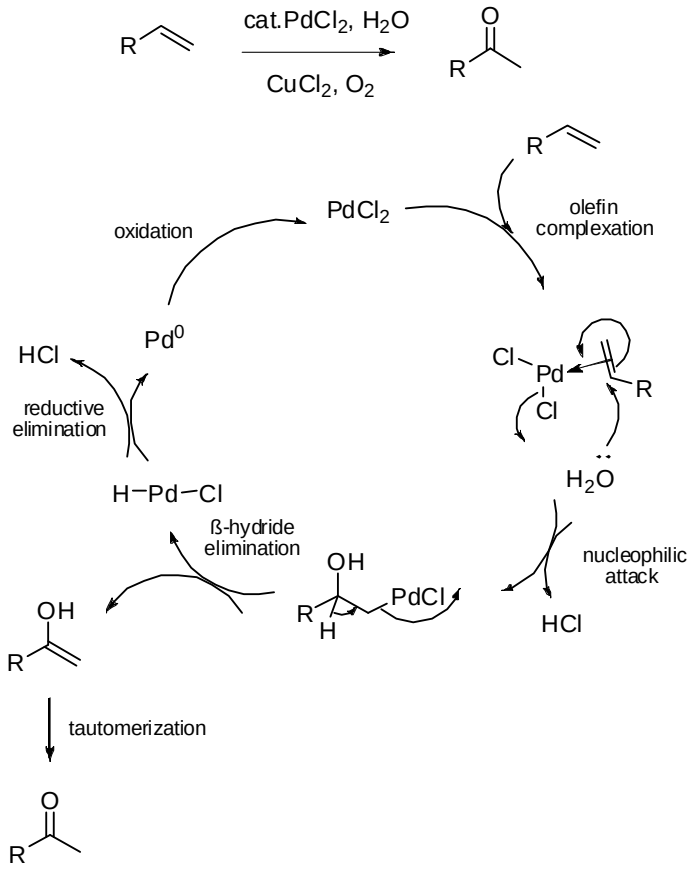
$$C_2H_4 + PdCl_4^{2-} + H_2O \longrightarrow CH_3CHO + Pd(0) + 2\,HCl + 2\,Cl^- \quad (1)$$

$$Pd(0) + 2\,CuCl_2 + 2\,Cl^- \longrightarrow PdCl_4^{2-} + 2\,CuCl \quad (2)$$

$$2\,CuCl + 1/2\,O_2 + 2\,HCl \longrightarrow 2\,CuCl_2 + H_2O \quad (3)$$

Net : $C_2H_4 + 1/2\,O_2 \longrightarrow CH_3CHO$

Wacker oxidation reaction



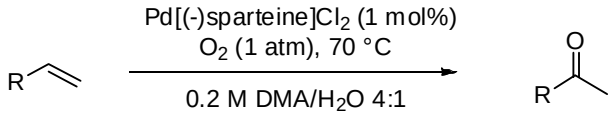
Scheme 36: General catalytic cycle of Wacker oxidation

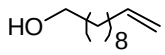
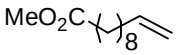
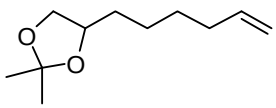
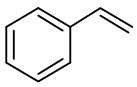
The catalytic cycle (Scheme 36) involves the coordination of alkenes to Pd(II) and,× subsequently, the nucleophilic attack of water on η^2-Pd-alkene complex followed by ß-hydride elimination afford in majority of cases methyl ketones from terminal alkenes. Catalytic amounts of copper chloride are used with oxygen to regenerate the active Pd(II) species.

The original protocol calls for stoichiometric amounts of copper (II) chloride as co catalyst, which has been recognized as a considerable limitation for the overall process. Sustainable alternatives have been developed, notably the application of *tert*-butylhydroperoxide for the oxidation of styrenes[9] or molecular oxygen for the oxidation of alkyl-substituted terminal alkenes.[10] The coordination of palladium with strong σ-donor ligands, that is, N-heterocyclic carbenes or sparteine proved to be crucial for these successful developments.

Recently, Sigman and Cornell discovered the direct palladium-catalyzed Wacker oxidation of terminal alkenes without the need for employing copper cocatalysts.[10] 1 mol% Palladium [(-)-sparteine] dichloride with 0.2 M substrate in a 4:1 DMA/H_2O solvent system proved to be efficient for the conversion of aliphatic alkenes to methyl ketones using molecular oxygen as the terminal oxidant (Table 11, entry 1-5). This palladium complex also proved to be applicable for the oxidation of 4-methylstyrene to the corresponding methyl ketone when an excess of *tert*-butylhydroperoxide (TBHP, 5.5 equiv) was employed (Table 11, entry 6).

Table 11: Palladium [(-)-sparteine]Cl_2 catalyzed Wacker oxidation

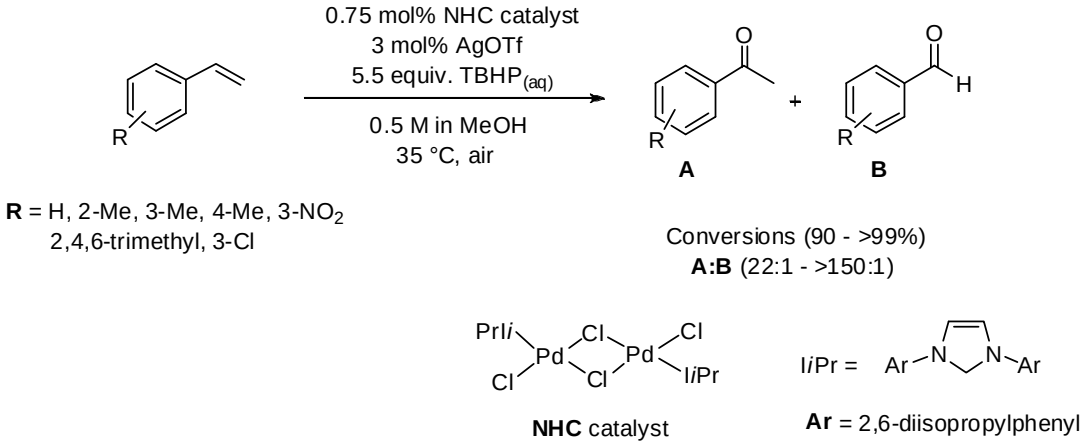


entry	substrate	reaction time (h)	yield(%)[a]
1	dodecene	18	85[b]
2	tridecene	18	83[b]
3		18	72
4		24	73
5		24	62[c]
6		24	92[d]

[a] Average isolated yield of multiple experiments. [b] Isolated yield reflects purity of SM (internal olefins). [c] 2.5 mol % Pd-[(-)sparteine]Cl_2. [d] 5 mol% Pd-[(-)sparteine]Cl_2, 5 equiv. TBHP, 0.25 M DMA or NMP.

Alternatively, a palladium (II)–NHC complex in the presence of catalytic amounts of AgOTf as co catalyst, again using TBHP as the terminal oxidant, was reported by the same authors to be efficient for the generally more challenging oxidation of styrenes, a process that is often

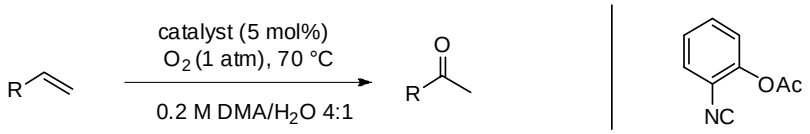
hampered by competing C=C bond cleavage (scheme 37).[9] High selectivity for the oxidation of primary aryl olefins to ketones (>95%) is demonstrated with minimal observed aldehyde formation. Different substitution patterns on the aryl ring lead to similar yields Moreover, Kaneda and co-workers disclosed that $PdCl_2$ is a Wacker catalyst that can be used under 6 atm oxygen pressure.[11]



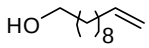
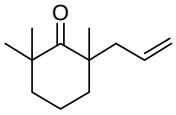
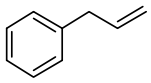
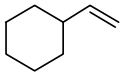
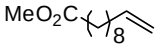
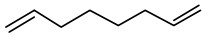
Scheme 37: NHC catalyzed Wacker oxidation of styrenes× derivatives reported by Sigman and co-workers.

Catalysts **105c, b** demonstrated its efficacy in the oxidation of terminal alkenes in the absence of any further co catalysts using molecular oxygen at ambient pressure. An initial screening revealed that both complexes gave very similar yields and selectivities in Wacker oxidation (Table 13, entries 5 and 11). Therefore, subsequently we evaluated **105b**, which can be isolated in high purity by recrystallization and stored without signs of decomposition. Compound **105b** effectively catalyzed the oxidation of terminal aliphatic alkenes (Table 12) by using dimethylacetamide (DMA)/water[9] as the solvent system. Careful GC analysis revealed that no isomerization or C=C bond cleavage had occurred, and that the corresponding methyl ketones were generated in high yields and excellent purity.

Table 12: Wacker oxidation of aliphatic alkenes



107

entry	catalyst	substrate	reaction time (h)	conversion (%)[a]
1	**105b**	1-octene	24	98 (75)
2	$[PdCl_2(\mathbf{107})_2]$[b,c]	1-octene	24	98
3	**105b**		48	97[d] (77)
4	**105b**		48	92 (71)
5	**105b**		48	75[e]
6	**105b**		48	84[e]
7	**105b**		48	98[e]
8	**105b**		48	93[f]

[a] Determined by GC using decane as the internal standard; isolated yields in parentheses, [b] 5 mol% $PdCl_2$, 10 mol% **107**, [c] 3 % isomerized alkene oxidation products, [d] reaction conditions: 0.125 M concentration of substrate, 6:1 DMA/ H_2O, [e] reaction conditions: 0.125 M concentration of substrate, 6:1 DMA/ H_2O, [f] diketone/monoketone ratio 4/3

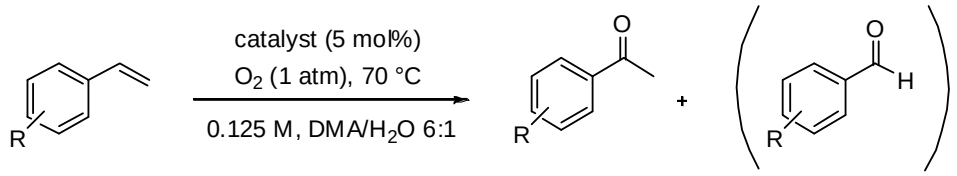
The Oxidation of long chain olefins 1-octene occurred efficiently to give ketones with 98% conversion (Table 12, entry 1). Terminal alkenes possessing oxygenated functional groups were found to be suitable substrates as well, and notably, hydroxyl groups were not oxidized under the reaction conditions (Table 12, entry 3). In case of 1,7-octadiene, diketone and monoketone products were obtained in 4:3 ratio (Table 12, entry 8).

As a control experiment, we performed the oxidation of 1-octene also with the palladium(II) complex of the monodentate isonitrile ligand **107**,[12] which also proceeded well but gave around 3% of oxidation products stemming from alkene isomerizations.

Turning to the more challenging styrenes because of their propensity for C=C bond cleavage under oxidative conditions, we were delighted to find that for these substrates also, **105b** is effective at ambient oxygen pressure in the absence of any further co catalyst (Table 13). A reaction temperature of 70 °C and a DMA/water mixture of 6:1 was found to give the highest ratios between methyl ketones and aldehydes (Table 13, entry 5). As shown for the oxidation of 4-methylstyrene, the bidentate bis(isontrile) ligand **72b** is clearly superior to the monodentate isonitrile ligand **107** (Table 13, entry 2) or palladium chloride alone (Table 13, entry 1). Electron-rich styrenes showed higher reactivity, but also better selectivity towards methyl ketone formation than electron-poor derivatives. Nevertheless, good yields and selectivities could be obtained for the latter also (Table 13, entries 8–11).

Increasing the catalyst loading had no beneficial effect on the reaction (Table 13, entry 10). On the other hand, attempts to lower the catalyst concentration were also not successful. While the conversion of substrates still proceeds well even at 1 mol% **105b**, substantially higher amounts of aldehydes are observed due to carbon–carbon bond cleavage (Table 13, entries 7–9), suggesting that the palladium isonitrile complexes are not stable under the reaction conditions and that background reactions involving palladium(0) alone occur over time. Control experiments showed that **72b** is stable in a 6:1 DMA/water mixture even at 100 °C for elongated times. However, **72b** showed appreciable decomposition in a 6:1 DMA/water mixture at a reaction temperature of 70 °C when palladium (II) chloride is present. In addition, when **72b** is employed in excess with respect to palladium, complete decomposition of **72b** is observed over time. Judged by the disappearance of the isonitrile band in the IR spectrum, we speculate that palladium (II) is capable of activating **72b** towards the attack of nucleophiles such as water present in the reaction; however, we did not observe the corresponding formamides that would result from addition of water to **72b**.

Table 13: Wacker oxidation of aromatic alkenes



entry	catalyst	R	reaction time (h)	conversion (%)[a]	ketone/ aldehyde
1	$PdCl_2$	4-Me	70	>99	4
2	[$PdCl_2$(**107**)$_2$]	4-Me	70	>99	6
3[b]	**105b**	4-Me	70	91	18
4[c]	**105b**	4-Me	40	>99	21
5	**105b**	4-Me	40	>99	26
6[d]	**105b**	4-Me	70	81	14
7[e]	**105b**	4-Me	40	98	14
8[f]	**105b**	4-Me	40	96	6
9[g]	**105b**	4-Me	40	90	8
10[h]	**105b**	4-Me	40	90	20
11	**105c**	4-Me	40	98	23
12	**105b**	H	70	84	17
13	**105b**	2-methyl naphthalene	70	88	11
14	**105b**	3-Cl	96	72	7
15	**105b**	4-Cl	96	98	7
16	**105b**	4-Br	96	50	9
17	**105b**	4-OMe	48	>99 (75)	21

[a] Determined by GC using decane as internal standard; isolated yields in parentheses, [b]DMA/water 2:1, [c] DMA/water 4:1, [d] Reaction temperature 100 °C, [e] 2.5 mol% **105b**, [f] 1 mol% **105b**, [g] 1 mol% **105b** + 2 mol% **72b,** [h] 10 mol% **105b**

5. Conclusion

The most relevant conclusion that could be drawn from these results is that palladium-bis(isonitrile) complex **105b** can be considered as a highly versatile catalyst for the Suzuki coupling and aerobic Wacker oxidation. Complex **105b** catalyzed Suzuki coupling of activated aryl chlorides and deactivated aryl bromides with phenylboronic acid proceeded very well. Wacker oxidation of terminal aliphatic and aromatic alkenes catalyzed by complex **105b** proceeded in good yields and chemoselectivities in the absence of further co catalyst at ambient pressures of oxygen. Palladium bis(isonitrile) catalyst was characterized by NMR spectroscopy and X-ray structure analysis, revealing a dissymmetric coordination of palladium by the two isonitrile moieties.

6. References

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D. Iron (II)-bis(isonitrile) Catalyzed Asymmetric Transfer Hydrogenation

1. Introduction

Catalysis is the key solution for clean, fast, efficient and selective processes in organic synthesis. Approximately, 80% of the chemical and pharmaceutical products in the industry are prepared by catalysts. During the last few decades, heavy or rare metals such as palladium (Pd), iridium (Ir), rhodium (Rh) and ruthenium (Ru) have dominated the research area of transition metal catalysis. However, their toxicity, low accessibility and high costs (Figure 19) are the main barriers for large scale applications[1] and thus, it is obligatory to explore more environment friendly and economical alternatives. Iron is the second most abundant metal on earth (4.7 wt%) and consequently, one of the most inexpensive and environmental friendly. Various iron salts and iron complexes are commercially accessible on a large scale or easy to synthesize.

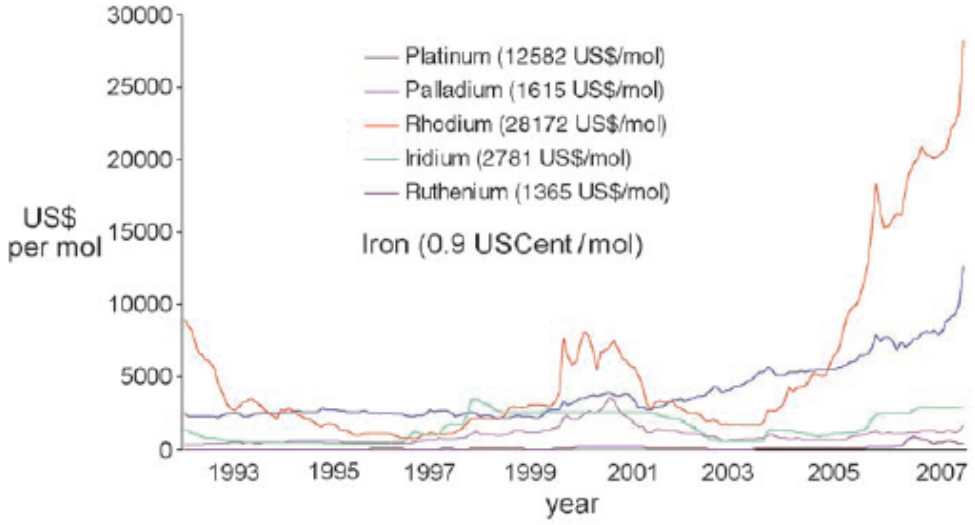


Figure 19: Market prices of transition metals (Pt, Pd, Rh, Ir, Ru) from 1993-2007.[1]

Despite its advantages, it is surprising that until recently, iron was relatively unexplored in the field of catalysis in comparison to other transition metals.

However, in the last few years, a number of examples demonstrated the potential usage of Iron[2] and a broad range of synthetic transformations, *e.g.* addition, substitution, cycloaddition, hydrogenation, reduction, oxidation, coupling reaction, isomerization, rearrangement and polymerization were catalyzed by iron.

In addition to metal catalysis, iron takes part in a number of important biochemical and biological activities. It is an integral part in human body where it binds to the oxygen transporting agent, hemoglobin, in the red blood corpuscles, and to the muscle oxygen storage protein myoglobin, and is stored by ferritin and haemosiderin. Iron also binds to the various metalloenzymes, redox proteins and is transported through the blood by transferrin. In nature, many redox reactions are dependent on iron-containing enzymes whereby electron transport is facilitated by changes in the oxidation state of the metal. Nitrogen fixation and photosynthesis are examples of processes in which iron-containing enzymes play vital roles.[3]

2. Asymmetric Transfer Hydrogenation

Chiral hydrogen transfer of prochiral ketones are widely used in the pharmaceutical industries[4] and has emerged as a convenient methodology to give enantiomerically pure secondary alcohols, based on the simplicity of the process and the safety regulations of the reagents.[5] However, these processes are mainly catalyzed by Ru, Rh or Ir bearing catalysts. Therefore, the use of iron catlysts is most desirable in this regard because of its low toxicity and low prices.

Transfer hydrogenation of ketones is one of the most appealing and interesting synthetic routes to alcohols and constitutes a good alternative to the widely used catalytic hydrogenation. In nature, oxidoreductases such as horse liver alcohol dehydrogenase catalyze transfer hydrogenation of carbonyl compounds to alcohols using some cofactors like NADH or NADPH.[6] Such biochemical reactions are normally very stereoselective. Transfer hydrogenation is a simple operation but the stereo-, chemo-, and regioselectivity are often different from well-established asymmetric hydrogenation.

Based on mechanistic point of view, three alternatives have been proposed for metal catalyzed hydrogen transfer of ketones (Figure 20), (i) direct transfer of a hydrogen atom of the alcohol to the carbonyl carbon through a concerted process involving a six-membered cyclic transition state (**A**), a mechanism accepted for aluminum-catalyzed Meerwein-Ponndorf-Verley (MPV) reductions and generally for main group elements[7], (ii) stepwise mechanism through the formation of a hydride metal intermediate and the migratory insertion of a C=O into a M–H bond (**B**), a mechanism suggested for rhodium(I) and ruthenium free-arene systems[8] and (iii) a concerted mechanism where a proton and a hydride are simultaneously transferred to the unsaturated substrate (**C**), a mechanism proposed by Noyori for the Ru arene derivatives.[9]

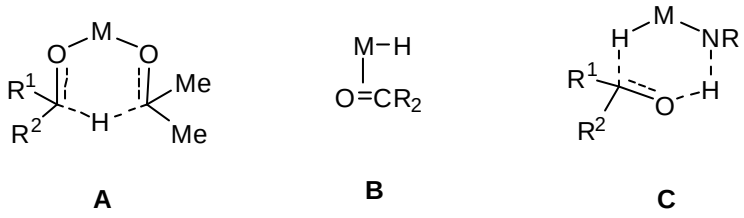
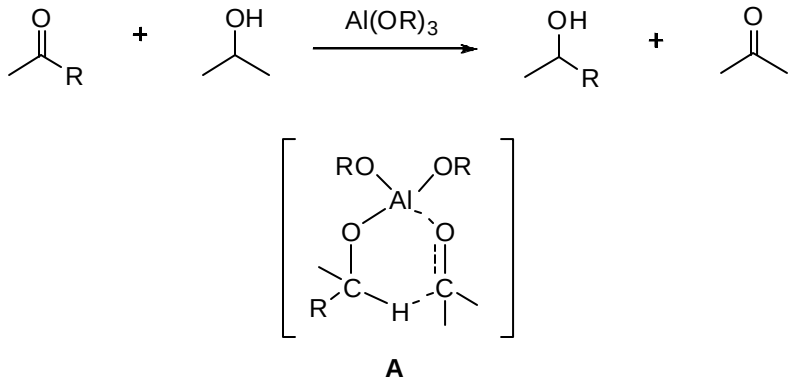


Figure 20: Key species involved in the three main mechanisms (**A**) concerted mechanism, (**B**) stepwise mechanism, (**C**) concerted mechanism of metal-catalyzed hydrogen transfer

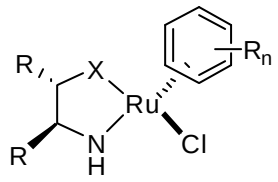
In the original version of MPV reduction, aluminum isopropoxide was used to promote transfer of hydrogen from isopropanol to a ketone (Scheme 38). The aluminium-catalyzed shift of the hydride from the carbon of an alcohol component to the carbonyl carbon of a second component proceeds *via* a six-membered transition state (**A**). This reaction can also be reversed, which is commonly referred as the Oppenauer oxidation, after its discoverer.



A

Scheme 38: Meerwein-Ponndorf-Verley reduction of ketones using isopropanol in excess

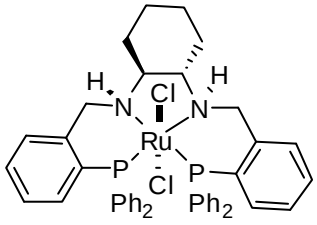
These hydrogen transfer reactions are equilibrium reactions that can be pushed to either direction by the use of an excess of either alcohol or ketone in the starting material. Thus, for the MPV reduction of a ketone, isopropanol is employed in excess because the resulting acetone may be continuously removed from the reaction mixture by distillation. For the Oppenauer oxidation acetone as ketone is used in excess.



106

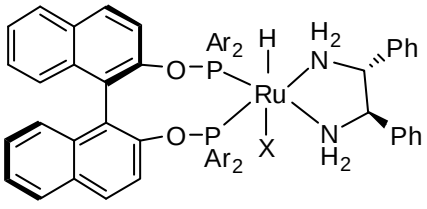
X = sulfonylated N, O

R_n = H: benzene
1-Me-4-$CH(CH_3)_2$: *p*-cym
1,3,5-$(CH_3)_3$: mes
1,2,4,5-$(CH_3)_4$: durene
1,2,3,4,5-$(CH_3)_5$: pmb



107

$P_2(NH)_2$-Ru

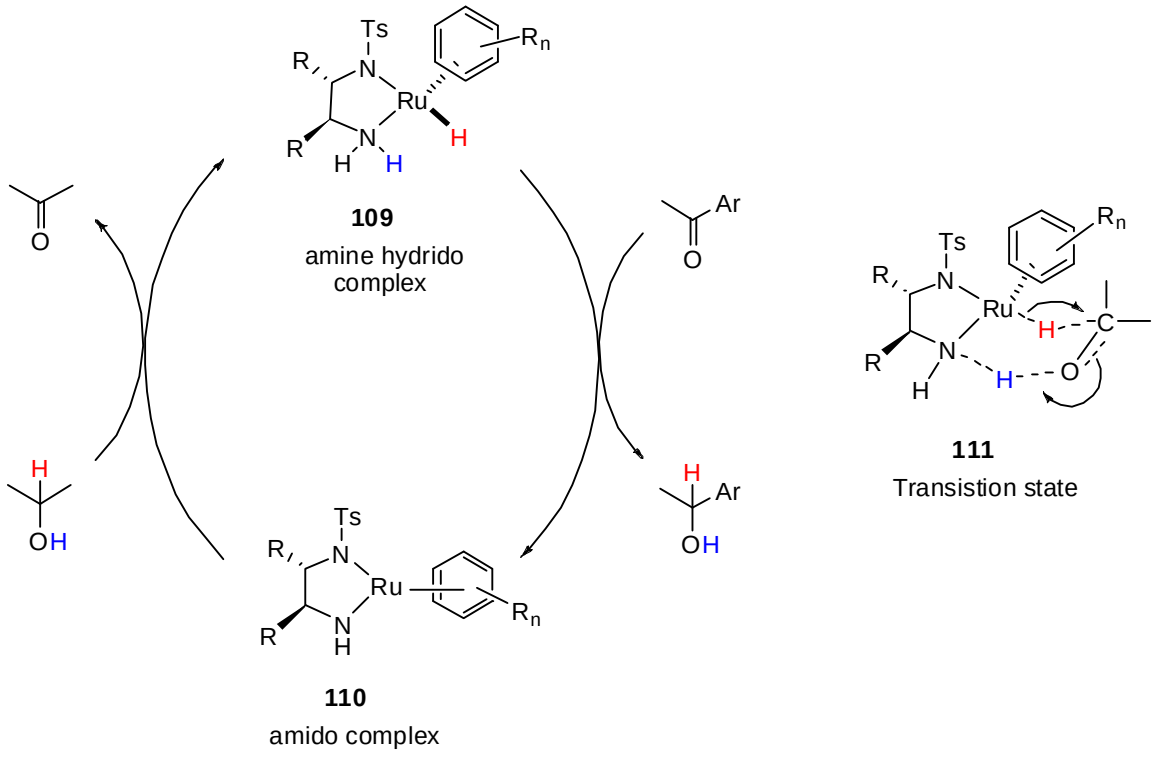


108

Ar = 3,5-$(CH_3)_2C_6H_3$
X = Cl: RuHCl[(*R*)-xybinop)][(*R*,*R*)-dpen]
X = BH_4: RuH(BH_4)[(*R*)-xybinop)][(*R*,*R*)-dpen]

Figure 21: Representative Ru catalysts bearing 1,2-diamine or alcohols

Later, Noyori and Ikariya and co-workers developed conceptually new chiral Ru catalysts bearing 1,2-diamines and amino alcohols as chiral ligands **106-108** (Figure 21) for highly efficient asymmetric transfer hydrogenation of ketones and imines.[9]



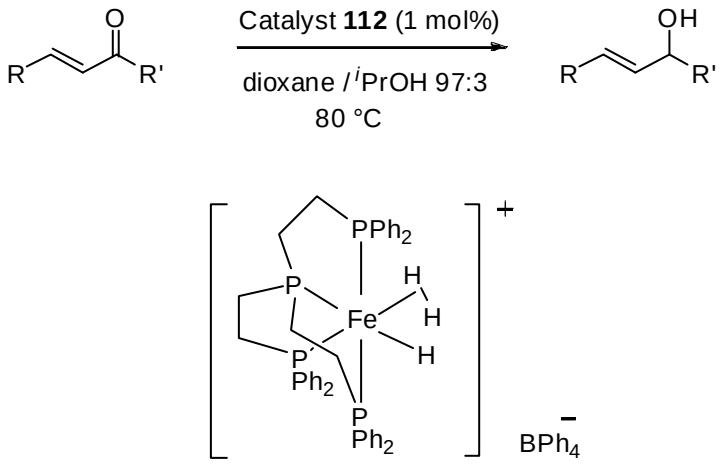
Scheme 39: Transfer hydrogenation mechanism involving interconversion of the Amido and Amine hydrido Ru complex via transition state **111**

Detailed structural studies, both in solid and in solution confirmed amido Ru complex as catalyst intermediate. Amido Ru complex (**110**) readily accepts a hydride from isopropanol to produce an amine hydrido Ru complex (**109**) (Scheme 39). The NH unit bound to Ru is acidic enough to activate ketones *via* hydrogen bonding. During the interconversion of amido and amine hydrido Ru complex, hydride is transfered from isopropanol to ketone reversibly *via* a six-membered transition state (**111**).

Most of the efficient and enantioselective catalysts for this reaction are based on ruthenium and rhodium[10] with high turnover frequencies (TOF's) in the range of 100 – 4000 h^{-1}. There

have been several attempts to develop an iron catalyst for these kinds of reactions, because these would be cheaper, relatively non toxic, using mild reaction conditions, and bearing operational simplicity and therefore, synthesis of chiral secondary alcohols *via* iron catalyzed asymmetric transfer hydrogenation has gained considerable attention.[1, 11] In this regard, Chirik's, Beller's and Nishiyama's groups have recently reported iron catalysts as useful for hydrosilylation of aldehydes and ketones.[12]

Also, Bianchini and co-workers[13] reported well defined dihydrogen complex **112** catalyzed chemoselective transfer hydrogenation of α,ß-unsaturated ketone in a mixture of dioxane and isopropanol (Scheme 40). However, the trend of this reduction was found to be quite irregular as the reaction was substrate-dependant. Thus, 3-methyl-2-cyclohexenone was reduced to the unsaturated alcohol with 31% conversion after 7 h, while 72% of 2-cyclohexenone was reduced to a mixture of unsaturated alcohol and saturated alcohol in 5 h. Other α, ß-unsaturated ketones were either reduced at the C=C double bond to the saturated ketone or were not reduced at all.

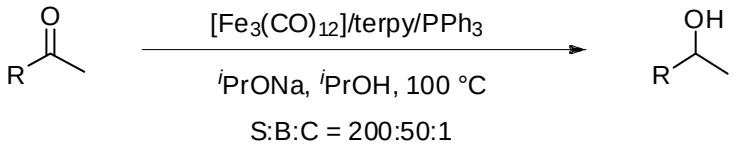


112

Scheme 40: Transfer hydrogenation of α,ß-unsaturated ketones catayzed by dihydrogen complex **112**

Beller and coworkers reported transfer hydrogenation of ketones catalyzed by 1 mol% $[Fe_3(CO)_{12}]$/terpy/PPh_3 or $FeCl_2$/terpy/PPh_3 (Scheme 41).[14] According to their report, sterically hindered and basic monodentate phosphines were found to be better than diphosphine ligands

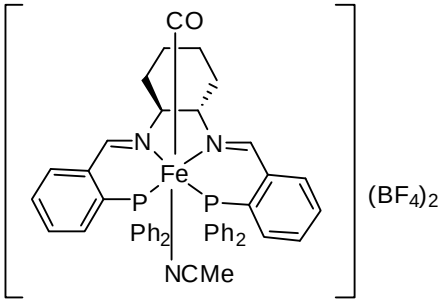
and the aryl ketones as well as dialkyl ketones were reduced to alcohols with excellent yields. Exact structural analysis was not observed with IR spectroscopy and NMR, but kinetic studies proposed a monohydride pathway from the alcohol to ketones.



Scheme 41: $[Fe_3(CO)_{12}]$/terpy/PPh_3 or $FeCl_2$/terpy/PPh_3 catalyzed ketone reduction

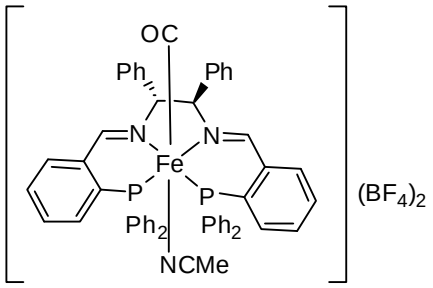
The same group also used a catalyst system comprising of iron porphyrin[15], that mimics the nature. The corresponding alcohols were isolated from 22% to 99% yields at 100 °C in the presence of 1 mol% of catalyst.

Despite tremendous progress in hydrogenations and transfer hydrogenations using Ru and Rh catalysts, only one catalytic asymmetric hydrogenation with iron catalysts was avaiable in literature.



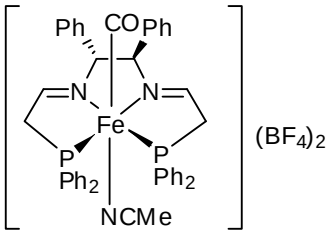
113

trans-[Fe(CO)(MeCN)((*R,R*)-cyP_2N_2)]$(BF_4)_2$

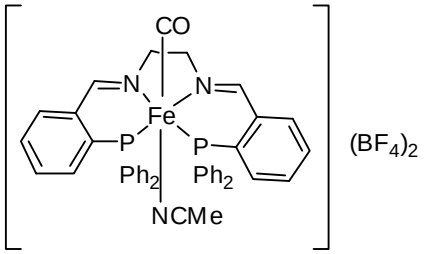


114

trans-[Fe(CO)(MeCN)((*R,R*)-ph-ethP_2N_2)]$(BF_4)_2$



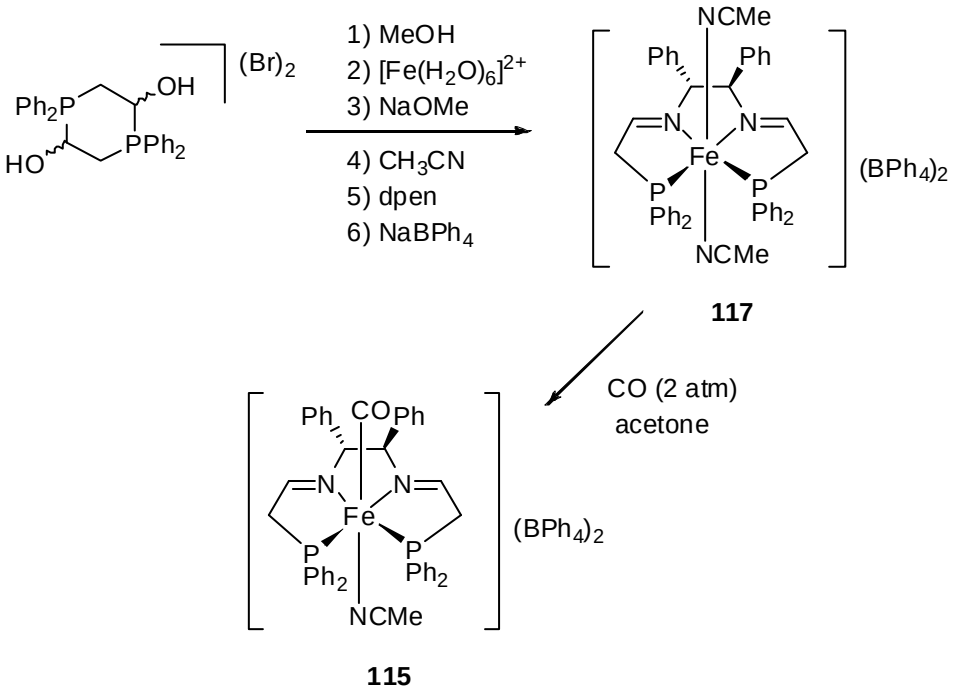
115



116

Figure 22: Structure of chiral iron complexes **113**, **114**, **115** and **116** described by Morris *et al.*

Complexes **113**, **114, 115** and **116** (Figure 22) were prepared by exchanging acetonitrile in the precursor complexes *trans*-$[Fe(NCMe)_2(P–N–N–P)]^{2+}$ with CO in acetone. Complexes **113**, **114** and **116** (Figure 22) were derived from *o*-diphenyl-phosphinobenzaldehyde, enantiopure 1,2–diamine and iron(II) precursor and found to have similar activity. Complex **115** was established to be the most active catalyst compared to complexes **113**, **114** and **116** and was prepared *via* an economical template synthesis route (Scheme 42). The synthesis consists of the deprotonation of dimeric phosphonium compound cyclo-$[PPh_2CH_2CH(OH)]_2(Br)_2$ to yield a very unstable diphenylphosphinoacetalaldehyde which is then trapped by $[Fe(H_2O)_6](BF_4)_2$ through coordination. Subsequent elimination of water from the metal complex yields an enantiomerically pure imine complex $[Fe(PPh_2CH_2CH{=}NCHPhCHPhNH_2)_2](BF_4)_2$ followed by formation of bisacetonitrile complex **117** , isolated as tetraphenylborate salt[16].



Scheme 42: Synthesis of Complex **115** via a template synthesis of the bis(acetonitrile) P-N-N-P complex **117.**

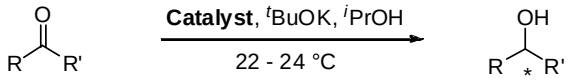
Complexes **113**, **114** and **116** are thermally stable as compared to complex **115** and thus can be handled in air for a few hours without appreciable decomposition. The enantiopure complexes

have diastereotopic phosphorus nuclei that are coupled to each other producing two doublets in their $^{31}P\{^{1}H\}$ NMR spectra. The CO infrared absorption occurs at around 2000 cm^{-1}, indicating little backdonation from the dicationic iron centre. The structure of complex **114** has been verified by single crystal X-ray diffraction.[18]

Complexes **113-115** are active at room temperature towards transfer hydrogenation of ketones in the presence of potassium *tert*-butoxide in isopropanol (Table 14). Enanatioselectivities up to 76% *ee* were obtained in the presence of complex **114** using 2-propanol as the hydrogen source. In addition, high catalyst activities (TOF up to 995 h^{-1}) were attained.[17] Morris *et al.* reported TOF up to 4900 h^{-1} and 99% *ee* for the transfer hydrogenation of ketones with complex **115**.[16]

In the reduction of acetophenone, complex **115** showed very high activity (4 times more active) compared to complex **113** and **114**. Excellent results were obtained for a range of ketones and the enantioselectivity of the complexes increases as **113**< **114**< **115**. For the phenyl-alkyl-ketones PhCOR, the rate of reduction decreases with the size of R, while the *ee* increases in the opposite order (Table 14, entry 1–8). Electron withdrawing groups in the para position accelerate the reaction relative to that of electron donating groups (Table 14, entry 9-13). Reduction of isomers of acetonaphthone were carried out very effectively using complex **115**.

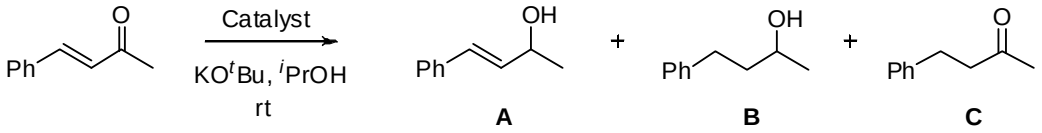
Table 14: Catalytic transfer hydrogenation of ketones catalyzed by Complexes **113-115**



entry	catalyst	substrate	cat./base/ketone	time (h)	conv %	ee %
1	**113**	Ph-CO-Me	1 : 8 : 400	0.4	95	29 (*S*)
2	**114**	"	1 : 8 : 600	0.5	68	63 (*S*)
3	**115**	"	1 : 8 : 2000	0.5	90	82 (*S*)
4	**113**	Ph-CO-Et	1 : 8 : 200	3.6	95	61(*S*)
5	**114**	"	1 : 8 : 600	0.5	75	70 (*S*)
6	**115**	"	1 : 8 : 1500	0.4	90	94 (*S*)
7	**114**	Ph-CO-^{t}Bu	1 : 8 : 200	0.25	93	96 (*S*)
8	**115**	"	1 : 8 : 500	3.3	35	99 (*S*)
9	**113**	(4'-Cl-C_6H_4)-CO-Me	1 : 8 : 200	0.2	94	26 (*S*)
10	**114**	"	1 : 8 : 600	0.5	81	38 (*S*)
11	**115**	"	1 : 8 : 1500	0.3	96	86 (*S*)
12	**113**	(4'-OMe-C_6H_4)-CO-Me	1 : 8 : 200	0.5	69	23 (*S*)
13	**115**	"	1 : 8 : 1000	0.66	65	54 (*S*)
14	**113**	2-aceto-naphthone	1 : 8 : 200	0.3	94	25 (*S*)
15	**114**	"	1 : 8 : 600	0.5	61	52 (*S*)
16	**115**	"	1 : 8 : 1000	0.17	90	84 (*S*)
17	**114**	^{i}Pr-CO-Me	1 : 8 : 600	0.25	63	12 (*S*)
18	**115**	"	1 : 8 : 1500	1	86	50 (*S*)
19	**113**	Me-Ph(CH_2)$_2$-CO-Me	1 : 8 : 200	0.6	100	29 (*S*)
20	**114**	"	1 : 8 : 200	0.25	91	57 (*S*)
21	**115**	"	1 : 8 : 1000	0.5	98	14 (*S*)

The carbonyl compounds, **113-115** also showed very impressive reactivity but poor selectivity for dialkylketone reduction (Table 14, entry 17-21). The reduction of *trans*-4-phenyl-3-buten-2-one to trans-4-phenyl-3-buten-2-ol using the precatalyst **114** shows the highest chemoselectivity toward the reduction of carbonyl group to produce allyl alcohol (Table 15).

Table 15: Transfer hydrogenation of *trans*-4-phenyl-3-buten-2-one



entry	catalyst	cat./KO*t*Bu/ketone	time (h)	A (% ee)	B (% ee)	C (% ee)
1	**113**	1 : 8 : 200	23	18 (45)	0	82 (27)
2	**114**	1 : 8 : 55	23	71 (68)	3	14 (61)
3	**115**	1 : 8 : 1000	0.5	82 (60)	1	4 (25)

A mechanism was suggested on the basis of above mentioned results. It was assumed that the imine linkage in the tetradentate ligand complex is reduced by the action of base and isopropanol to an amine intermediate such as $[FeH(CO)\{(R,R)\text{-}cyP_2(NH)_2\}]^+$. This could suggest that an outer sphere attack by an H–Fe–N–H motif on the ketone group might be possible and the complex might be expected to transfer a hydride from iron and a proton from nitrogen to polar bonds. However, other catalysts that do not utilize an outer sphere H–M–N–H attack still provide this selectivity in certain cases (complexes **113** and **114**). The mechanism of action of these catalysts is currently under investigation.

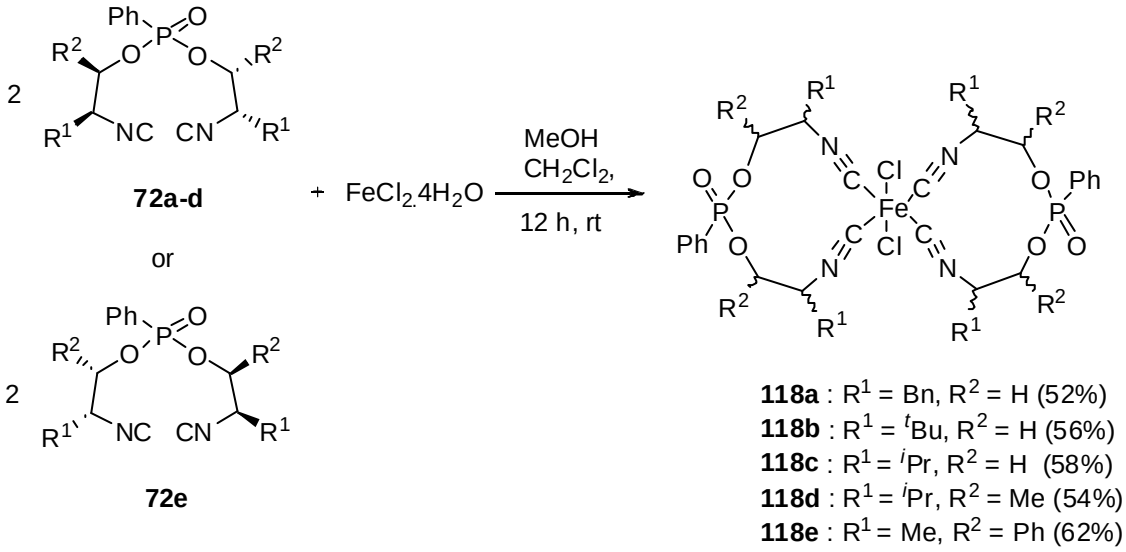
3. Iron(II) Bis(isonitrile) complexes

3.1 Synthesis

Our investigations began with the synthesis of iron complexes containing enantiopure bidentate bis(isonitrle) ligands (BINC). Chiral oxazolines (**71a-e**) were transformed to

bis(isonitrile) upon metallation followed by trapping of resulting anion with phenylphosphonic dichloride (Section B, Scheme 21 and 22).[19]

The reaction of $FeCl_2.4H_2O$ with BINC (**72a-e**) in methanol led to the formation of orange to yellowish colored $FeCl_2(BINC)_2$ complexes (**118a-e**) with good yields at room temperature (Scheme 43)[20]. $FeCl_2(BINC)_2$ complexes are quite stable in air and completely soluble in dichloromethane, chloroform, methanol, acetonitrile, THF and isopropanol.



Scheme 43: Synthesis of Iron Bis(isonitrile) complexes **118a-e**.

The presence of broad intense absorption in the higher energy region of IR spectrum compared to free bis(isonitrile) ligands and the broad signals in ^1H NMR is the evidence for the formation of iron-bis(isonitrile) complexes (**118a-e**). Attempts to grow X-ray quality crystals of complex **118b** from several solvents failed. However, exchange of chlorides with trichlorotin resulted in growth of suitable yellow colored crystals of $[Fe(^tBuBINC)_2(SnCl_3)_2]$ (**119d**) (Figure 23) from methanol-pentane mixture in two weeks. $[Fe(^tBuBINC)_2(SnCl_3)_2]$ was prapared at room temperature reaction of $FeCl_2(^tBuBINC)_2$ (**118b**) with excess of $SnCl_2.2H_2O$ in chloroform for 12 h.

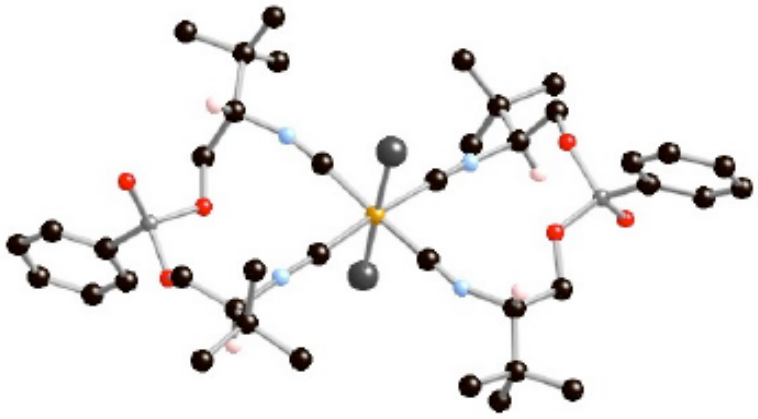


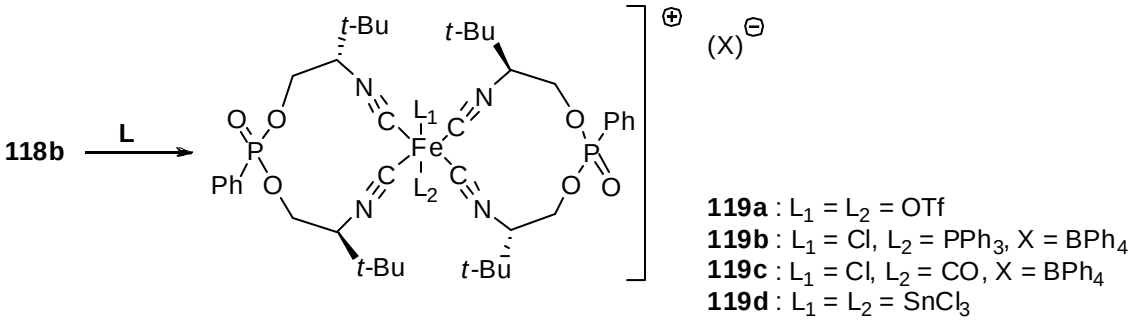
Figure 23: X-ray structure of complex **119d** (Cl atoms on Sn were omitted for clarity)

X-ray analysis of the so obtained Fe(**118b**)$_2$($SnCl_3$)$_2$ revealed that the bidentante isontrile ligands had coordinated iron(II) in a square planar geometry with the trichlorostannyl ligands taking the axial positions to overall result in a distorted octahedral complex. Notably, the iron-isonitrile unit has by enlarge a linear geometry (169°) with Fe-C and isonirile C-N bond lengths averaging 1.86 Å and 1.14 Å, respectively (Table 16), indicating that no or little back bonding from the metal to the ligand takes place. Other interatomic data of the compound **119d** includes the average Fe-Sn bond length of 2.466 Å.[21]

Table 16: Selected bond lengths [Å] and angles [°] of **119d**.

Bond lengths [A°]		Bond angles [°]	
Fe-Sn1	2.468	Sn1-Fe-Sn2	177.7
Fe-Sn2	2.464	C1-Fe-C20	89.2
Fe-C1	1.87	C1-Fe-C40	91.0
Fe-C20	1.85	C20-Fe-C21	93.3
Fe-C21	1.91	C21-Fe-C40	86.8
Fe-C40	1.82	C1-N1-C2	176
N1-C1	1.17	C15-N2-C20	164
N2-C20	1.15	C21-N3-C22	175
N3-C21	1.10	C35-N4-C40	162
N4-C40	1.18		

The chloride ligand in complex **118b** can also be easily displaced by other ligands such as CO, PPh_3 and OTf to obtain **119** as shown in scheme 44. Complexes **119b** and **119c** were isolated as their tetraphenylborate salts.

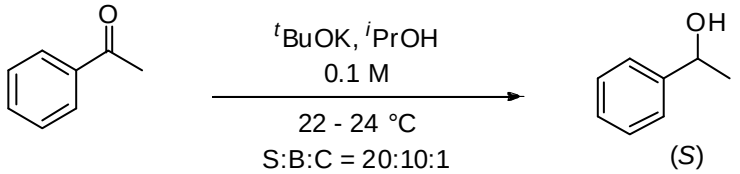


Scheme 44: Synthesis of Iron Bis(isonitrile) complexes **119a-d**.

3.2 Transfer Hydrogenation of Aromatic Ketones

Complexes **118(a-e**) – **119(a-c)** were tested as catalyst precursors for transfer hydrogenation of acetophenone to 1-phenylethanol in basic isopropanol and the results are summarized in Table 17. Complex **118b** was found to be an active catalyst at room temperature (Table 17, entries 2 *vs* 4) and showed good activity with 90% conversion and 64% *ee*. Lowering the loading of complex **118b** led to the decrease in the extent of conversion (Table 17, entry 3). Under hydrogenation using hydrogen at 50 bar, complex **118b** showed moderate conversion and selectivity (Table 17, entry 5). On the basis of this result it was concluded that complex **118b** works better under transfer hydrogenation conditions. As revealed by the data presented in Table 17, the exchange of one or both chloride ligands with triflate (Table 17, entry 9), PPh_3 (Table 17, entry 10) and CO (Table 17, entry 11) didn't show appreciable results.

Table 17: Transfer Hydrogenation of Acetophenone Catalyzed by complexes **118** and **119**



entry	complex	time (h)	conv %[a]	ee %[b]	mol %
1	**118a**	23	17	-	5
2	**118b**	8	90	64	5
3	**118b**	5	41	60	2
4	**118b**[c]	23	41	36	5
5	**118b**[d]	6	59	52	5
6	**118c**	8	71	54	5
7	**118d**	24	6	10	5
8	**118e**	24	24	17	5
9	**119a**	8	71	40	5
10	**119b**	23	17	-	5
11	**119c**	24	22	-	5

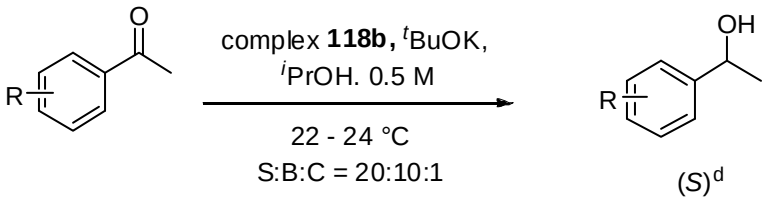
[a] Determined by GC using decane internal standard. [b] Determined by HPLC.
[c] Temperature 45 °C. [d] Under 50 bar H_2 pressure.

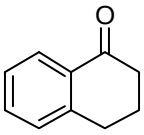
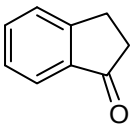
The substitution pattern in the isonitrile ligands appears to play an important role to render **118** an efficient catalyst in transfer hydrogenations. While the *iso*-propyl derivative **118c** still showed appreciable activity and selectivity (Table 17, entry 6), the benzyl complex **118a** and derivatives **118d** and **118e** (Table 17, entry 7, 8) being substituted at the β-position of the isonitrile were by enlarge inactive. It was assumed that the presence of additonal chiral centre might lead to an increase in the enantioselectivity due to steric reasons, but observed decrease in selectivity and conversion may be attributed to blocking the access of substrate to the iron center. Since we assume (*vide infra*) that both, iron and the isonitrile moiety play an integral role in the hydride transfer to the ketone, small conformational changes in the iron-bis(isonitrile) complexes might sufficiently disturb the required arrangement of these two moieties to give catalytic turnover. The use of a strong base such as ^{t}BuOK was very essential for the catalysis, as no reaction was observed without the base. The optimal ratio of the catalyst to the base was 1: 10.

Complex **118b** was also extensively studied with a variety of substrates. Replacement of methyl group of acetophenone with bulky groups (Table 18, entry 2, 3, 4) brought down the conversion as well as the enantioslectivity. This finding demonstrated that the rate of reduction and enantioselectivities decreased with the more hindered aromatic ketones. Hydrogenation of the ketone with 1-phenylmethyl group (Table 18, entry 5) proceeded with reduced conversion and *ee*.

The acetophenone with electron donating group such as *p*- and *o*-OMe acetophenone showed lower reactivity with moderate selectivity (Table 18, entry 6, 8), whereas *m*-OMe acetophenone was found to be reduced very fast with moderate selectivity (Table 18, entry 7). Aromatic ketones with electron withdrawing group such as *p*- and *m*-Cl acetophenone showed excellent conversion with moderate selectivity (Table 18, entry 3, 4). In contrast, *o*-Br substituted acetophenone showed moderate activity as well as selectivity (Table 18, entry 5). This result is opposite to the results reported by Morris and co-workers,[16] in which *o*-Cl substitution has no significant influence on the reactivities of the substrates. The acetonaphthone isomers (Table 18, entry 12, 13) and cyclic ketones (Table 18, entry 14, 15) were also reduced efficiently with lower selectivity.

Table 18: Transfer Hydrogenation of Aromatic Ketones catalyzed by complex **118b**

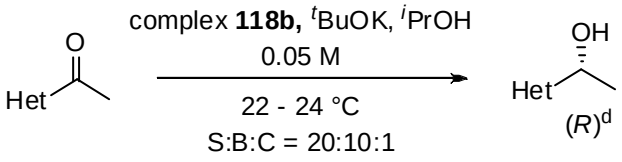


entry	substrate	time (h)	conv %[a]	ee %[b]
1[c]	Ph-CO-Me	8	90	64
2	Ph-CO-Et	6	73	64
3	Ph-CO-*i*Pr	3	36	36
4[c]	Ph-CO-(*cyclo*-C_6H_{11})	5	55	18
5	$PhCH_2$-CO-Me	1	99	34
6	(4'-Cl-C_6H_4)-CO-Me	12	94	60
7	(3'-Cl-C_6H_4)-CO-Me	1	>99	67
8	(2'-Br-C_6H_4)-CO-Me	24	60	67
9	(4'-OMe-C_6H_4)-CO-Me	6	50	58
10	(3'-OMe-C_6H_4)-CO-Me	1	93	54
11	(2'-OMe-C_6H_4)-CO-Me	3	56	52
12[c]	2-aceto-naphthone	1	84	64
13	1-aceto-naphthone	1	48	41
14		3	62	46
15[c]		24	89	33

[a] Determined by GC using decane internal standard. [b] Determined by HPLC. [c] 0.1 M concentration of substrate. [d] Absolute configuration was determined by comparison of the sign of rotation with literature value.[22, 23]

3.3 Transfer Hydrogenation of Heteroaromatic and Pyridyl Ketones

Table 19: Transfer Hydrogenation of Heteroaromatic Ketones catalyzed by **118b**



entry	hetero	time (h)	conv %[a]	ee %[b]
1	2-acetylfuran	3	>99	30
2	2-acetylthiophene	1	70	53 (*S*)
3	2-acetylpyridine	6	85	41
4[c]	3-acetylpyridine	1	95	61
5	4-acetylpyridine	1	99	55 (*S*)

[a] Determined by GC using decane internal standard. [b] Determined by HPLC. [c] 0.1 M concentration of substrate. [d] Absolute configuration was determined by comparison of the sign of rotation with literature value.[24]

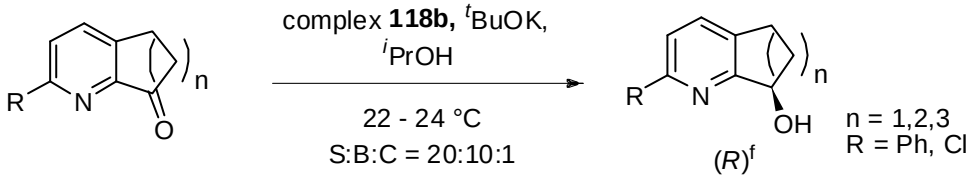
Furthermore, Iron complex **118b** was also tested with some more variety of substrates such as heteroaromatic ketones. It also showed appreciable results, thereby, confirming its ability to reduce versatile substrates.

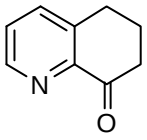
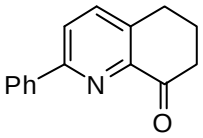
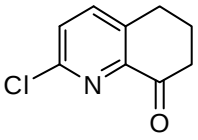
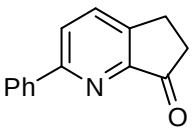
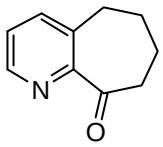
Turning to heteroaromatic methylketones (Table 19), we observed high turnover for the carbonyl reduction, allowing reaction times as little as one hour to achieve complete conversion. Enantioselectivities remained moderate, however, a reversal of the absolute stereochemistry in the products with respect to the aromatic ketones was observed with the exception of 2-acetylthiophene (Table 19, entry 2) and 4-acetylpyridine (Table 19, entry 4). Thus it is very

much clear from above results that heteroaromatic ketones react faster than simple aromatic ketones because of extra possible coordination provided by heteroatom. Keeping this conclusion in mind, several pyridyl ketones with rigid backbone were synthesized and examined in complex **118b** catalyzed transfer hydrogenation. Chiral Pyridyl alcohols are very useful intermediates in the synthesis of ligands for asymmetric catalysis.[25]Till date only kinetic resolution of racemic pyridyl alcohols were reported by Pfaltz and co-workers,[26] but there is no report on hydrogenation of pyridyl ketones to chiral pyridyl alcohols. Here, we have described the transfer hydrogenation of pyridyl ketones with excellent conversions and enantioselectivities.

Pyridine with six membered fused ring was reduced with 80% yield and 91% *ee* (Table 20, entry 1). In contrast, α-tetralone (Table 18, entry 14), bearing no nitrogen in aromatic ring showed diminshed reactivity and selectivity. This comparision illustrates the importance of presence of a heteroaromatic atom, which can represent an additional coordination point for the metal, giving rise to a better enanti-discrimination. Increasing the size of aliphatic cyclic ring fused to pyridine ring also showed excellent conversion and enantioselectivity (Table 20, entry 2). It was interesting to note that a substituent in 2-position is detrimental to the enantioselectivity (entries 2-4), which might be an indication that the pyridine nitrogen is in proximity or even interacting with the active centre of the catalyst.When a six-membered ring is fused to the pyridine ring with phenyl substitution at α position, the enantioselectivtiy is higher than that with a five membered ring analogue (Table 20, entry 2, 4). Cl group α to the pyridine N-atom and six-membered ring was found to be hydrogenated with excellent yield and enenatioslectivity (Table 20, entry 3).

Table 20: Transfer Hydrogenation of Pyridyl Ketones Catalyzed by **118b**



entry	substrate	time (h)	conv %[a]	ee %[b]
1[c, e]		24	80	91
2[d, e]		3	98	72
3[d]		15	93	84
4[d, e]		6	89	52
5[c]		24	83	83

[a] Determined by GC using decane as internal standard. [b] Determined by chiral HPLC. [c] 0.2 M concentration of substrate. [d] 0.05 M concentration of the substrate. [e] Isolated yield. [f] Absolute configuration was determined by comparison of the sign of rotation with literature value.[25, 26]

3.4 Proposed Mechanism

Infra red spectroscopy (IR) has been used to get a better understanding of the reaction mechanism. The IR spectrum of a solution of iron bis(isonitrile) complex **118b** (6 mg, 0.007 mmol) in isopropanol (1mL) showed a strong broad absorption of the isonitrile NC strech at higher frequency (2177 cm^{-1}, **B**, Figure 24) than that of free bis(isonitrile) ligand **72b** (2140 cm^{-1}, **A**, Figure 24). The high value of υ (NC) is attributed to a strong σ- bonding interaction between the isonitrile carbon and the charged metal centre. This σ- bonding interaction becomes stronger in the presence of isopropanol. The solution of **118b** in ^{i}PrOH was then treated with 10 equivalents of ^{t}BuOK, resulting in the complete disappearance of the isonitrile band within 10 minutes and the appearance of a new band at 1638 cm^{-1} (**C**, Figure 24).The presence of this broad intense absorption at very low energy is the evidence for the reduction of isonitrile groups in the iron complex **118b** to corresponding imine N=C. The latter is assigned to the presence of a C=N double bond, indicating the reduction of isonitrile to the corresponding imine. In contrast, we could find no indication for a Fe-H band, which would have been expected around 1900 cm^{-1}. Moreover, in NMR studies no signals at negative ppm (δ_H = -8 to -12 ppm),[27] typical for such species, were observed.

Therefore, we propose that the reaction proceeds by a outer sphere hydride transfer mechanism as shown in Figure 25,[28] being different from the reported mechanisms for transfer hydrogenations with ruthenium involving achiral isonitrile ligands.[29] We speculate that the ketone binds via its carbonyl group or alternatively through the respective heteroatom in the case of heteroaromatic substrates to the iron centre of the catalyst. Hydride transfer then occurs from the reduced isonitrile group.

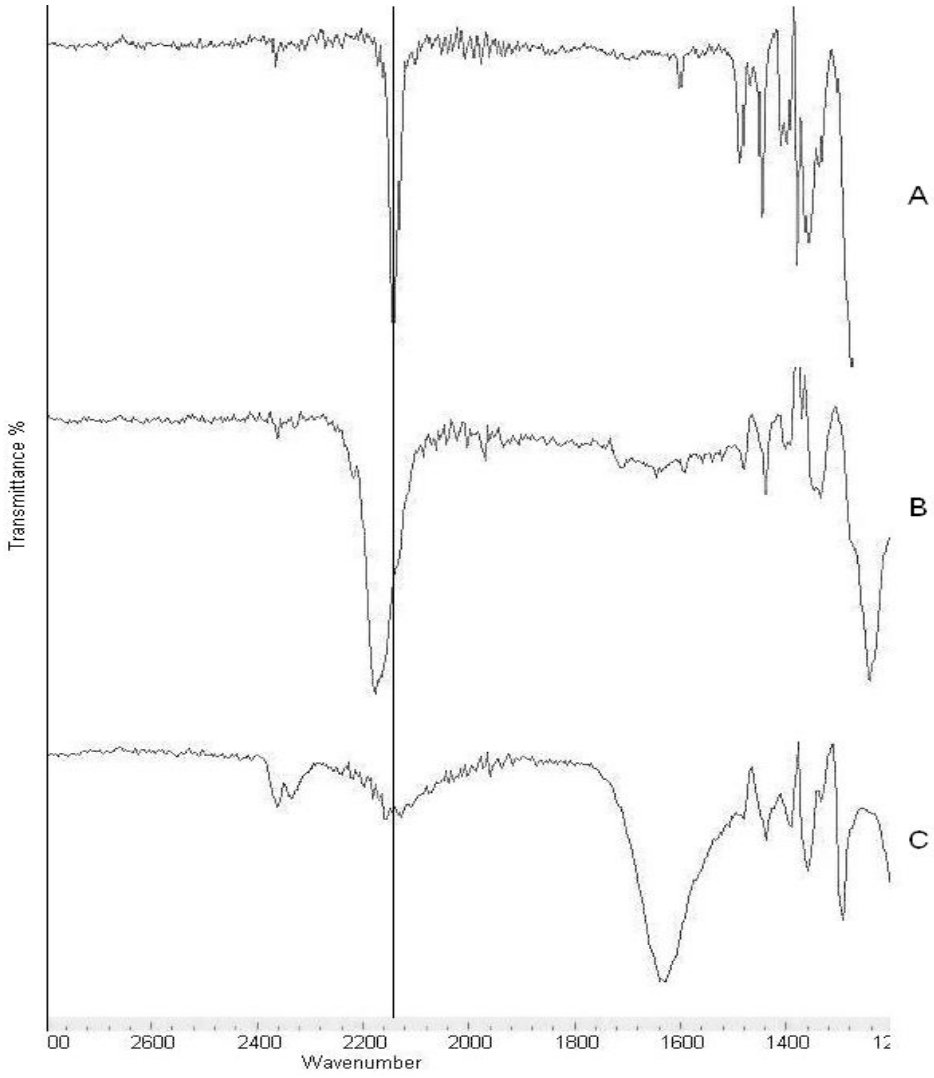


Figure 24 IR spectrums in ^{i}PrOH (A) Free Ligand **72b**, (B) Iron complex **118b**, (C) Iron complex **118b** in the presence of 10 equiv. ^{t}BuOK

This mechanism is different from the reported mechanism. The mechanism consists of following steps: (a) iron bis(isonitrile) **118b** was thought to undergo reduction of NC (Figure 25) to imine by basic isopropanol (confirmed by IR), (b) coordination of ketone to iron centre, (c) hydride transfer from imine carbon *via* five-membered transition state to carbonyl group, (d) formation of alcohol by protonation by isopropanol, (e) hydride elimination from isopropoxide generated acetone, (f) regeneration of the active iron species.

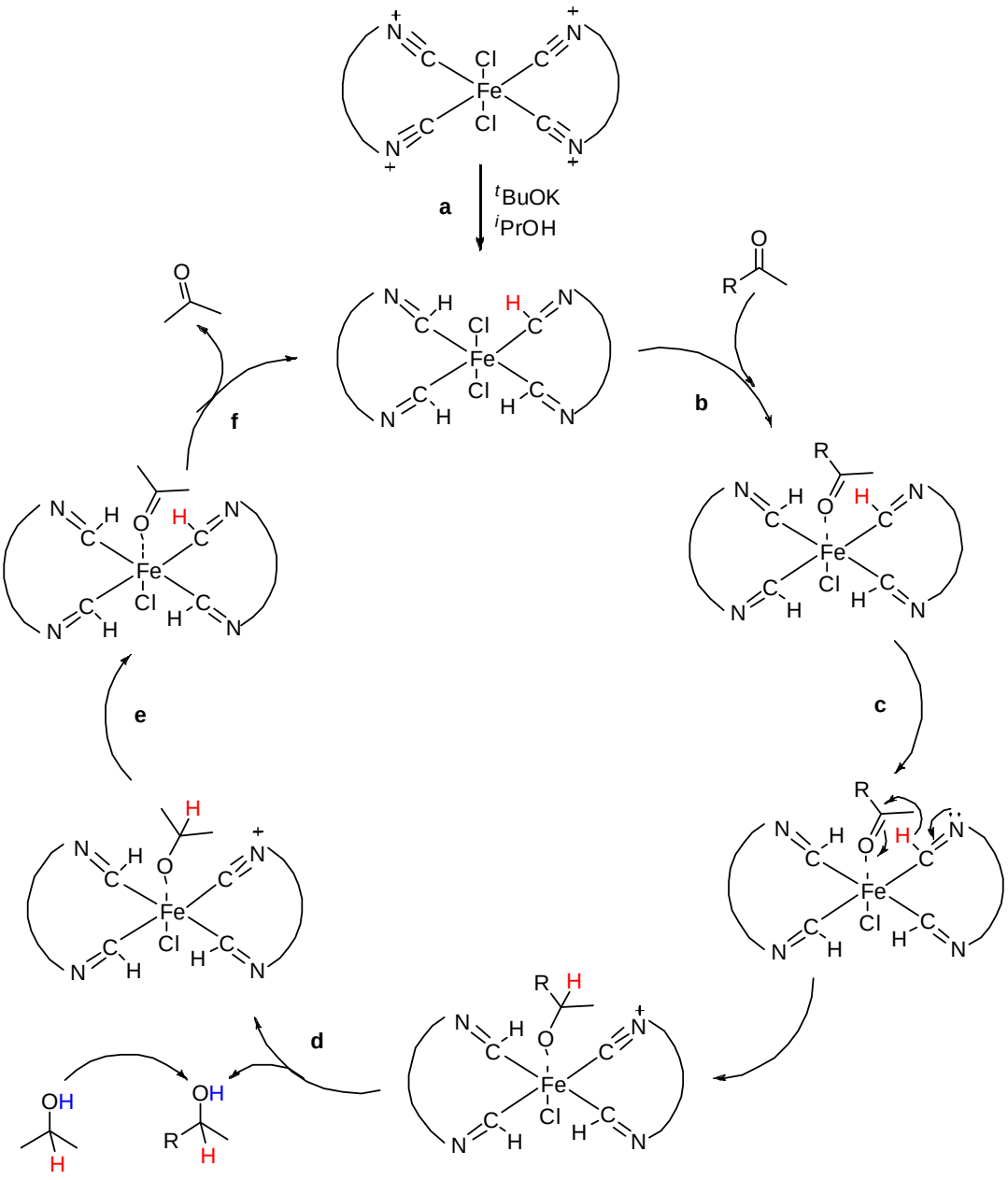


Figure 25: The proposed mechanism for Transfer Hydrogenation catalyzed by **118b**

4. Conclusion

In conclusion, we could develop a new type of iron catalyst (**118**) being effective in asymmetric transfer hydrogenations of ketones. The noteworthy feature of the iron complexes employed in our study are coordinating isonitrile groups that might serve as acceptors for hydrogen that is subsequently delivered to the ketone being activated by the iron centre. In addition, this is the first report that demonstrates the ability of isonitriles to be able to serve as chiral ligands in asymmetric catalyses.

5. References

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E. Cu(I), Rh(I) and Ir(I)-bis(isonitrile) complexes

1. Cyclopropanation

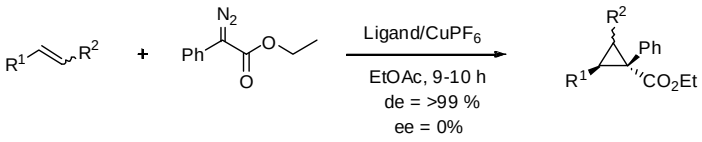
Optically active cyclopropanes play an important role as intermediates in the synthesis of insecticides and drugs.[1] In this perspective, metal catalyzed cyclopropanation is one of the most important methods for the synthesis of cyclopropane derivatives and has been widely applied in organic synthesis. Chiral ligands such as semicorrine,[2] bisoxazolines,[3] bipyridines[4] and Schiff's bases[5] are the most efficient ligands for copper-catalyzed alkene cyclopropanation with diazoacetate. Several rhodium catalysts[6] were also reported to promote the cyclopropanation of styrene with aryldiazoacetates, in which both good diastereoselectivity and enantioselectivity are achieved. However, non-rhodium catalysts showed poor enantioselection in this reaction.[6a]

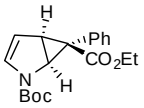
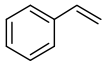
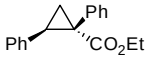
1.1 Cu(I)-bis(isonitrile) complexes catalyzed cyclopropanation

Being a unique ligand for a broad variety of transition metal complexes, we investigated Cu(I)-bis(isonitrile) complexes in the asymmetric alkene cyclopropanation reaction using ethyl phenydiazoacetate. Because of its susceptibility to oxidation, the catalyst was freshly made *in situ*. We chose to optimize the conditions for cyclopropanation using N-Boc pyrrole as a substrate. Thus, in the presence of 5 mol% $CuPF_6$/BINC **72b** N-Boc pyrrole could react with ethyl phenyldiazoacetate to afford the racemic cyclopropanation product in moderate yields and high diastereoselectivity. The results of our investigations are given in Table 21. Optimization studies revealed that the yield was strongly influenced by reaction conditions (Table 21). Under the screened conditions, ethylacetate gave the best result with a maximum 57% yield of cyclopropanated product at 40 °C (Table 21, entries 1–9). Changing the solvent to toluene gave no cyclopropanation product (Table 21, entry 6), whereas dichloromethane and 1,2-dichloroethane gave lower yields (49-42% yield) (Table 21, entry 4, 5). Employing higher catalyst loadings (Table 21, entry 7, 8) did not improve the yield. The additional rigid BINC **72f** did not prove to be beneficial in this reaction (Table 21, entry 10). More promising results in terms of yield were obtained using styrene (Table 21, entry 11, 12). Excellent

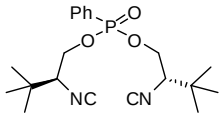
diastereoselctivity as well as yield were obtained using 10 mol% of BINC **72b**/Cu(I). Again, it was noted that no enantioselectivity was observed in this reaction. The relative configuration of the major diastereomer was determined by NOESY NMR. The required ethylphenyldiazoacetate was prepared in a standard manner from *p*-toluolsulfonyl azide and ethyl phenylacetate in acetonitrile at 0 °C.[7]

Table 21: BINC **72b,f** catalyzed cyclopropanation of alkenes

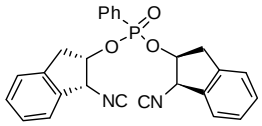


entry	ligand	alkene	temp.(°C)	solvent	yield (%)	product
1[a]	**72b**		40	EtOAc	57	
2[a]	**72b**		40	Hexanes/EtOAc (1/1)	32	
3[a]	**72b**		40	CH_3CN	24	
4[a]	**72b**		40	CH_2Cl_2	49	
5[a]	**72b**		80	$ClCH_2CH_2Cl$	42	
6[a]	**72b**		110	toluene	-	
7[b]	**72b**		40	EtOAc	37	
8[c]	**72b**		40	EtOAc	37	
9[a]	**72b**		rt	EtOAc	18	
10[a]	**72f**		40	EtOAc	21	
11[a]	**72b**		40	EtOAc	60	
12[b]	**72b**		40	EtOAc	87	

[a] 5 mol% ligand/Cu(I). [b] 10 mol% ligand/Cu(I). [c] 20 mol% ligand/Cu(I).



72b



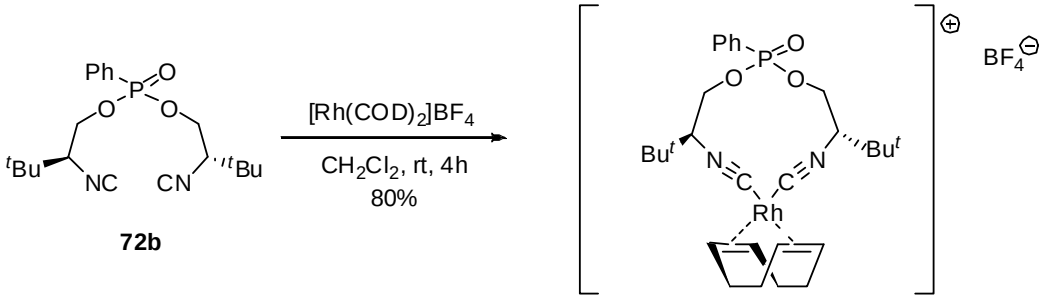
72f

2. Imine hydrogenation

Enantioselective hydrogenation of olefins and ketones were studied widely in contrast to enantioselective hydrogenation of prochiral imines to corresponding chiral amines although the reaction has considerable significance. Chiral aromatic amines are particularly sought after due to applications in the pharmaceutical, agrochemical and fine chemical industries. In this respect, metal-catalyzed asymmetric reductions of imines have attracted much interest in the last decade and have been the subject of several studies.[8] Till now, a range of Rh, Ir and Ru complexes have been investigated in detail.[9]

2.1 Rh(I) and Ir(I)-bis(isonitrile) complexes catalyzed imine hydrogenation

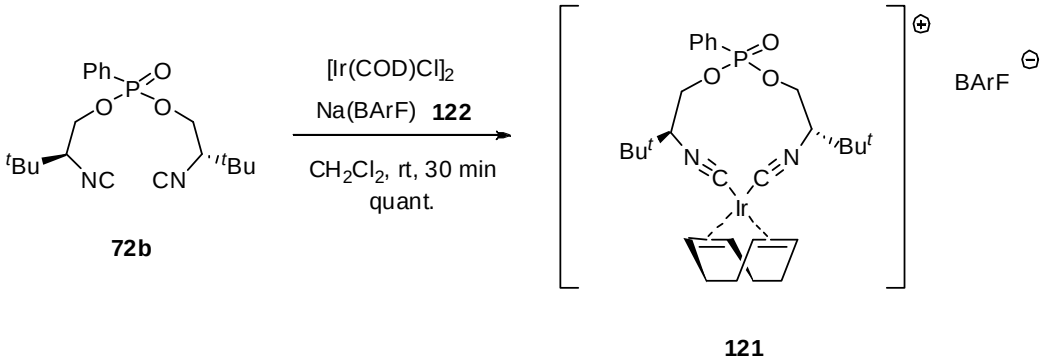
We have synthesized cationic rhodium (I) and iridium (I) complexes with bis(isonitrile) ligand **72b** and studied their catalytic activity in asymmetric imine hydrogenation. Rhodium-bis(isonitrile) complexe of the type [Rh(^{t}Bu-BINC)(COD)]BF_4 (**120**) was prepared according to scheme 45. Reaction of $[Rh(COD)_2]BF_4$ with one equivalent of bis(isonitrile) **72b** under an inert atmosphere formed the cationic complex [Rh(^{t}Bu-BINC)(COD)]BF_4 (**120**) in quantitative yields.



72b **120**

Scheme 45: Preparation of [Rh(^{t}Bu-BINC)(COD)]BF_4 (**120**)

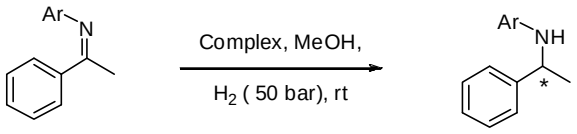
Similarly, [Ir(^{t}Bu-BINC)(COD)]BArF (**121**) was synthesized in excellent chemical yields by treating the dicholoromethane solution of ^{t}Bu-BINC **67b** and $[Ir(COD)Cl]_2$ with Na(BArF) (**122**) at room temperature.



Scheme 46: Preparation of [Ir(*t*Bu-BINC)(COD)]BArF (**121**)

The new rhodium and iridium complexes **120**, **121** were tested in the asymmetric hydrogenation of a range of aromatic imines. Under the given reaction conditions, the cationic rhodium and iridium complexes **120** and **121** afforded N-arylamines in high yields, but no enantioselectivity was seen in this class of compounds. Table 22 shows that 50 bar of hydrogen pressure is optimum in the hydrogenation of imines, using cationic rhodium and iridium complexes **120** and **121** as the catalyst precursors. In contrast to rhodium complex **120**, the best results were obtained with iridium complex **121**. Decreasing the catalyst loading of iridium complexes **121** to 1 mol% resulted in significant decrease in imine formation from 99 to 81% in 14 h (Table 22, entries 3).

Table 22: Hydrogenation of imines catalyzed with the iridium and rhodium complexes



entry	Ar	complex	mol %	time (h)	conv.%	ee %
1	Bn	**120**	1	24	>99	-
2	Ph	**121**	5	1	>99	-
3	Ph	**121**	1	14	81	-
4	*(p*-OMe)Ph	**121**	5	3	>99	-

3. Conclusion

We have shown that bis(isonitrile) ligands form very stable complexes with Cu(1), Rh(1) and Ir(1). Cu-BINC complex catalyzed cyclopropanation reactions with excellent reactivity, whereas cationic rhodium-BINC complex and iridium-BINC complex **120** and **121** formed efficient imine hydrogenation catalysts displaying high conversions at 50 bar hydrogen pressure. The catalyst precursors are readily prepared, easily handled and air-stable.

Bis(isonitrile) complexes are capable to perform the above mentioned reaction with moderate reactivites. Nevertheless, the obtained results are not capable of competing with the best values in literature. Therefore, no further exploration regarding these transformation were undertaken

4. References

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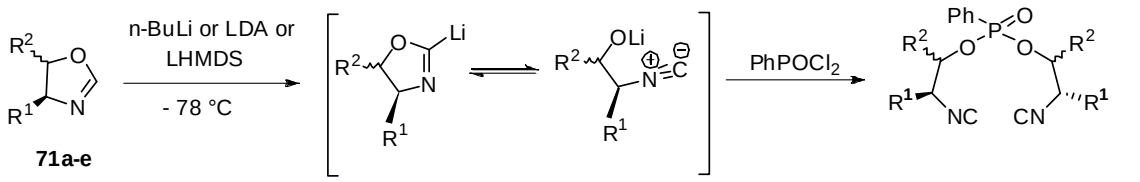
F. Summary

Synthesis of Chiral Novel Bis(isonitrile) Ligands

This thesis describes the development and application of new chiral bis(isonitrile) ligands (BINC) in catalysis. These BINC ligands are capable of forming very stable complexes with various transition metals such Pd, Fe, Cu, Rh and Ir.

Specifically, the syntheses of a wide variety of sterically and electronically different bis(isonitrile) ligands **72** can be prepared by structural variation of the oxazolines **71** and phosphorus chloride (Scheme 47). Preparation of the requisite bis(isonitrile) ligands **72a-e** was achieved in moderate yields via lithiation of 2-oxazolines (**71a-e**) following the procedure of Meyers and Novachek and subsequent treatment with phenylphosphonic dichloride at low temperature (Scheme 47).



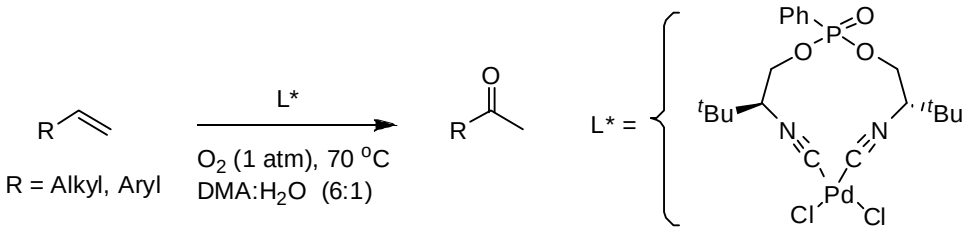
72a : R^1 = Bn, R^2 = H
72b : R^1 = ^{t}Bu, R^2 = H
72c : R^1 = ^{i}Pr, R^2 = H
72d : R^1 = Me, R^2 = Ph (2S, 3R)
72e : R^1 = ^{i}Pr, R^2 = Me (2R, 3S)

Scheme 47: Synthesis of bis(isonitrile) ligands **72a-e**

Efficient aerobic Wacker oxidation of styrenes using novel palladium bis(isonitrile) catalysts

Chiral pseudo C_2-symmetrical palladium (II) bis(isonitrile) complexes were found to catalyze the Wacker oxidation of aliphatic and especially styrenes in the absence of further cocatalysts gives rise to methyl ketones in a highly chemoselective manner (Scheme 48). The palladium

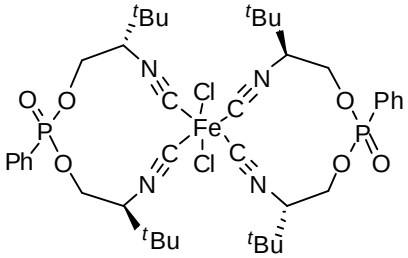
bis(isonitrile) catalyst was characterized by NMR spectroscopy and X-ray structure analysis, revealing a dissymmetric coordination of palladium by the two isonitrile moieties.



Scheme 48: Wacker oxidation of aliphatic and aromatic alkenes using bis(isonitrile) palladium complexes.

Asymmetric Transfer Hydrogenation of Aromatic and Heteroaromatic ketones using Chiral Novel bis(isonirile) iron complexes

We have also achieved the first version of iron complex of chiral bis(isonitrile) ligand (**118b**), catalyzing asymmetric transfer hydrogenation of aromatic, heteroaromatic and pyridyl ketones under mild conditions.

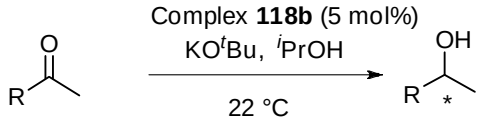


118b

Figure 26: Iron (^{t}Bu-BINC) catalyst

Complex **118b** was found to be an active catalyst at room temperature for transfer hydrogenation of substituted acetophenones, cyclic ketones, heteroaromatic and pyridyl ketones to corresponding alcohols in basic isopropanol. Excellent conversion with moderate enantioselectivity was observed in substituted acetophenones and

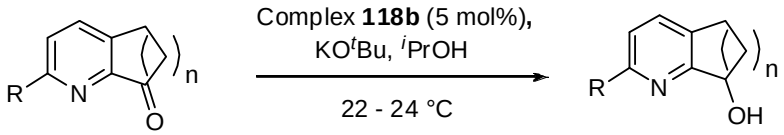
heteroaromatic ketones (Equation 1) using iron bis(isonitrile) complex **118b**. In contrast, several pyridyl ketones with rigid backbones were reduced with excellent conversions and enantioselectivities (Equation 2) to corresponding chiral Pyridyl alcohols.



1

R = substituted acetophenone, heteroaromatic ketones

Conv. upto 99 %
ee up to 69 %



2

n = 1,2,3
R = Ph, Cl

Conv. upto 99 %
ee up to 91 %

G. Experimental

General

^{1}H NMR-Spectra were recorded on Bruker Avance 300, Bruker Avance 400, Bruker Avance 600, Varian Inova 600, Bruker DRX-400 with a H/C/P/F QNP gradient probe and Bruker Avance 500 with a dual carbon/proton CPDUL cryoprobe. The chemical shift δ is given in [ppm], calibration was set on chloroform-d_1 (7.26 ppm) or tetramethylsilane (0.00 ppm) as internal standard. The spectra were evaluated in 1st order and the coupling constants are given in Hertz [Hz]. The following abbreviations for the spin multiplicity were used: s = singlet, d = doublet, t = triplet, q = quartet, qt = quintet, m = multiplet, dt = doublet of a triplet, dd = double doublet, ddd = doublet of a double doublet, sept = septet. The used deuterated solvents are given separately.

^{13}C NMR-Spectra were recorded on Bruker Avance 300, Bruker Avance 400, Bruker Avance 600, Varian Inova, Bruker DRX-400 with a H/C/P/F QNP gradient probe and Bruker Avance 500 with a dual carbon/proton CPDUL cryoprobe. The chemical shift δ is given in [ppm], calibration was set on chloroform-d_1 (77.16 ppm), or tetramethylsilane (0.00 ppm) as internal standard.

Melting points were measured on a Büchi SMP 20 in a silicon oil bath. The melting points are uncorrected.

Infrared-Spectra were recorded on a Bio-Rad Excalibur FTS 3000 spectrometer, equipped with a Specac Golden Gate Diamond Single Reflection ATR-System. The wave numbers are given in [cm^{-1}].

Masspectrometry was performed on Varian MAT 311A, Finnigan MAT 95, Thermoquest Finnigan TSQ 7000, Nermag quadrupoles, VG ZAB high-resolution double-focusing and VG Autospec-Q tandem hybrid with EBEqQ configuration. The percentage set in brackets gives

the peak intensity related to the basic peak (I = 100%). High resolution mass spectrometry (HRMS): The molecular formula was proven by the calculated precise mass.
Elemental analysis was prepared by the micro analytic section of the University of Regensburg using a Vario EL III or Mikro-Rapid CHN (Heroes).

Optical rotation was measured at rt on a 241 MC Perkin-Elmer polarimeter at a wavelength of 589 nm (Na-D) in a 1 dm or 0.1 dm cell. The concentration is given in [g/100 ml].

X-ray analysis was performed by the crystallography laboratory of the University of Regensburg (STOE-IPDS, Stoe & Cie GmbH).

Chiral HPLC was performed in the analytic department of the University of Regensburg or on a Kontron Instruments 325 System (HPLC 335 UV detector, λ = 254 nm, Chiracel OD/OD-H, OJ and AS respectively served as chiral stationary phase.

Gaschromatography (GC) was measured in the analytic department of the University of Regensburg or on Fisons Instruments GC 8000 series (Data Jet Integrator, CP-chiralsil-DEX-CP column).

Thin layer chromatography (TLC) was prepared on TLC-aluminium sheets (Merck, silica gel 60 F_{254}, 0.2 mm). Detection in UV-light λ = 254 nm, staining with I_2, Mostain, molybdatophosphoric-acid (5% in ethanol), $KMnO_4$ solution or vanillin-sulfuric acid. GC conversions for the reactions were determined relative to decane as an internal standard

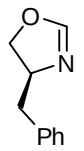
Column chromatography was performed in glass columns (G2 or G3). As a stationary phase silica gel Merck-Geduran 60 (0.063-0.200 mm) or flash silica gel Merck 60 (0.040-0.063 mm) was used.

Solvents: Absolute solvents were prepared according to usual lab procedures or taken from the MB-SPS solvent purification system. Ethylacetate, hexanes (40-60 °C) and dichloromethane were purified by distillation before use. Further solvents and reagents were of p.a. quality. THF, diethyl ether and toluene were distilled over sodium/benzophenone.

Isopropanol was dried over sodium and DMA was dried over vacuum activated 4 Å molecular sieves.

Reactions with oxygen- and moisture sensitive reactants were performed in oven dried and in vacuo heated reaction flasks under a pre-dried inert gas (nitrogen or argon) atmosphere. For cooling to temperatures < -40 °C a cryostat Haake EK 90 or dry ice/*iso*-propanol mixture was used.

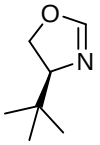
Synthesis of oxazolines



(*S*)-Benzyl-2-oxazoline (71a):

(*S*)-Phenylalinol (3 g, 19.8 mmol), and DMF-DMA (2.77 mL, 1.05equiv) and Amberlite IR-120 resin (150 mg) in benzene (50 mL) were refluxed for 16 h in a flask equipped with a liquid/solid extraction apparatus containing 15 g of 4Å molecular sieves. The reaction mixture was filtered of resin, washed with 10% $KHCO_3$ (30 mL) and brine and dried. The solution was concentrated and subjected to Kugelrohr distillation 55°C to obtain 1.78 g (56%) of the compound **71a** as a clear liquid.

IR (neat): υ 3062, 3029, 1629, 1091 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.68 (dd, *J* = 8.1, 13.8 Hz, 1H), 3.09 (dd, *J* = 5.7, 13.7 Hz, 1H), 3.93 (t, *J* = 7.7, 1H), 4.16(t, *J* = 8.8 Hz, 1H), 4.34-4.45 (m, 1H), 6.82 (d, *J* = 1.9 Hz ,1H), 7.20-7.34 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 41.57, 66.46, 70.43, 126.49, 128.49, 129.13, 137.69, 154.73.

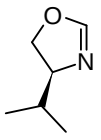


(*S*)-*tert*-butyl-2-oxazoline (71b):

With a water bath to moderate the exotherm, (*S*)-*tert*-leucinol (10.2 g, 86.8 mmol), and DMF-DMA (13.8 mL, 1.2 equiv) were combined, neat. After the mixture was stirred with for 4 h,

the volatiles were removed by rotory evaporation and the mixture was twice azeotropically concentrated with 30 ml of hexane. TsOH (40 mg) was added to the resultant mixture, and the mixture was diluted with hexanes (150 mL), fitted with a liquid/solid extraction apparatus containing 30 g of 4Å molecular sieves and refluxed for 48 h. The solution was washed with 10% $KHCO_3$ (30 mL) and brine and dried. The hexanes were removed by distillation at atmospheric pressure. The mixture was then distilled at reduced pressure 74-75 °C to obtain 5 g (50%) of the compound **71b** as a clear liquid.

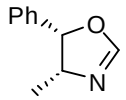
IR (neat): υ 1635, 1395, 1366, 1102 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 0.811 (s, 9H), 3.73--3.79 (m, 1H), 3.90 (t, *J*= 8.5 Hz, 1H), 4.04 (dd, *J* = 8.9, 10.6 Hz, 1H), 6.724 (d, *J* = 1.94 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.76 ($CH_{3\ t\text{-}Bu}$), 33.26 ($CH_{3\ t\text{-}Bu}$), 67.32 ($CH_{\ t\text{-}Bu}$), 74.94 (C_{oxa}), 154.13($C{=}N_{oxa}$).



(*S*)–*iso*-propyl-2-oxazoline (71c):

With a water bath to moderate the exotherm, *S*-valinol (4 g, 38.8 mmol), and DMF-DMA (6.19 mL, 46.60 mmol) were combined neat. After the mixture was stirred with for 4 h, the volatiles were removed by rotory evaporation and the mixture was twice azeotropically concentrated with 15 mL of hexane. TsOH (16.8 mg) was added to the resultant mixture, and the mixture was diluted with hexanes (150 mL), fitted with a liquid/solid extraction apparatus containing 14.6 g of 4Å molecular sieves and refluxed for 48 h. The solution was washed with 10% $KHCO_3$ (15 mL) and brine and dried. The hexanes were removed by distillation at atmospheric pressure. The mixture was then distilled at reduced pressure 69-70 °C to obtain 3 g (40%) of the compound **71a** as a clear liquid.

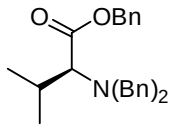
IR (neat): υ 1632, 1386, 1368, 1094 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 0.79, 0.87 (d, *J* = 2.2, 6.8 Hz, 3H), 1.56-1.70 (m, 1H), 3.72-3.86 (m, 2H), 4.03-4.15 (m, 1H), 6.71 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.23 ($CH_{3\ iPr}$), 18.61 ($CH_{3\ iPr}$), 32.42 (CH_{iPr}), 68.82(C_{oxa}), 71.32 (C_{oxa}), 154.13 ($C{=}N_{oxa}$).



(4*R*,5*S*)-4-methyl-5-phenyl-2-oxazoline (71d):

A solution of L-(-) norephedrine (1 g, 6.6 mmol), triethyl orthoformate (1.1 g, 7.3 mmol), and trifluoroacetic acid (17 mol %) in 1,2-dichloroethane (20 mL) was heated at reflux for 7 h under N_2. After cooling, the reaction mixture was poured, with vigorous stirring, into ice cold 20% $KHCO_3$ (1.5 mL/mmol), and the organic layer was separated. The combined organic layer was washed with saturated brine, dried over anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure to leave a light yellowish solid (639 mg, 60%).

IR (neat): υ 1632 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 0.75 (d, *J* = 6.8 Hz, 3H), 4.34 – 4.47 (m, 1H), 5.52 (d, *J* = 10.1 Hz, 1H), 6.97 (d, *J* = 1.9 Hz, 1H), 7.17 – 7.36 (m, 5H). ^{13}C NMR (75 MHz): δ = 16.70, 63.01, 81.72, 125.1, 126.9, 127.3, 135.4, 152.9. Mass (CI- MS), m/z (rel. intensity): $[M+H^+]$ 162, $[MNH_4^+]$ 179.

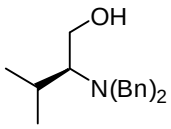


(*S*)-benzyl-2-(dibenzylamino)-3-methylbutanoate (76):

A solution of benzyl bromide (2.62 gm, 15.24 mmol) in ethanol (4 mL) was slowly added to solution of *S*-valine (0.5 gm, 3.81 mmol) and K_2CO_3 (2.1 gm, 15.24 mmol) in a 5:1 mixture of ethanol-water (22 mL). The reaction mixture was heated under reflux for 14 h. The solvent was removed under reduced pressure and water was added to the residue. The resulting slurry was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure. The resulting crude mixture was purified by column chromatography to get colorless oily product (1.2 gm, 73%).

^1H NMR ($CDCl_3$, 300 MHz): δ = 0.80 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.8 Hz, 3H), 2.14-2.30 (m, 1H), 2.95 (d, *J* = 10.97 Hz, 1H), 3.32 (d, *J* = 14 Hz, 2H), 4.0 (d, *J* = 14

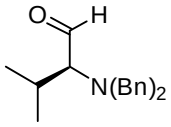
Hz, 2H), 5.26 (quart. *J* =12.3, 42 Hz, 2H), 7.2- 7.5(m, 15 H). ^{13}C NMR (75 MHz): δ = 19.58, 19.99, 27.31, 54.64, 65.74, 68.15, 126.9, 128.3, 129.4, 128.6, 128.7, 128.8, 136.2, 139.5, 171.9.



(*S*)-2-(dibenzylamino)-3-methylbutan-1-ol (77):

A solution of benzyl protected amino acid (4.8 gm, 12.39 mmol) in dry THF (25 mL) was slowly added to suspension of $LiAlH_4$ (0.94 gm, 24.77 mmol) in a dry THF (25 mL) at 0 °C. The reaction mixture was warmed to room temperature and quenched with NH_4Cl at 0 °C. The resulting slurry was extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and evaporated under reduced pressure. The resulting crude mixture was purified by column chromatography to get colorless oily product in quantitative yield.

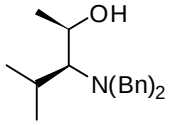
^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.90 (d, *J* = 6.6 Hz, 3H), 1.15 (d, *J* = 6.8 Hz, 3H), 1.99-2.16 (m, 2H), 2.49- 2.81 (m, 1H), 3.02 (bs, 1H), 3.45 (t, 1H), 3.52-3.64 (m, 1H), 3.67(d, *J* = 13.4 Hz, 1H), 3.89 (d, *J* = 13.2 Hz, 1H), 7.22-7.36 (m, 10H). ^{13}C NMR (75 MHz): δ = 21.16, 22.78, 27.64, 54.24, 59.26, 64.69, 127.2, 128.5, 129.2, 139.7.



(*S*)-2-(dibenzylamino)-3-methylbutanal (78):

A solution of dichloromethane (21 mL) and oxalyl chloride (0.8 mL, 9.2 mmol) was placed in a 100mL three neck flask equipped with two dropping funnels containing DMSO (1.6 mL, 22.5 mmol) dissolved in dichloromethane (5 mL) and the alcohol (2.9 gm, 10.2 mmol) dissolved in dichloromethane (10 mL) respectively. The DMSO was added to the stirred oxalyl chloride solution at -78 °C. The reaction mixture was stirred for 4-5 minutes and the alcohol was added within 5-10 min; stirring was continued for next 30 minutes Triethylamine (7.1 mL, 51.2 mmol) was addedand the reaction mixture was allowed to warm to room temperature. Water was added and the aqueous layer was extracted with dichloromethane.

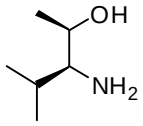
The organic layers were combined, washed with saturated NaCl and dried over sodium sulfate and concentrated under reduced pressure. The crude aldehyde was used without any purification.



(2*R*,3*S*)-3-(dibenzylamino)-4-methylpentan-2-ol (79):

The solution of aldehyde (100 mg, 0.36 mmol) in ether (0.5 mL) was added dropwise under nitrogen to a solution of methymagnesium iodide (0.6 mmol) in ether (2 mL). After one hour stirring the reaction mixture was quenched with saturated NH_4Cl solution and the aqueous phase was extracted with ether. The combined organic layers were washed with brine solution and dried over Na_2SO_4. The crude mixture was purified by column chromatography (80 mg, 76%).

^{1}H NMR ($CDCl_3$, 600 MHz): δ = 0.96 (d, *J* = 6.6 Hz, 3H), 1.21 (d, *J* = 6.6 Hz, 3H), 1.23 (d, *J* = 6.6 Hz, 3H), 2.13 – 2,19(m, 1H), 2.50 (dd, J = 4.9, 9 Hz, 1H), 2.81 (bs, 1H), 3.76 (d, J = 13.6 Hz, 2H), 3.80 – 3,86 (m, 1H), 3.89 (d, J = 13.6 Hz, 2H), 7.23 – 7.28 (m, 2H), 7.29 – 7.35 (m, 8H). ^{13}C NMR (75 MHz): δ = 19.53, 20.88, 23.33, 18.34, 56.59, 66.05, 67.40, 127.25, 128.48, 129.19, 139.96.

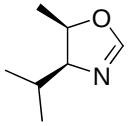


(2*R*,3*S*)-3-amino-4-methylpentan-2-ol (81):

To a solution of the dibenzylamino alcohol (50 mg, 0.168 mmol) in 2 mL of dry MeOH was added 9 mg of 20% $Pd(OH)_2$-C in one portion. The mixture was stirred under 1 atmosphere of hydrogen, and the reaction was monitored by TLC. After completion of the reaction, the catalyst was removed by filtration through celite and washed with 5 mL of MeOH. The solvent was removed under reduced pressure to afford the pure product (15 mg, 78%).

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 0.89 (d, *J* = 6.6 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.6 Hz, 3H), 1.44 – 1.55 (m, 1H), 1.74 (bs, 3H), 2.37 (dd, *J* = 4.7, 8.5 Hz, 1H), 3-79 – 3.90

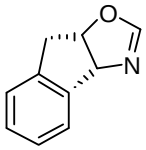
(m, 1H). ^{13}C NMR (75 MHz): δ = 16.43, 19.63, 19.68, 31.60, 61.91, 67.28. Mass (EI- MS), m/z (rel. intensity): $[M\text{-}C_2H_5O]^+$ 72.2, $[M\text{-}C_3H_7]^+$ 74.1.



(4*S*,5*R*)-4-isopropyl-5-methyl-2-oxazoline (71e):

With a water bath to moderate the exotherm, amino alcohol (4 g, 34.2 mmol), and DMF-DMA (5.4 mL, 41.02 mmol) were combined neat. After the mixture was stirred with for 4 h, the volatiles were removed by rotory evaporation and the mixture was twice azeotropically concentrated with 15 mL of hexane. TsOH (16.8 mg) was added to the resultant mixture, and the mixture was diluted with hexanes (150 mL), fitted with a liquid/solid extraction apparatus containing 14.6 g of 4Å molecular sieves and refluxed for 48 h. The solution was washed with 10% $KHCO_3$ (15 mL) and brine and dried. The hexanes were removed by distillation at atmospheric pressure. The mixture was then distilled at reduced pressure to obtain 1.7 g (39 %) of the compound as a clear liquid.

IR (neat): 1626 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.967 (d, *J* = 6.6 Hz, 3H), 1.05 (d, *J* = 6.6 Hz, 3H), 1.22 (d, *J* = 6.6 Hz, 3H), 1.73 – 1.90 (m, 1H), 3.54 – 3.63 (m, 1H), 4.61 – 4.74 (m, 1H), 6.789 (d, *J* = 2.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.44, 20.16, 21.54, 27.77, 73.44, 77.79, 154.04. Mass (EI- MS), m/z (rel. intensity): $[M+H^+]$ 128.1, $[MNH_4^+]$ 145.



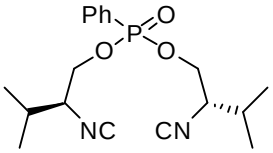
(3a*R*,8a*S*)-8,8a-dihydro-3aH-indeno[1,2]oxazole (71f):

A solution of (1R,2S)-2-amino-2,3-dihydro-1H-inden-1-ol (500 mg, 3.35 mmol), triethyl orthoformate (548 mg, 3.7 mmol), and trifluoroacetic acid (17 mol %) in 1,2-dichloroethane (9 mL) was heated at reflux for 7 h under N_2. After cooling, the reaction mixture was poured, with vigorous stirring, into ice cold 20% $KHCO_3$ (1.5 mL/mmol), and the organic layer was separated. The combined organic layer was washed with saturated brine, dried over

anhydrous Na_2SO_4, filtered, and evaporated under reduced pressure to leave a light yellowish solid (501 mg, 94%).

IR (neat): υ 3037, 2972, 1646, 1614, 1477, 1256 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 3.25 (dd, *J* = 17.99, 1.64 Hz, 1H), 3.46 (dd, *J* = 17.99, 6.9 Hz, 1H), 5.27 (ddd, *J* = 7.9, 6.9, 1.6 Hz, 1H), 5.54 (dd, *J* = 7.9, 1.8 Hz), 6.8 (d, *J* = 1.8 Hz), 7.25 - 7.29 (m, 3H), 7.46 – 7.50 (m, 1H). ^{13}C NMR (75.5 MHz): δ = 39.62, 75.63, 81.96, 125.27, 125.36, 127.51, 128.57, 139.46, 141.62, 154.74. MS (CI-MS), m/z (rel. intensity): $[M+H^+]$ 160.1, $[MNH_4^+]$ 177.1.

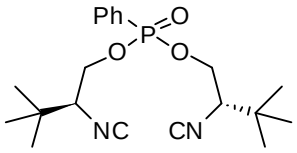
Synthesis of BINC Ligands:



Bis((*S*)-2-isocyano-3-methylbutyl) phenylphosphonate (*i*Pr-BINC, 72c):

To a solution of diisopropylamine (0.2 mL, 1.42 mmol) in 4 mL of THF was added under nitrogen atmosphere at 0 °C n-butyl lithium (15 % in hexane, 0.5 mL, 1.15 mmol). After stirring for 15 min the solution was cooled down to –78 °C and *i*-Propyl-2-oxazoline (**71c**, 100 mg, 0.885 mmol) dissolved in 4 mL THF was added. After stirring for 30 min, phenylphosphonic dichloride (0.07 mL, 0.53 mmol) was added followed by immediate removal of the cooling bath, and the solution was allowed to stir at room temperature for 2 hours. Aqueous NH_4Cl solution was added followed by work up of the mixture with ethyl acetate and brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. Yellowish viscous liquid was obtained after purification on silica (113 mg, 61%).

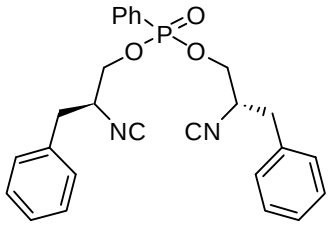
(hexanes/ethyl acetate 2:3, R_f = 0.52). $[\alpha]^{20}_D$ + 36 (c = 1.0, $CHCl_3$). IR (neat): υ 2969, 2141, 1595, 1475, 1442, 1253 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.80-7.90 (m, 2H), 7.58 - 7.66 (m, 1H), 7.48-7.55 (m, 2H), 4.03-4.28 (m, 4H), 3.63-3.76 (m, 2H), 1.88-2.03 (m, 2H), 1.03 (d, 6H), 1.01 (d, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.3 (CN), 133.37 (d, *J* = 2.8 Hz), 131.88 (d, *J* = 10.5 Hz), 128.85(d, *J* = 15.4 Hz), 126.05 (d, *J* = 190.9 Hz), 65.49 (rel. intens. 2), 60.80 (rel. intens. 2), 28.83, 28.78, 19.40, 19.34, 17.09, 16.97. ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 20.78 (s). MS (EI-MS), m/z (rel. intensity): $[M+H^+]$ 349, $[MNH_4^+]$ 366. HRMS: calcd. for $C_{18}H_{25}O_3N_2P$ $[M^{\cdot+}]$: 348.160, found: 348.1603.



Bis((*S*)-2-isocyano-3,3-dimethylbutyl) phenylphosphonate (^{t}Bu-BINC, 72b):

To a solution of diisopropylamine (0.09 mL, 0.630 mmol) in 2 mL of THF was added under nitrogen atmosphere at 0 °C n-butyl lithium (15 % in hexane, 0.22 mL, 0.512 mmol). After stirring for 15 min the solution was cooled down to –78 °C and *t*-Butyl-2-oxazoline (**71b**, 50 mg, 0.394 mmol) dissolved in 2 mL THF was added. After stirring for 30 min, phenylphosphonic dichloride (0.03 mL, 0.236 mmol) was added followed by immediate removal of the cooling bath, and the solution was allowed to stir at room temperature for 2 hours. Aqueous NH_4Cl solution was added followed by work up of the mixture with ethyl acetate and brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. White colored solid was obtained after purification on silica (52 mg, 59 %).

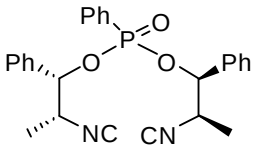
m.p 67 °C, (hexanes/ethyl acetate 2:3, R_f = 0.56). $[\alpha]^{20}_D$ + 83 (c = 1.0, $CHCl_3$). IR (KBr): υ 2964, 2140, 1594, 1475, 1442, 1394, 1370, 1346, 1246, 926 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.87 (dd, 2H, *J* = 7 Hz, 13.8 Hz), 7.61(t, 1H, *J* = 7.5 Hz), 7.45-7.54 (m, 2H), 4.28-4.36 (m, 1H), 4.16- 4.27 (m, 2H), 4.01 (q, 1H, *J* = 9.2 Hz), 3.68 (dd, 1H, *J*= 3.1, 9.1 Hz), 3.54 (dd, 1H, *J*= 3.8, 8.9 Hz), 1.03 (s, 18 H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.37 (CN), 133.45 (d, $C_{Ar\text{-}p}$, *J* = 3.05 Hz)), 132.06 (d, $C_{Ar\text{-}o}$, *J* = 10.3 Hz), 128.96 (d, $C_{Ar\text{-}m}$, *J* = 15.5 Hz), 126.4 (d, C_{ipso}, *J* = 191 Hz), 65.07 (C*H*t-Bu), 64.77 (CH$\underline{C}H_2$), 33.56 ($C_{t\text{-}Bu}$), 33.50 ($C_{t\text{-}Bu}$), 26.37($CH_{3\ t\text{-}Bu}$). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 20.96 (s). MS (EI-MS), m/z (rel. intensity): $[M+H^+]$ 377, $[MNH_4^+]$ 394. HRMS: calcd. for $C_{20}H_{29}O_3N_2P$ $[M^{\cdot+}]$: 376.190, found: 376.191.



Bis((*S*)-2-isocyano-3-phenylpropyl) phenylphosphonate (Bn-BINC, 72a):

To a solution of Benzyl-2-oxazoline (**71a**, 500 mg, 3.11 mmol) in 40 mL of THF was added under nitrogen atmosphere –78 °C n-butyl lithium (15 % in hexane, 1.7 mL, 4.04 mmol) for 10 minutes. After stirring for 30 min, phenylphosphonic dichloride (0.3 mL, 1.9 mmol) was added followed by immediate removal of the cooling bath, and the solution was allowed to stir at room temperature for 2 hours. Aqueous NH_4Cl solution was, followed by work up of the mixture with ethyl acetate. Yellowish viscous liquid was obtained after purification on silica (276 mg, 33 %).

(hexanes: ethyl acetate = 2:3, R_f = 0.47). $[\alpha]^{20}_D$: + 3.4 (c = 1.5, $CHCl_3$). IR (KBr): υ 2140, 1593, 1495, 1253, 961, 746 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.83-7.91 (m, 2H), 7.61-7.66 (m, 1H), 7.49-7.56 (m, 2H), 7.17-7.36(m, 10H), 4.11-4.28 (m, 3H), 3.97-4.06 (m, 3H), 2.97 (t, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.01(CN), 134.82, 133.60 (d, *J* = 3.05 Hz), 132.06 (d, *J* = 10 Hz), 129.38, 129.04(d, *J* = 15 Hz), 129.02, 127.76, 126.06(d, *J* = 191 Hz), 65.80, 56.09, 37.64. ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 20.77 (s). MS (ES-MS), m/z (rel. intensity): $[M+H^+]$ 445, $[MH^+ + H_2O]$ 463. HRMS: calcd. for $C_{26}H_{26}O_3N_2P$ $[MH^+]$: 445.168, found: 445.167.

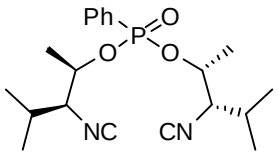


Bis((1*S*,2*R*)-2-isocyano-1-phenylpropyl) phenylphosphonate (72d):

To a solution of HMDS (0.112 mL, 0.525 mmol) in 2 mL of THF was added under nitrogen atmosphere at 0 °C n-butyl lithium (1.6 M, 0.25 mL, 0.404 mmol). After stirring for 15 min the solution was cooled down to –10 °C and oxazoline (**71d**, 50 mg,

0.311 mmol) dissolved in 2 mL THF was added. After stirring for 30 min, phenylphosphonic dichloride (0.026 mL, 0.187 mmol) was added followed by immediate removal of the cooling bath, and the solution was allowed to stir at room temperature for 2 hours. Aqueous NH_4Cl solution was added followed by work up of the mixture with ethyl acetate and brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. Colorless oil was obtained after purification on silica (64 mg, 77%).

IR (neat): υ 2137 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 1.02 (d, *J* = 6.6 Hz, 3H), 1.29 (d, *J* = 6.8 Hz, 3H), 3.71 – 3.78 (m, 1H), 4.08 – 4.14 (m, 1H), 5.06 (dd, *J* = 4.6, 9.2 Hz, 1H), 5.57(dd, *J* = 5, 9.2 Hz, 1H), 7.35 (d, *J* = 7.3Hz, 2H), 7.17 (t, 2H), 7.25 – 7.25 (m, 1H), 7.32 – 7.37 (m, 2H), 7.45 – 7.51 (m, 4H), 7.52 – 7.55(m, 2H), 7.62 – 7.68 (m, 2H). ^{13}C NMR (151 MHz): δ = 17.01, 17.70, 54.71, 55.02, 78.42, 78.68, 127.05, 127.35, 128.36, 128.37, 129.23, 131.51, 132.84, 133.93, 134.94, 158.1, 158.3. Mass (LSI- MS), m/z (rel. intensity): [$M+H^+$] 445. HRMS: calcd. for $C_{26}H_{26}O_3N_2P$ [MH^+]: 445.2, found: 445.168.

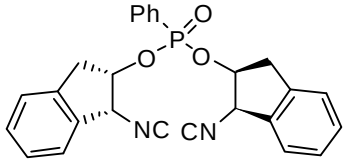


Bis((2*R*,3*S*)-3-isocyano-4-methylpentan-2-yl) phenylphosphonate (72e):

To a solution of diisopropylamine (94 µL, 0.665 mmol) in 2 mL of THF was added under nitrogen atmosphere at 0 °C n-butyl lithium (1.6 M, 0.3 mL, 0.512 mmol). After stirring for 15 min the solution was cooled down to –10 °C and oxazoline (**71e**, 50 mg, 0.394 mmol) dissolved in 2 mL THF was added. After stirring for 30 min, phenylphosphonic dichloride (0.033 mL, 0.236 mmol) was added followed by immediate removal of the cooling bath, and the solution was allowed to stir at room temperature for 2 hours. Aqueous NH_4Cl solution was added followed by work up of the mixture with ethyl acetate and brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. Colorless oil was obtained after purification on silica (70 mg, 70 %).

IR (neat): υ 2969, 2139, 1440, 1392, 1250, 986 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.914 (dd, *J* = 6.6, 9.2 Hz, 6H), 0.995 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 6.6 Hz, 3H), 1.316 (d, *J* = 6.3 Hz, 3H), 1.538 (d, *J* = 6.2 Hz, 3H), 1.74 – 1.85 (m, 1H), 1.86 – 1.97(m, 1H), 3.375 (t, *J* = 6 Hz, 1H), 3.67 (t, *J* = 6.2 Hz, 1H), 4.50 – 4.70 (m, 2H), 7.45 – 7.53 (m, 2H), 7.56 – 7.63 (m, 1H), 7.76 – 7.85 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 158.54, 133.06 (d, *J* = 3 Hz),

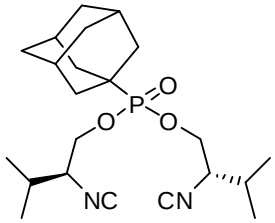
131,64 (d, *J* = 10 Hz), 128.7 (d, *J* = 15.4 Hz), 127.7 (d, *J* = 190.5 Hz), 71.44, 66.25, 29.63, 28.94, 28.60, 19.31, 18.18, 17.53, 16.76. Mass (EI- MS), m/z (rel. intensity): $[M - H]^+$ 375.2. HRMS: calcd. for $C_{20}H_{29}O_3N_2P$ $[MH^+]$: 376.191, found: 376.1905.



Bis((1*R*,2*S*)-1-isocyano-2,3-dihydro-1H-inden-2-yl) phenylphosphonate (72f):

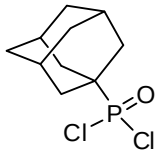
To a solution of oxazoline (**71f**, 100 mg, 0.628 mmol) in 8 mL of THF was added under N_2 atmosphere -78 °C n-BuLi (15% in hexane, 0.691 mmol) dropwise. After stirring for 30 min, phenylphosphonic dichloride (0.053 mL, 0.377 mmol) was added followed by immediate removal of the cooling bath, and the solution was allowed to stirred at room temperature for 1 h. Aqueous NH_4Cl solution was added, followed by work up of mixture with ethyl acetate. Desired product is unstable on silica column.

IR (neat): υ 3049, 2361, 2144, 1728, 1682, 1439, 1248 cm^{-1}. ^1H NMR ($CDCl_3$, 600 MHz): δ = 3.12 (dd, *J* = 16.12, 6.13 Hz, 1H), 3.2 (dd, *J* = 16.12, 5.7 Hz, 1H), 3.35 (dd, *J* = 16.37, 5.9 Hz, 1H), 3.42 (dd, *J* = 16.37, 5.3, 1H), 5.09 (d, *J* = 5.5 Hz, 1H), 5.12 (d, *J* = 5.5 Hz, 1H), 5.18 (dddd, *J* = 7.7, 6.13, 5.7, 5.5 Hz), 5.32 (dddd, *J* = 8.0, 5.95, 5.3, 5.5 Hz), 7.19 (d, *J* = 6.5 Hz, 1H), 7.26 - 7.37 (m, 5H), 7.42 – 7.45 (m, 2H), 7.48 – 7.52 (m, 2H), 7.58 – 7.63 (m, 1H), 7.90 – 7.96 (m, 2H). ^{13}C NMR (150.9 MHz): δ = 36.97, 37.62, 59.77, 59.89, 75.26, 75.56, 124.53, 124.69, 125.30, 125.42, 127.98, 128.08, 128.69, 128.79, 129.91, 130.01, 132.09, 132.16, 133.29, 135.79, 138.43, 138.64, 159.82, 159.87. ^{31}P NMR (121.5 MHz): δ = 20.59. MS (CI-MS), m/z (rel. intensity): $[MH^+]$ 441.2, $[MNH_4^+]$ 458.2.



Bis((*S*)-2-isocyano-3-methylbutyl) admantylphosphonate (72g):

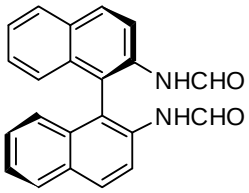
To a solution of diisopropylamine (0.1 mL, 0.747 mmol) in 2 mL of THF was added under nitrogen atmosphere at 0 °C n-butyl lithium (15 % in hexane, 0.32 mL, 0.575 mmol). After stirring for 15 minutes the solution was cooled down to –78 °C and *i*-Propyl-2-oxazoline (**71c**, 50 mg, 0.442 mmol) dissolved in 2 mL THF was added. After stirring for 30 min, admantylphosphonic dichloride (**74**, 67 mg, 0.265 mmol) was added followed by immediate removal of the cooling bath, and the solution was allowed to stir at room temperature for 2 hours. Aqueous NH_4Cl solution was added followed by work up of the mixture with ethyl acetate and brine. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. Colorless viscous liquid was obtained after purification on silica (43 mg, 40 %).
(hexanes/ethyl acetate 2:1, R_f = 0.43). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 4.01-4.21 (m, 4H), 3.61-3.71 (m, 2H), 1.85-2.1 (m, 8H), 1.63-1.82 (m, 9H), 1.0-1.10 (m, 12H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.08 (CN), 65.29, 61.17, 36.35, 35.26, 34.98, 28.99, 26.92, 19.45, 17.22. ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 34.57 (s). MS (CI-MS), m/z (rel. intensity): [$M+H^+$] 407, [MNH_4^+] 424.



Admantylphosphonic dichloride (74):

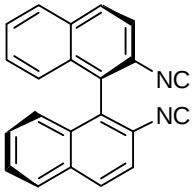
To a solid mixture of admantylbromide (500 mg, 2.33 mmol) and aluminum tribromide (900 mg, 3.4 mmol) phosphorus trichloride (5 mL, 53.47 mmol) was added dropwise at room temperature. The mixture was refluxed for 5 h, then allowed gradually to cool down to room temperature. The mixture was filtered and washed with benzene. The addition of CCl_4 gives a suspension, which is hydrolyzed by ice water. The organic layer is separated, dried over Na_2SO_4 and concentrated under vacuum to give yellow crystalline product (547 mg, 93%).

IR (neat): υ 1265 (P-O) cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.0-2.24 (m, 9H), 1.7 – 1.86 (m, 7H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 48.86 (d, *J* = 88.2 Hz), 35.838 (d, *J* = 29 Hz), 34.96 (d, *J* = 4.4 Hz), 27.49 (d, *J* = 15.5 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 65.78 (s).



(*R*)-N,N'-(1,1'-binaphthyl-2,2'-diyl)diformamide (86):

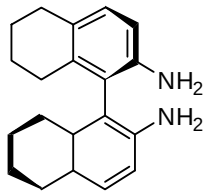
To a saturated solution of the (R)-diamine (20 mg, 0.070 mmol) in ether at 0°C was added dropwise acetic formic anhydride (4 equiv., 25 mg). After stirring for 1 h at 0 °C the mixture was cooled to -78 °C and the solvent was evaporated after 1 h. Product obtained was used for next step without purification.



(*R*)-2,2'-diisocyano-1,1'-binaphthyl (87):

To a cooled solution of formamide (34 mg, 0.099 mmol) in dichlorormethane (0.8 mL) at 0°C was added triethylamine (0.072 mL, 0.515 mmol) and diphosgene (0.017 mL, 0.138 mmol). The reaction was warmed to room temperature and stirred overnight. The mixture was washed with $NaHCO_3$ and water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. Yellowish solid was obtained after purification on silica (27 mg, 89%).

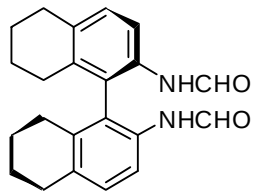
$[\alpha]^{20}_{D}$: - 79.6 (c = 0.5, $CHCl_3$).IR (neat): υ 3057, 2924, 2114, 1504, 815, 748 cm^{-1} ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.146 (d, *J* = 8.5 Hz, 2H), 7.41 (t, *J* = 7.5 2H), 7.59 (t, *J* = 7.9 Hz, 2H), 7.66 (d, *J* =8.7 Hz, 2H), 7.99 (d, *J* = 8.3 Hz, 2H), 8.07 (d, *J* = 8.7 Hz, 2H). ^{13}C NMR (75 MHz): δ = 123.57, 124.09, 126.02, 127.90, 128.26, 128.56, 130.75, 130.86, 131.78, 133.08, 167.14. MS (EI-MS), m/z (rel. intensity): $[M^{+\cdot}]$ 304.1. HRMS: calcd. for $C_{22}H_{12}N_2$ $[M^{+\cdot}]$: 304.099, found 304.100.



(*R*)-2,2'-diamino-H_8-1,1'-binaphthyl (BINAM, 84):

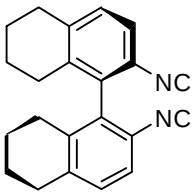
25 mg (0.088 mmol) of (R)-diamine, 3 mg of 10 % Pd/C and 1 mL of methanol were placed into a autoclave and stirred under 50 bar H_2 at 100 °C for 1 h. The reaction mixture was cooled to rt, the metal catalyst was filtered off and washed with dichloromethane. The combined filtrated were concentrated in vacuum to give 14 mg (70 %) of desired product, which was purified by silica chromatography.

IR (neat): υ 3456, 3365, 2926, 1607, 1275, 1441, 1302, 1285, 829, 807 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.63 – 1.77 (m, 8H), 2.13 – 2.34 (m, 4H), 2.72 (t, J = 6.3 Hz, 4H), 3.24 (s, 4H), 6.62 (d, J = 8.1 Hz, 2H), 6.92 (d, J = 7.9 Hz, 2H). ^{13}C NMR (75 MHz): δ = 23.27, 23.47, 27.0, 29.39, 113.12, 122.0, 127.7, 129.3, 136.3, 141.6. MS (EI-MS), m/z (rel. intensity): [$M^{+\cdot}$] 294.1.



(*R*)-N,N'-(H_8-1,1'-binaphthyl-2,2'-diyl)diformamide (88):

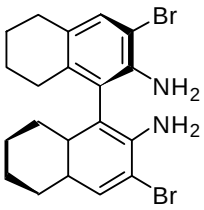
To a saturated solution of the diamine (68 mg, 0.233 mmol) in ether at 0°C was added dropwise acetic formic anhydride (4 equiv., 82 mg). After stirring for 1 h at 0 °C the mixture was cooled to -78 °C and the solvent was evaporated after 1 h. Product obtained was used for next step without purification.



(*R*)-2,2'-diisocyano-H_8-1,1'-binaphthyl (89):

To a cooled solution of formamide (80 mg, 0.229 mmol) in dichlorormethane (2 mL) at 0 °C was added triethylamine (0.166 mL, 1.2 mmol) and diphosgene (0.039 mL, 0.322 mmol). The reaction was warmed to room temperature and stirred overnight. The mixture was washed with $NaHCO_3$ and water. The organic layer was dried over Na_2SO_4 and concentrated under vacuum. Yellowish solid was obtained after purification on silica (62 mg, 86%).

$[\alpha]^{20}_D$: + 83.3(c = 1, $CHCl_3$). IR (neat): υ 2035, 2860, 2113, 1869, 1462, 833, 813 cm^{-1}. IR (neat): υ cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.6 – 1.8 (m, 8H), 2.0 – 2.1 (m, 2H), 2.2 – 2.4 (m, 2H), 2.7 – 2.9 (m, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 2H). ^{13}C NMR (75 MHz): δ = 22.28, 22.64, 27.26, 29.83, 123.03, 130.09, 133.73, 136.69, 139.87, 164.74. MS (EI-MS), m/z (rel. intensity): [$M^{+\cdot}$] 312.2. HRMS: calcd. for $C_{22}H_{20}N_2$ [$M^{+\cdot}$]: 312.41, found 312.16..

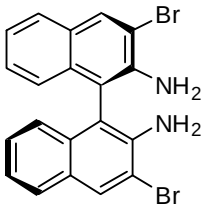


3,3′-dibromo (*R*)-BINAM (90):

To a stirred solution of (R)-5,5',6,6',7,7',8,8'-octahydro- 1,1'- binaphthyl-2,2'-diamine (56 mg, 0.192 mmol) in dry THF (1 mL)was added NBS (68 mg, 0.383 mmol) at 0 °C. The reaction mixture was stirred at 0 °C for 1 minute. The mixture was then quenched with saturated $NaHCO_3$ and saturated Na_2SO_3 at 0 °C, and extracted with ethylacetate. The combines organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography (hexanes/ethyl acetate = 40:1) to afford desired product (79 mg, 92%).

IR (neat): υ 3471, 3375, 2930, 2855, 2359, 2334, 1603, 1452, 907, 732 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz): δ = 1.60- 1.74 (m, 8H), 2.03 – 2.26 (m, 4H), 2.70 (t, J = 6.0 Hz, 4H),

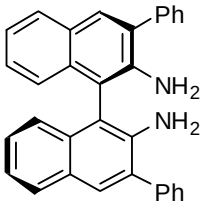
3.72 (brs, 4H), 7.21 (s, 2H). ^{13}C NMR (75 MHz): δ = 22.98, 23.16, 26.76, 29.06, 127.04, 122.39, 129.04, 132.3, 135.7, 139.2. MS (EI-MS), m/z (rel. intensity): [MH^+] 449.0



(*R*)-3,3'-dibromo-1,1'-binaphthyl-2,2'-diamine (91):

To a stirred solution of (R)-3,3'-Dibromo-5,5',6,6',7,7',8,8'-octahydro-1,1'- binaphthyl-2,2'-diamine (24 mg, 0.0533 mmol) in benzene (1 mL)was added DDQ (61 mg, 0.266 mmol) at room temperature, and the mixture was refluxed for 5 minutes. Upon consumption of starting material, the reaction mixture was directly purified by column chromatography to afford desired product (9.3 mg, 40% yield, >94% *ee*).

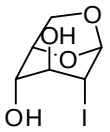
[α] + 80.7 (c 0.5, $CHCl_3$). IR (neat): υ 3472, 3371, 2956, 2925, 2854, 2365, 1730, 1596 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.14 (bs, 4H), 6.98 (d, *J* = 7.6 Hz, 2H), 7.19 – 7.31 (m, 4H), 7.73 (d, *J* = 7.6 Hz, 2H), 8.17 (s, 2H). ^{13}C NMR (75 MHz): δ = 112.66, 113.38, 123.43, 123.84, 127.36, 127.36, 127.41, 128.65, 132.24, 132.46, 140.33. MS (EI-MS), m/z (rel. intensity): [MH^+] 440.8. HPLC (Chiralpak AD-H, hexane/^{i}PrOH 95/5, 0.5 ml/min, 254 nm).



(*R*)-3,3'-diphenyl-1,1'-binaphthyl-2,2'-diamine (92):

A mixture of (R)-3,3'-Dibromo-1,1'- binaphthyl-2,2'-diamine (20 mg, 0.045 mmol), $Pd(OAc)_2$ (1 mg, 0.0045 mmol), PPh_3 (5 mg, 0.018 mmol), $Ba(OH)_2$. $8H_2O$ (57 mg, 0.18 mmol) and phenylboronic acid (35 mg, 0.14 mmol) in DME (0.5 mL) and H_2O (45 µL) was refluxed for 20 h. After cooling to room temperature, the mixture was poured into water and extracted with ethylacetate. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography to afford white solid (11 mg, 57 %).

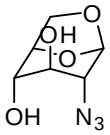
^{1}H NMR ($CDCl_3$, 300 MHz): δ =2.67 (bs, 4H), 7.12 – 7.18 (m, 2H), 7.20 – 7.30 (m, 4H), 7.37 – 7.45 (m, 2H), 7.46 – 7.54 (m, 4H), 7.59 – 7.67 (m, 4H), 7.75 – 7.84 (m, 4H). ^{13}C NMR (75 MHz): δ = 113, 122.7, 123.9, 126.8, 127.7, 128.2, 128.3, 128.9, 129.4, 129.8, 130.8, 133, 139.3, 140.8. MS (EI-MS), m/z (rel. intensity): [$M^{+\cdot}$] 436.2.



1,6-anhydro-2-deoxy-2-iodo-ß-D-glucopyranose (100):

A mixture of glucal (340 mg, 2.33 mmol), bis-(tributylstannyl) oxide (0.95 mL, 1.86 mmol) and 3 Å molecular sieves (4 gm/ 100 mL) in acetonitrile (10 mL) was refluxed for 3 h. After cooling to room temperature iodine (355 mg, 2.8 mmol) was added and mixture was stirred at room temperature for 2 h. Solvent was evaporated after 2 h and crude product was purified by column chromatography to afford colorless oily product (210 mg, 78 %).

^{1}H NMR (D_2O, 300 MHz): δ = 3.34 (s, 1H), 3.55 – 3.70 (m, 2H), 3.86 – 3.91 (m, 1H), 4.09 – 4.13 (m, 1H), 4.16 (dd, J = 1, 7.4 Hz, 1H), 4.48 – 4.55 (m, 1H), 5.67 (s, 1H). ^{13}C NMR (75 MHz): δ = 28.8, 67.1, 73.9, 76.6, 77.9, 105.1. MS (ESI-MS), m/z (rel. intensity): [M + $HCOO^-$] 316.9, [MCl^-] 306.9.

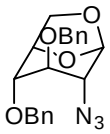


1,6-anhydro-2-deoxy-2-azido-ß-D-glucopyranose (101):

A mixture of 1,6-anhydro-2-deoxy-2-iodo-ß-D-glucopyranose (210 mg, 0.77 mmol) and sodium azide (15q mg, 2.32 mmol) in DMF (1.4 mL) and H_2O (0.2 mL) was stirred at 120 °C for 2 h. The mixture was concentrated under vacuum and the residue was dissolved in EtOH (0.62 mL) and H_2O (0.07 mL) and treated with charcoal under reflux for 30 min. The mixture was filtered through Celite, concentrated and purify by column chromatography to furnish white solid (115 mg, 80 %).

^{1}H NMR (DMSO-d_6, 300 MHz): δ = 3.02 (s, 1H), 3.42 (s, 1H), 3.5 – 3.6 (m, 2H), 3.93 (d, J = 7 Hz, 1H), 4.43 (d, J = 4.9 Hz, 1H), 5.26 (d, J = 3.6 Hz, 1H), 5.35 – 5.43 (m, 2H). ^{13}C NMR

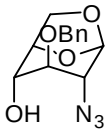
(75 MHz): δ = 62, 64.8, 70.6, 41.4, 76.3, 99.7. MS (ESI-MS), m/z (rel. intensity): [M + $HCOO^-$] 232.1, [MCl^-] 222.1.



1, 6-anhydro-2-azido-3,4-di-O-benzyl-2-deoxy-ß-D-glucopyranose (102):

A solution of benzyl bromide (40 mg, 0.235 mmol) in DMF (1 mL) was slowly added to solution of azide (20 mg, 0.11 mmol) and NaH (60 % in petether, 10 mg, 0.235 mmol) in DMF (2 mL) at 0 °C. The reaction mixture was allowed to reach room temperature and the solvent was removed under vacuum. The resulting crude mixture was purified by column chromatography to afford desired product (33 mg, 83 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.3 (s, 1H), 3.4 (s, 1H), 3.74 (dd, J = 6, 7 Hz, 1H), 4.03 (dd, J = 0.8, 7.4 Hz, 1H), 4.49 – 4.68 (m, 5H), 5.52 (s, 1H), 7.28 – 7.43 (m, 10H). ^{13}C NMR (75 MHz): δ = 59.9, 65.4, 71.4, 72.4, 74.4, 75.9, 76.2, 100.6, 127.8, 127.9, 128.0, 128.1, 128.6, 137.3, 137.4. MS (ESI-MS), m/z (rel. intensity): $[MNH_4]^+$ 385.1.

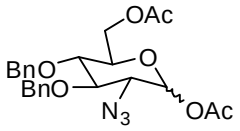


1, 6-anhydro-2-azido-3-O-benzyl-2-deoxy-ß-D-glucopyranose (103):

To a solution of 1, 6-anhydro-2-azido-3,4-di-O-benzyl-2-deoxy-ß-D-glucopyranose (12 mg, 0.033 mmol) in dichloromethane (0.6 mL) was added $TiCl_4$ (4 µL) at room temperature. After 45 min, the solution was poured into ice water, and the organic layer was washed with $NaHCO_3$, water, dried over Na_2SO_4 and concentrated. The crude mixture was purified by column chromatography to give 1,6-anhydro-2-azido-3-O-benzyl-2-deoxy-ß-D-glucopyranose (7.2 mg, 82 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.65 (d, *J* = 10.7 Hz, 1H), 3.52 (s, 1H), 3.61 (m, 1H), 3.67 (d, *J* = 9.8 Hz, 1H), 3.783 (dd, *J* = 6, 7 Hz, 1H), 4.24 (dd, *J* = 0.5, 7 Hz, 1H), 4.54 (d, *J* = 5.5 Hz, 1H), 4.62 (s, 1H), 4.63 (s, 1H), 5.45 (s, 1H), 7.29 – 7.41 (m, 5H).. ^{13}C NMR (75 MHz): δ

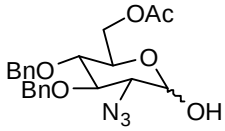
= 59.61, 65.08, 68.82, 72.53, 76.29, 77.98, 100.08, 127.73, 128.2, 128.6, 137.1. MS (ESI-MS), m/z (rel. intensity): [M + $HCOO^-$] 322, [MCl^-] 312.



1, 6-diacetae-2-azido-3,4-di-O-benzyl-2-deoxy-ß-D-glucopyranose (104):

The anhydro compound **103** (8mg, 0.022 mmol) was dissolved in 9:1 Ac_2O-CF_3CO_2H (10 mL) and the solution was stirred for 16 h at room temperature. Solvents were removed and residual traces of acid were removed with toluene. Purification by column chromatography gave the anomeric mixture of diacetate (9 mg, 90 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.04 (s, 3H), 3.52 (s, 1H), 2.16 (s, 3H), 3.55 – 3.70 (m, 2H), 3.90 – 4.04 (m, 2H), 4.277 (d, *J* = 3 Hz, 2H), 4.56 – 4.65 (m, 1H), 4.82 – 4.99 (m, 3H), 6.241 (d, J = 3.5 Hz, 1H), 7.27 – 7.45 (m, 10H). ^{13}C NMR (75 MHz): δ = 20.82, 20.98, 62.35, 62.44, 62.74, 65.07, 71.31, 73.93, 75.15, 75.34, 75.73, 75.84, 76.83, 77.20, 80.57, 83.13, 90.40, 92.72, 128.11, 128.27, 128.62, 128.66, 137.23, 137.45, 168.83, 170.59. MS (ESI-MS), m/z (rel. intensity): $[MNH_4]^+$ 487.1.

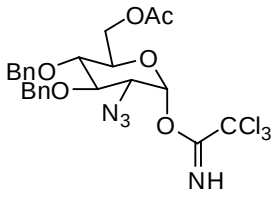


6-acetae-2-azido-3,4-di-O-benzyl-2-deoxy-ß-D-glucopyranose (105):

Benzylamine (0.2 mL, 1.83 mmol) was added at room temperature to a solution of anomeric acetate **104** (86 mg, 0.183 mmol) in THF (7mL). The mixture was stirred for 2 days at room temperature, by which time starting material was disappeared. The solution was neutralized with IR- 120 (H^+) resin, filtered and concentrated. Column chromatography of the residue gave anomeric alcohol (56 mg, 72 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.05 (s, 3H), 3.34 – 3.62 (m, 3H), 3.97 – 4.26 (m, 3H), 4.30 – 4.40 (m, 1H), 4.55 – 4.65 (m, 1H), 4.80 – 4.96 (m, 3H), 5.26 – 5.31 (m, 1H), 7.25 – 7.43 (m, 10H). ^{13}C NMR (75 MHz): δ = 20.89, 62.85, 63.98, 67.43, 69.21, 73.22, 75.15, 75.67, 75.74, 77.15, 77.95, 80.15, 83.09, 92.03, 96.18, 128.03, 128.10, 128,20, 128.60, 137.35,

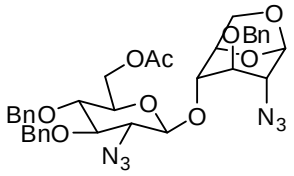
137.48, 137.59, 137.63, 170.97. MS (ESI-MS), m/z (rel. intensity): $[MH]^+$ 428.1, $[MNH_4]^+$ 445.1.



6-acetae-2-azido-3,4-di-O-benzyl-2-deoxy-ß-D-glucopyranose trichloroacetimidate (106):

1,8-Diazabicyclo[5.4.0]undec-7-ene (4 µL, 0.025 mmol) was added at 0 °C to a stirred mixture of anomeric alcohol **105** (107 mg, 0.250 mmol), trichlroacetonitrile (50.2 µL, 0.501 mmol), and activated powdered molecular sieves (4 Å, 30 mg) in dry dichlromethane (7 mL). This mixture was stirred for 3 h at 0 °C. The reaction mixture was directly poured onto column using silica gel equilibrated with 2 % triethyamine to furnish desired product (86 mg, 60 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.03 (s, 3H), 3.63 – 3.75 (m, 2H), 4.03 – 4.13 (m, 2H), 4.20 – 4.37 (m, 2H), 4.62 (d, *J* = 10.7 Hz, 1H), 4.85 – 4.98 (m, 3H), 6.421 (d, *J* = 3.6 Hz, 1H), 7.27 – 7.46 (m, 10H), 8.75 (s, 1H). ^{13}C NMR (75 MHz): δ = 20.82, 62.23, 63.08, 71.76, 75.39, 75.69, 77.28, 80.24, 90.81, 94.55, 128.15, 128.18, 128.27, 128.33, 128.61, 128.69, 137.16, 137.45, 160.71, 170.54.

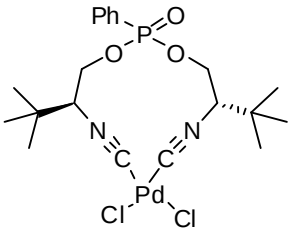


1,6-anhydro-2-azido-3-O-benzyl-4-O-(6-acetate-3,4-di-O-benzyl-2-deoxy-2-azido-ß-D-glucopyranosyl)-2-deoxy- ß-D-glucopyranose (95):

A mixture of the imidate (**106**, 20 mg, 0.035 mmol), the alcohol (**103**, 14 mg, 0.049 mmol) and activated powdered 4 Å molecular sieves (20 mg) in dry toluene (0.3 mL) was stirred at room temperature and then cooled to – 78 °C. $BF_3.Et_2O$ (0.5 µL, 10 mol %) was added to the mixture which was then stirred for 3 h. The mixture was diluted with dichloromethane and

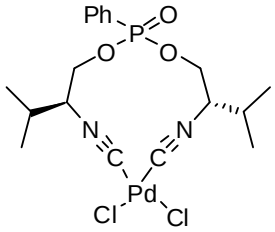
washed with water, dried and concentrated. The residue was purified by column chromatography to give disaccharide (19 mg, 80 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.96 (s, 3H), 3.24 (s, 1H), 3.30 – 3.45 (m, 2H), 3.46 – 3.59 (m, 2H), 3.7 – 3.83 (m, 2H), 3.86 (t, 1H), 4.04 – 4.2 (m, 3H), 4.27 – 4.39 (m, 2H), 4.55 – 4.73 (m, 4H), 4.80 – 4.95 (m, 3H), 5.52 (d, 1H), 7.22 – 7.4 (m, 15H). MS (ESI-MS), m/z (rel. intensity): [MH^+] 687.2, [MNH_4]$^+$ 704.2.



[$PdCl_2$(^{t}BuBINC)] (105b):

A mixture of ^{t}Bu diisonitrile ligand (**72b**, 50 mg, 0.133 mmol) and $PdCl_2(PhCN)_2$ (50 mg, 0.131 mmol) in dichloromethane (2mL) was stirred at room temperature for 16 h. The mixture was filtered through a small pad of celite and washed with dichloromethane. The filtrate was concentrated to a volume of approx. 0.5 ml. The crude product was precipitated by addition of 1 ml of hexane and solvent was decanted after stirring for 10 minutes. This procedure was repeated thrice. The resulting solid was washed with diethyl ether (3 x 1 ml) to give **105b** (67 mg, 91% yield) as an off white solid. Crystals suitable for X-ray-crystaollography were obtained from benzene at room temperature. IR (neat) υ (CN) 2237; (P=O) 1250, (Pd-Cl) 343, 321 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.05 (s, 9H), 1.12 (s, 9H), 3.93 (dd, 1H, *J* = 10.3 Hz, 3.19 Hz), 3.98 (ddd, 1H, *J* = 10.5 Hz, 11.08 Hz, 7.6 Hz), 4.16 (dd, 1H, *J* = 7.6 Hz, 4.2 Hz), 4.18 (ddd, 1H, *J* = 3.6 Hz, 10.9 Hz, 3.2 Hz), 4.29 (ddd, 1H, *J* = 7.6 Hz, 11.08 Hz, 4,2 Hz), 4.49 (ddd, 1H, *J* = 8.4 Hz, 10.9 Hz, 10.3 Hz), 7.55-7.64 (m, 2H), 7.65-7.74 (m, 1H), 7.77 -7.88 (m, 2H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 26.29, 33.95, 62.94, 64.20, 67.95, 68.72, 119.67 (CN), 120.94 (CN), 125.23, 129.26, 131.81, 133.9. ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 21.05 (s). Anal. Calc. for $C_{20}H_{29}Cl_2N_2O_3PPd$: C, 43.38; H, 5.28; N, 5.06. Found: C, 42.88; H, 5.50; N, 4.83.



[$PdCl_2$(^{i}PrBINC)] (105c):

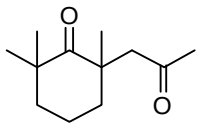
A mixture of ^{i}Pr diisonitrile ligand (**72c**, 50 mg, 0.144 mmol) and $PdCl_2(PhCN)_2$ (55 mg, 0.144 mmol) in dichloromethane (2mL) was stirred at room temperature for 16 h. The mixture was filtered through a small pad of celite and washed with dichloromethane. The filtrate was concentrated to a volume of approx. 0.5 ml. The crude product was precipitated by addition of 1 ml of hexane and solvent was decanted after stirring for 10 minutes. This procedure was repeated thrice. The resulting solid was washed with diethyl ether (3 x 1 ml) to give [$PdCl_2$(^{i}PrBINC)] (68 mg, 90% yield) as a off white solid.

IR (neat) υ (CN) 2237; (P=O) 1245 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.87-1.148 (m, 12H), 2.03-2.31 (m, 2H), 3.95- 4.69 (m, 6H), 7.51-7.70 (m, 3H), 7.80- 7.80-8.12 (m, 2H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 18.60, 18.91, 19.32, 19.41, 29.39, 29.47, 64.48, 65.29, 65.42, 65.61, 125.71(J = 188.7 Hz), 129.38 (*J* = 15.6 Hz), 131.99 (*J* = 10.6 Hz). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 20.93 (s). Anal. Calc. for $C_{18}H_{25}Cl_2N_2O_3PPd$: C, 41.12; H, 4.19; N, 5.33. Found: C, 40.10; H, 5.02; N, 5.02.

Representative procedure for the Wacker oxidation of alkenes:

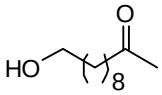
In a flame dried 10 ml schleck tube equipped with a sidearm and stir bar, a mixture of [$PdCl_2$(DiNC)] (**105**, 14 mg, 5 mol %) and 4 ml of a 6:1 (v/v) solution of DMA:H_2O mixture were heated at 70 °C for 10 minutes to assure complete solubility of the catalyst. The tube was allowed to cool to room temperature and connected with a condenser and a one way joint with a balloon of O_2. The tube was evacuated (50 mbar) and refilled with O_2 three times. The reaction mixture was stirred vigorously for 10 minutes upon which the alkene (0.5 mmol) was added. For the indicated reaction time the mixture was then heated at 70 °C. After cooling to room temperature, the reaction mixture was analyzed by GC using decane as internal standard. For product isolation the reaction mixture diethylether was added and washed twice with 1N HCl. The aqueous layers were combined and extracted thrice with

diethylether. The organic layers were combined and washed with brine, dried over Na_2SO_4 and filtered. The product was purified by flash silica chromatography.



2, 2, 6-trimethyl-6-(2-oxopropyl)-cyclohexanone (Table 12, entry 4):

^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.76(dd, 2H, *J*= 18Hz, 279 Hz), 2.02 (s, 3H), 1.72-1.95 (m, 3H), 1.43-1.65 (m, 3H), 1.14 (s, 3H), 1.09 (s, 3H), 1.07 (s, 3H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 220.6, 206.9, 55.6, 44.9, 44.32, 38.9, 36.9, 30.1, 27.87, 27.7, 26.9, 18.2.

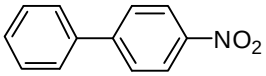


10-hydroxy-2-undecanone (Table 12, entry 3):

^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.62 (t, 2H, *J*= 6.6Hz), 2.41(t, 2H, *J*= 7.4Hz), 2.12 (s, 3H), 1.47-1.65 (m, 5H), 1.21-1.42 (m, 10 H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 209.6, 63.2, 43.9, 32.9, 30.0, 29.54, 29.49, 29.46, 29.28, 25.9, 23.9.

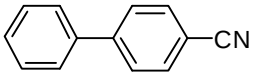
Suzuki couplings:

An oven dried Schlenk tube was evacuated and backfilled with nitrogen and charged with [$PdCl_2$(DiNC)] (**105**, 5 mol %), the boronic acid (1.5 equiv.), aryl halide (1 equiv.) and K_3PO_4 (2 equiv.). The flask was evacuated and backfilled with nitrogen and DMA (2ml/ 0.25mmol of aryl halide).The reaction mixture was stirred at 120 °C for 16 h. The reaction mixture was diluted with ether and washed with 1M NaOH and the aqueous layer was extracted with ether. The combined organic layers were washed with brine, dried over sodium sulfate, filtered and concentrated in vacuum. The crude material was purified by flash chromatography on silica gel.



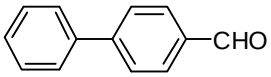
4-nitrobiphenyl (Table 10, entry 1):

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.31 (d, 2H, *J* = 9 Hz), 7.74 (d, 2H, *J* = 9 Hz), 7.63 (dd, 2H, *J* = 2 Hz, 6 Hz), 7.42- 7.53 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.8, 147.2, 138.9, 129.3, 120.1, 127.9, 127.6, 124.3.



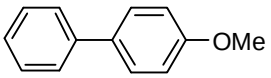
4-cyanobiphenyl (Table 10, entry 2):

^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.67- 7.75 (m, 4H), 7.57- 7-61 (m, 2H), 7.40- 7.52 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 145.8, 139.3, 132.7, 129.3, 128.8, 127.9, 127.4, 119.1, 111.



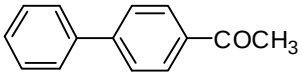
biphenyl-4-carbaldehyde (Table 10, entry 3):

^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.06 (s, 1H), 7.96 (d, 2H, *J* = 8.5 Hz), 7.76 (d, 2H, J = 8.24), 7.64 (dd, 2H, J = 1.6 Hz, 7 Hz), 7.39-7.52 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 192.1, 147.3, 139.8, 135.3, 130.4, 129.2, 128.6, 127.8, 127.5.



4-methoxybiphenyl (Table 10, entry 4):

^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.53- 7.59 (m, 4H), 7.42- 7.49 (m, 2H), 7.30- 7.35 (m, 1H), 7.0 (d, 2H, *J* = 9 Hz), 3.87 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 159.3, 140.9, 133.9, 128.9, 128.3, 126.9, 126.8, 114.4, 55.5.

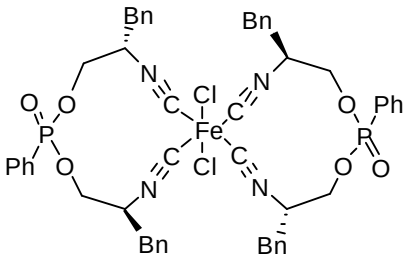


1-(biphenyl-4-yl)ethanone (Table 10, entry 5):

^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (d, 2H, *J* = 8.5 Hz), 7.62- 7.71 (m, 4H), 7.37- 7.51 (m, 3H), 2.65 (s, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 197.9, 145.9, 140.1, 136, 129.14, 129.10, 128.4, 127.46, 127.41, 26.9.

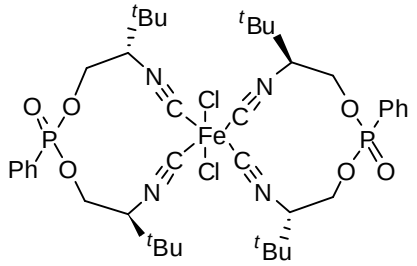
Typical procedure for synthesis of Bis(isonitrile) iron complexes 118a-e:

To $FeCl_2.4H_2O$ (1 equiv.) in dry MeOH was added a solution of bis(isonitrile) ligand (**72**, 2 equiv.) dissolved in minimum amount of dichloromethane. The reddish solution was obtained which was stirred for 12 h at room temperature after which no bis(isonitrile) was seen by TLC. The solvent was removed under pressure and residue was washed with hexane thrice. Yellowish orange colored solid was obtained after drying under vacuum.



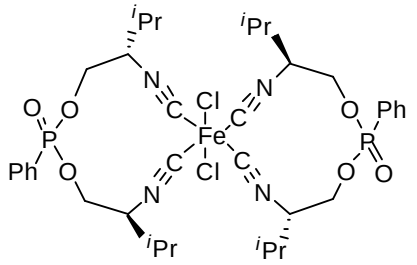
Complex 118a:

Yield: 52 %. IR (KBr): υ 3446, 2163, 1496, 1455, 1244, 1131, 1012, 958 cm^{-1}. ^{1}H NMR (CD_2Cl_2, 400 MHz): δ 2.73.5 – 1.5 (m, 4H), 3.7 – 4.7 (m, 6H), 7.70 – 8.0 (m, 2H), 7.1 – 7.68 (m, 13H). ^{31}P NMR (CD_2Cl_2, 162 MHz): δ 19.56, 19.69, 19.78, 19.86, 20.12, 20.30. MS (LSI-MS), m/z (rel. intensity): $[M\text{-}Cl]^+$ 978.8.



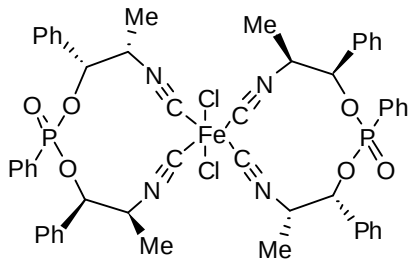
Complex 118b:

Yield: 56 %. IR (KBr): υ 2963, 2165, 1473, 1439, 1247, 1131, 1020, 988 cm^{-1}. ^{1}H NMR (CD_2Cl_2, 400 MHz): δ 0.5 – 1.4 (m, 18H), 3.3 – 4.9(m, 6H), 7.4 – 7.70 (m, 3H), 7.72 – 7.9 (m, 1H), 7.92 – 8.19 (m, 1H). ^{31}P NMR (CD_2Cl_2, 162 MHz): δ 20.19 (bs). MS (LSI-MS), m/z (rel. intensity): $[M\text{-}Cl]^+$ 843.2. HRMS: calcd. for $C_{40}H_{58}O_6N_4P_2FeCl$ $[M\text{-}Cl]^+$: 843.2, found: 843.287.



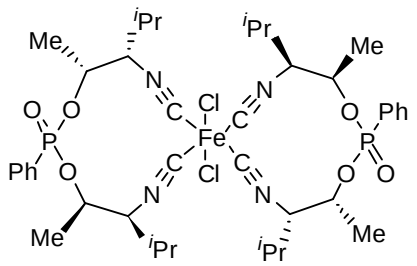
Complex 118c:

Yield: 58 %. IR (KBr): υ 2967, 2161, 1466, 1439, 1243, 1131, 1024, 988 cm^{-1}. ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 0.6 – 1.5 (m, 12H), 1.7 – 2.5 (m, 2H), 3.4 – 4.8 (m, 6H), 7.2 – 8.15 (m, 5H). ^{31}P NMR (CD_2Cl_2, 121 MHz): δ 19.93 (s). MS (LSI-MS), m/z (rel. intensity): $[M\text{-}Cl]^+$ 787.2.



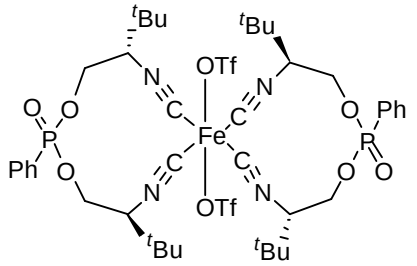
Complex 118d:

Yield: 62 %. IR (KBr): υ 3525, 2936, 2162, 1454, 1252, 1130, 992 cm^{-1}. ^{31}P NMR (CD_2Cl_2, 243 MHz): δ 17.17, 17.31, 17.61, 17.76, 17.80, 18.07. MS (LSI-MS), m/z (rel. intensity): $[M-Cl]^+$ 978.8.



Complex 118e:

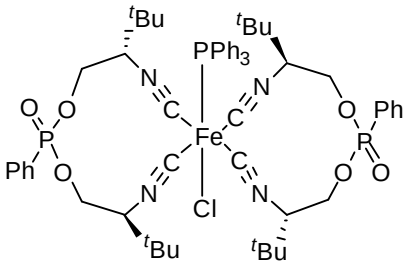
Yield: 54 %. IR (KBr): υ 2967, 2167, 1439, 1248, 1131, 990 cm^{-1}. ^{31}P NMR (CD_2Cl_2, 243 MHz): δ 16.04, 16.57, 17.17, 17.34, 17.66. MS (LSI-MS), m/z (rel. intensity): $[M-Cl]^+$ 843.3.



Complex 119a:

Trifluoromethanesulfonic acid (HOTf, 9 μL) was added to the stirring solution of complex **118b** (25 mg, 0.03 mmol) in degassed benzene (2 mL). The reaction mixture darkens immediately to give a reddish precipitate. After 10 min of gentle stirring, the benzene was removed via syringe and the precipitate was washed with copious amounts of dry ether, followed by drying under vacuum to isolate Fe(^{t}Bu-BINC)$_2$(OTf)$_2$. Yield: 19 mg, 63 %. IR

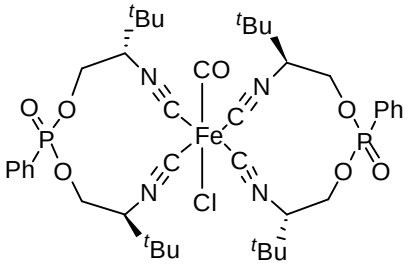
(KBr): υ 3435, 2973, 2224, 1221, 1134, 1022 cm^{-1}. MS (LSI-MS), m/z (rel. intensity): $[M\text{-}OTf+Cl+H]^+$ 957.3.



Complex 119b:

Triphenylphosphine (16.4 mg, 0.063 mmol) was added to the solution of complex **118b** (50 mg, 0.06 mmol) in methanol (19 mL). After stirring the reaction mixture for 12 h, $NaBPh_4$ (19.5 mg, 0.06 mmol) was added and stirring was continued for next 4 h. The solvent was removed under pressure and residue was washed with hexane thrice. Yellowish colored solid was obtained after drying under vacuum.

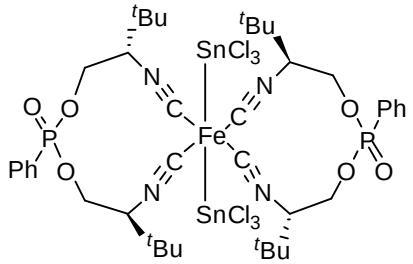
Yield: 43 mg, 53 %. IR (KBr): υ 3056, 2966, 2166, 1479, 1250, 1131, 990 cm^{-1}. MS (ES-MS), m/z (rel. intensity): $[M^+]$ 1105.3.



Complex 119c:

Under nitrogen complex **118b** (50 mg, 0.06 mmol) was dissolved in methanol (25 mL). Resulting reaction solution was perched with CO gas (1 atm) and stirred for 12 h under 1 atm of CO. Solvent was evaporated under vacuum followed by addition of $NaBPh_4$ (19.5 mg, 0.06 mmol) solution in methanol (50 mL). After stirring for next 4 h, the solvent was removed under pressure and residue was washed with hexane thrice to afford greenish solid.

MS (ES-MS), m/z (rel. intensity): $[M^+]$ 871.2, $[M^+\text{-}CO]^+$ 843.2.



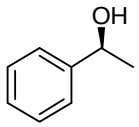
Complex 119d:

To a solution of complex **118b** (50 mg, 0.057 mmol) in chloroform (37 mL) was added $SnCl_2.2H_2O$ (128 mg, 0.57 mmol). After stirring the mixture for 12 h, the excess of $SnCl_2.2H_2O$ was removed by filtration. The solution was concentrated to small volume and again excess of $SnCl_2.2H_2O$ was removed by filtration. This step was repeated 3 to 4 times. The resulted solvent was removed under pressure to obtain a yellowish compound. Crystals suitable for X-ray studies were obtained from MeOH/pentane.

IR (KBr): υ 2966, 2160, 1472, 1440, 1338, 1172, 1021 cm^{-1}.

General procedure for the iron catalyzed asymmetric transfer hydrogenation:

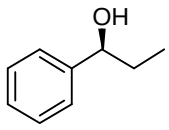
In a 10 mL schlenk tube, the iron complex (**118**, 5mol %, 15 mg, 0.0169 mmol), KO^{t}Bu (10 equiv., 19 mg, 0.169 mmol) and 2-propanol (1.7 mL, for 0.2 M concentration of substrate) were stirred under nitrogen at room temperature for 5 minutes. The substrate (20 equiv.) was added to this mixture and stirred for the time period mentioned in the table. The conversion and enantiomeric excess of the products were determined by GC using decane as internal standard and chiral HPLC respectively. The products were also identified by ^{1}H NMR and ^{13}C NMR spectroscopy and the data obtained matches with literature values. Absolute configuration was determined by comparison of the sign of rotation of the isolated products with literature value.



(*S*)-1-phenylethanol (Table 18, entry 1):

The title compound was prepared according to the general procedure as described above in 90% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 64% ee (OJ: 95/5, heptane/isopropanol, 1mL/min, 215-254 nm); t_r (major) = 10.90 (*S*); t_r (minor) = 12.49 (*R*) min.

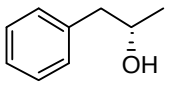
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.20-7.4 (m, 5H), 4.86 (q, *J* = 6.6, 12.8 Hz, 1H), 2.29 (s, 1H), 1.48 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.17, 70.36, 125.44, 127.46, 128.24, 145.88.



(*S*)-1-phenylpropan-1-ol (Table 18, entry 2):

The title compound was prepared according to the general procedure as described above in 73% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 64% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (minor) = 16.39 (*R*), t_r (major) = 19.06 (*S*) min.

^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.22-7.40 (m, 5H), 4.57 (t, *J* = 6.6 Hz, 1H), 2.11 (s, 1H), 1.65-1.91 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 10.18, 31.89, 76.01, 126.02, 127.49, 128.41, 144.64.

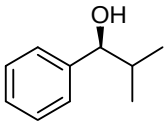


(*S*)-1-phenylpropan-2-ol (Table 18, entry 5):

The title compound was prepared according to the general procedure as described above in 99% conversion. The product was analyzed by HPLC to determine the enantiomeric excess

34% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 12.50 (*S*), t_r (minor) = 14.08 (*R*) min.

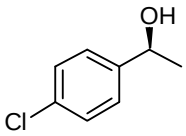
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.35-7.21 (m, 5H), 4.01 (m, 1H), 2.78 (dd, *J* = 13.4, 5.0 Hz, 1H), 2.70 (dd, *J* = 7.8, 13.4 Hz, 1H), 2.01 (br s, 1H), 1.25 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 129.4, 128.5, 126.5, 68.8, 45.8, 22.8.



(*S*)-2-methyl-1-phenylpropan-1-ol (Table 18, entry 3):

The title compound was prepared according to the general procedure as described above in 36% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 36% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 13.21 (*S*), t_r (minor) = 15.97 (*R*) min.

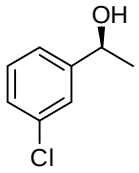
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.38-7.24 (m, 5H), 4.37 (d, *J* = 6.8 Hz, 1H), 1.96 (octet, 1H, *J* = 6.8 Hz), 1.82 (brs, 1H), 1.01 (d, *J* = 6.8 Hz, 3H), 0.80 (d, *J* = 6.8 Hz, 3H).



(*S*)-1-(4-chlorophenyl)ethanol (Table 18, entry 6):

The title compound was prepared according to the general procedure as described above in 94% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 60% ee (OD-H: 99/1, heptane/isopropanol, 0.5 mL/min, 215 – 254 nm); t_r (minor) = 45.81(*R*), t_r (major) = 52.46 (*S*) min.

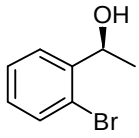
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.20-7.34 (m, 4H), 4.83 (q, *J* = 6.6, 12.8 Hz, 1H), 2.34 (s, 1H), 1.43 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.25, 69.69, 126.82, 128.59, 133.02, 144.26.



(*S*)-1-(3-chlorophenyl)ethanol (Table 18, entry 7):

The title compound was prepared according to the general procedure as described above in >99% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 67% ee (OJ: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 19.85 (*S*), t_r (minor) = 23.78 (*R*) min.

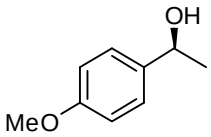
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.34-7.39 (m, 1H), 7.19-7.30 (m, 3H), 4.84 (q, *J* = 6.6, 12.9 Hz, 1H), 2.16 (s, 1H), 1.46 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.23, 69.79, 123.56, 125.64, 127.53, 129.80, 134.36, 147.87.



(*S*)-1-(2-bromophenyl)ethanol (Table 18, entry 8):

The title compound was prepared according to the general procedure as described above in 60% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 67% ee (OD-H: 99/1, heptane/isopropanol, 0.5 mL/min, 215 – 254 nm); t_r (minor) = 40.82 (*R*), t_r (major) = 45.08 (*S*) min.

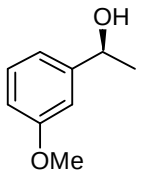
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.57 (dd, J = 1.6, 7.6 Hz, 1H), 7.50 (dd, J = 1.06, 7.9 Hz, 1H), 7.29-7.38 (m, 1H), 7.08-7.16 (m, 1H), 5,21 (q, *J* = 6.6, 12.8 Hz, 1H), 2.24 (s, 1H), 1.47 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.59, 69.19, 121.72, 126.69, 127.87, 128.78, 132.66, 144.63.



(*S*)-1-(4-methoxyphenyl)ethanol (Table 18, entry 9):

The title compound was prepared according to the general procedure as described above in 50% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 58% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (minor) = 29.31 (*R*), t_r (major) = 33.09 (*S*) min.

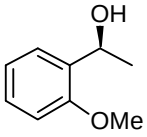
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.25-7.32 (m, 2H), 6.84-6.91 (m, 2H), 4.83 (q, *J* = 6.6, 12.8 Hz, 1H), 3.79 (s, 3H), 2.07 (s, 1H), 1.46 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.04, 55.30, 69.93, 113.84, 126.69, 138.07, 158.95.



(*S*)-1-(3-methoxyphenyl)ethanol (Table 18, entry 10):

The title compound was prepared according to the general procedure as described above in 93% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 54% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (minor) = 31.08 (*R*), t_r (major) = 37.42 (*S*) min.

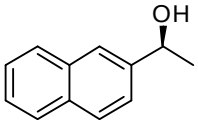
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.22-7.30 (m, 1H), 6.90-6.96 (m, 2H), 6.80 (ddd, *J* = 8.20, 2.54, 1.06 Hz, 1H), 4.84 (q, *J* = 6.5, 12.8 Hz, 1H), 3.80 (s, 3H), 2.20 (bs, 1H), 1.47 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.16, 55.22, 70.29, 110.91, 112.86, 117.72, 129.53, 147.65, 159.75.



(*S*)-1-(2-methoxyphenyl)ethanol (Table 18, entry 11):

The title compound was prepared according to the general procedure as described above in 56% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 52% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 19.28 (*S*), t_r (minor) = 21.32 (*R*) min.

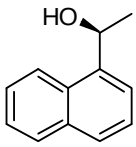
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.34 (dd, *J* = 1.65, 7.4 Hz, 1H), 7.21-7.30 (m, 1H), 6.93-7.01 (m, 1H), 6.85-6.92 (dd, *J* = 0.8, 8.2 1H), 5.09 (q, *J* = 6.6, 12.9 Hz, 1H), 3.86 (s, 3H), 2.7 (bs, 1H), 1.51 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.88, 55.27, 66.51, 110.43, 120.81, 126.11, 128.30, 133.46, 156.55.



(*S*)-1-(naphthalen-2-yl)ethanol (Table 18, entry 12):

The title compound was prepared according to the general procedure as described above in 84% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 64% ee (OJ: 90/10, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 14.34 (*S*), t_r (minor) = 18.43 (*R*) min.

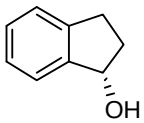
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.78-7.88 (m, 4H), 7.43-7.54 (m, 3H), 5.06 (q, *J* = 6.3, 12.9 Hz, 1H), 2.04 (s, 1H), 1.58 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.17, 70.55, 123.83, 123.85, 125.83, 126.18, 127.71, 127.96, 128.34, 132.94, 133.34, 143.21.



(*S*)-1-(naphthalen-1-yl)ethanol (Table 18, entry 13):

The title compound was prepared according to the general procedure as described above in 48% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 41% ee (OJ: 90/10, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 11.82 (*S*), t_r (minor) = 16.35 (*R*) min.

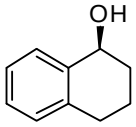
^{1}H-NMR (300 MHz; $CDCl_3$): δ 1.46 (d, *J* = 6.79 Hz, 3H), 3.09 (br s, 1H), 5.38 (q, *J* = 6.04, 6.79 Hz, 1H), 7.30-7.50 (m, 4H), 7.61-7.90 (m, 3H); ^{13}C NMR (75 MHz, CDCl3) δ 24.1, 6.5, 121.8, 122.9, 125.2, 125.3, 125.6, 127.4, 128.5, 130.0, 133.4, 141.2.



(*S*)-2,3-dihydro-1H-inden-1-ol (Table 18, entry 15):

The title compound was prepared according to the general procedure as described above in 89% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 33% ee (OJ: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (minor) = 24.40 (*R*), t_r (major) = 28.20 (*S*) min.

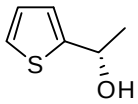
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.37-7.45 (m, 1H), 7.20-7.29 (m, 3H), 5.22 (t, *J* = 6.3 Hz, 1H), 2.98-3.19 (m, 1H), 2.74-2.88 (m, 1H), 2.4-2.54 (m, 1H), 2.1-2.38 (bs, 1H), 1.85-2.0 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.81, 35.86, 76.40, 124.25, 124.47, 127.35, 128.52, 143.34, 144.98.



(*S*)-1,2,3,4-tetrahydronaphthalen-1-ol (Table 18, entry 16):

The title compound was prepared according to the general procedure as described above in 62% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 46% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (minor) = 15.91 (*R*), t_r (major) = 17.33 (*S*) min.

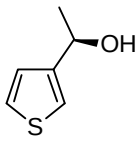
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.41-7.46 (m, 1H), 7.18-7.24 (m, 2H), 7.08-7.15 (m, 1H), 4.77 (t, *J* = 5.2 Hz, 1H), 2.65-2.9 (m, 2H), 1.7-2.09 (m, 5H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.83, 29.27, 32.28, 68.15, 126.19, 127.59, 128.69, 129.03, 137.14, 138.82.



(*S*)-1-(2-Thienyl)ethanol (Table 19, entry 1):

The title compound was prepared according to the general procedure as described above in 70% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 53% ee (OJ: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 25.72 (*S*), t_r (minor) = 33.38 (*R*) min.

^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.19-7.24 (m, 1H), 6.91-6.99 (m, 2H), 5.07 (q, *J* = 6.3, 12.9 Hz, 1H), 2.94 (s, 1H), 1.56 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.25, 66.11, 120.22, 124.37, 126.66, 149.99.

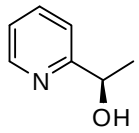


(*R*)-1-(3-Thienyl)ethanol (Table 19, entry 2):

The title compound was prepared according to the general procedure as described above in 36% conversion. The product was analyzed by HPLC to determine the enantiomeric excess

62% ee (OJ: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 25.08 (*R*), t_r (minor) = 30.51 (*S*) min.

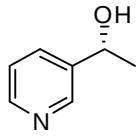
^{1}H-NMR (300 MHz; $CDCl_3$): δ 1.52 (d, *J* = 6.8 Hz), 1.89 (s, 1H), 4.97 (q, *J* = 6.8 Hz,1H), 7.09-7.10 (m, 1H), 7.18-7.20 (m, 1H), 7.29-7.31 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 147.4, 126.1, 125.7, 120.2, 66.5, 24.5.



(*R*)-1-(pyridin-2-yl)ethanol (Table 19, entry 3):

The title compound was prepared according to the general procedure as described above in 85% conversion. The product was analyzed by HPLC to determine the enantiomeric excess41% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 18.66 (*R*), t_r (minor) = 21.61 (*S*) min.

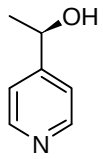
^{1}H-NMR (300 MHz; $CDCl_3$): δ 8.54 (d, *J* = 5.3 Hz, 1H), 7.68-7.72 (m, 1H), 7.28 (d, *J* = 9.3 Hz, 1H), 4.90 (q, *J* = 6.4 Hz, 1H), 4.34 (s, 1H), 1.5 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.19, 69.01, 119.82, 122.22, 136.87, 148.09, 163.25.



(*R*)-1-(pyridin-3-yl)ethanol (Table 19, entry 4):

The title compound was prepared according to the general procedure as described above in 95% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 61% ee (OJ: 90/10, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 7.21 (*R*), t_r (minor) = 9.33 (*S*) min.

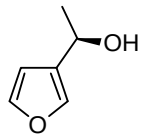
^{1}H-NMR (300 MHz; $CDCl_3$): δ 8.38 (d, *J* = 2.4 Hz, 1H), 8.29 (dd, *J* = 1.3, 4.6 Hz, 1H), 7.64-7.75 (m, 1H), 7.15-7.24 (m, 1H), 4.85 (q, *J* = 6.4 Hz, 1H), 4.6 (bs, 1H), 1.44 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.19, 67.45, 123.58, 133.60, 141.84, 146.99, 147.96.



(*S*)-1-(pyridin-4-yl)ethanol (Table 19, entry 5):

The title compound was prepared according to the general procedure as described above in 99% conversion. The product was analyzed by HPLC to determine the enantiomeric excess55% ee (AS-H: 90/10, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (minor) = 17.74 (*S*), t_r (major) = 31.69 (*R*) min.

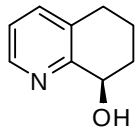
^{1}H-NMR (300 MHz; $CDCl_3$): δ 8.42 (d, *J* = 4.5 Hz, 1H), 7.27 (d, *J* = 4.5 Hz, 2H), 4.86 (q, *J* = 6.4 Hz, 1H), 4.13 (s, 1H), 1.46 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 25.10, 68.53, 120.56, 149.40, 155.53.



(*R*)-1-(furan-3-yl)ethanol (Table 19, entry 6):

The title compound was prepared according to the general procedure as described above in >99% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 30% ee (OJ: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (minor) = 21.05 (*S*), t_r (major) = 23.41 (*R*) min.

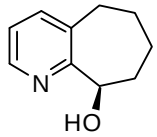
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.35-7.40 (m, 1H), 6.32 (dd, 1H, *J* = 3.2 and 1.2 Hz), 6.22 (d, 1H, *J* = 3.2 Hz), 4.88 (q, 1H, *J* = 6.4 Hz), 2.30 (br s, 1H), 1.54 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.6, 141.8, 110.1, 105.0, 63.5, 21.2.



(*R*)-8-hydroxy-5, 6, 7, 8-tetrahydroquinoline (Table 20, entry 1):

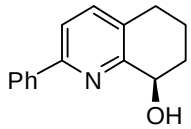
The title compound was prepared according to the general procedure as described above and purified by flash chromatography in 80% yield. The product was analyzed by HPLC to determine the enantiomeric excess 91% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 15.94 (*R*), t_r (minor) = 22.73 (*S*) min.

^{1}H-NMR (300 MHz; $CDCl_3$): δ 8.30-8.29 (m, 1H), 7.31 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.01 (dd, *J* = 7.7, 4.8 Hz, 1H), 5.15 (s, 1H), 4.68 (dd, *J* = 7.2, 5.4 Hz, 1H), 2.79-2.60 (m, 2H), 2.16-2.06 (m, 1H), 1.98-1.65 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.03, 146.46, 137.05, 131.90, 122.19, 67.85, 31.03, 28.44, 18.84.



(*R*)-9-hydroxy-6, 7, 8, 9-tetrahydro-5H-cycloheptapyridine (Table 20, entry 2):

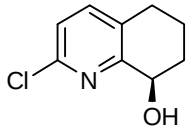
The title compound was prepared according to the general procedure as described above in 83% conversion. The product was analyzed by HPLC to determine the enantiomeric excess 83% ee (AS-H: 99/1, heptane/isopropanol, 0.5 mL/min, 215 – 254 nm); t_r (major) = 21.46 (*R*), t_r (minor) = 27.12 (*S*) min.



(*R*)-8-hydroxy-2-phenyl-5, 6, 7, 8-tetrahydroquinoline (Table 20, entry 3):

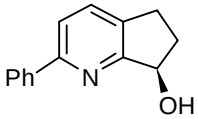
The title compound was prepared according to the general procedure as described above and purified by flash chromatography in 98% yield. The product was analyzed by HPLC to

determine the enantiomeric excess 72% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (minor) = 12.54 (*S*), t_r (major) = 31.41 (*R*) min.



(*R*)-8-hydroxy-2-chloro-5, 6, 7, 8-tetrahydro-2-quionoline (Table 20, entry 4):

The title compound was prepared according to the general procedure as described above and purified by flash chromatography in 93% yield. The product was analyzed by HPLC to determine the enantiomeric excess 84% ee (OJ: 99/1, heptane/isopropanol, 0.5 mL/min, 215 – 254 nm); t_r (major) = 25.48 (*R*), t_r (minor) = 30.0 (*S*) min.

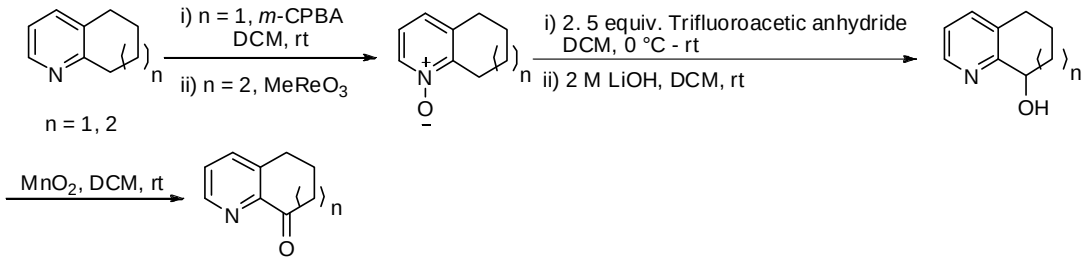


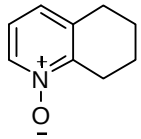
(*R*)-2-phenyl-7-hydroxy- 6, 7-dihydro-5H-cyclopentapyridine (Table 20, entry 5):

The title compound was prepared according to the general procedure as described above and purified by flash chromatography in 89% yield. The product was analyzed by HPLC to determine the enantiomeric excess 52% ee (OD-H: 99/1, heptane/isopropanol, 1 mL/min, 215 – 254 nm); t_r (major) = 32.41 (*R*), t_r (minor) = 57.29 (*S*) min.

Synthesis of Pyridyl Ketones:

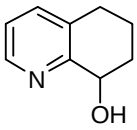
General scheme for the synthesis of six and eight membered pyridyl ketones:





5, 6, 7, 8-tetrahydroquinoline-N-oxide:

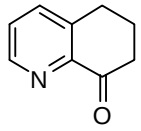
To the cold solution of *m*-CPBA (1.2 equiv.) in dichloromethane (30 mL), 5, 6, 7, 8-tetrahydroquinoline (1 g, 7.5 mmol) in dichloromethane was added drop wise. After removing the ice bath the reaction mixture was stirred at rt overnight. An additional 0.6 equiv. *m*-CPBA was added and stirred for 5 h. The organic layer was washed with dilutes NaOH to remove remaining peroxides. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was used for next step without further purification.



8-hydroxy-5, 6, 7, 8-tetrahydroquinoline:

Trifluoroacetic anhydride (4 mL) was added slowly to cold solution of crude 5, 6, 7, 8-tetrahydroquinoline-N-oxide in 10 mL of dichloromethane. The reaction mixture was allowed to warm up to rt and was stirred overnight. The volatile compounds were removed under pressure and remaining organic phase was dissolved in dichloromethane and 2M LiOH solution was added to it. The combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (839 mg, 78 %).

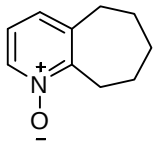
(Triethylamine/ethyl acetate 1:9, R_f = 0.4). ^{1}H-NMR (300 MHz; $CDCl_3$): δ 8.30-8.29 (m, 1H), 7.31 (dd, *J* = 7.7, 0.6 Hz, 1H), 7.01 (dd, *J* = 7.7, 4.8 Hz, 1H), 5.15 (s, 1H), 4.68 (dd, *J* = 7.2, 5.4 Hz, 1H), 2.79-2.60 (m, 2H), 2.16-2.06 (m, 1H), 1.98-1.65 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 158.03, 146.46, 137.05, 131.90, 122.19, 67.85, 31.03, 28.44, 18.84.



5, 6, 7, 8-tetrahydroquinoine-8-one:

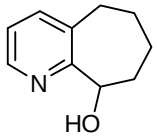
A mixture of activated MnO_2 (262 mg) and 8-hydroxy-5, 6, 7, 8-tetrahydroquinoline (25 mg, 0.168 mmol) in chloroform (3 mL) was refluxed for 7 h. The mixture was filtered and washed with diethyether. The combined organic layers were concentrated under vacuum and purified by column chromatography to obtain white solid (22 mg, 88 %).

(Triethylamine/ethyl acetate 1:9, R_f = 0.2). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.15 – 2.26(m, 2H), 2.82(t, 2H, *J* = 6.3Hz), 3.04 (t, 2H, *J* = 6.03 Hz), 7.37 (dd, 1H, *J* = 4.4, 7.4 Hz), 4.16 - 7.65 (dt, 1H, *J* = 0.8, 7.6 Hz), 8.71 (dt, 1H, J = 0.8, 4.6 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.70, 29.17, 39.68, 126.99, 137.64, 140.76, 14918.



6, 7, 8, 9-tetrahydro-5H-cycloheptapyridine-N-oxide:

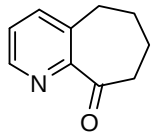
To stirred solution of 6, 7, 8, 9-tetrahydro-5H-cycloheptapyridine (500 mg, 3.4 mmol) and methyltrioxorhenium (42.4 mg, 5 mol%) in dichloromethane (5 mL) was slowly added hydrogen peroxide 0.7 mL (30 % aq.) at 0 °C. The reaction mixture was allowed to warm to rt and catalytic amount of MnO_2 was added to destroy the remaining hydrogen peroxide. The mixture was filtered and the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4 and concentrated. The crude product was used for next step without further purification.



9-hydroxy-6, 7, 8, 9-tetrahydro-5H-cycloheptapyridine:

Trifluoroacetic anhydride (10 mL) was added slowly to cold solution of 6, 7, 8, 9-tetrahydro-5H-cycloheptapyridine-N-oxide in dichloromethane. The reaction mixture was allowed to warm up to rt and was stirred overnight. The volatile compounds were removed under pressure and remaining organic phase was dissolved in dichloromethane and 2M LiOH solution was added to it. The combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (299 mg, 54 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.03 – 1.20(m, 1H), 1.22 – 1.40 (m, 1H), 1.65 – 1.82 (m, 1H), 1.83 – 2.03 (m, 2H), 2.06 – 2.19 (m, 1H), 2.53 – 2.73(m, 2H), 4.66 (dd, 1H, *J* = 2.4, 11 Hz), 5.81 (s, 1H), 7.02 (dd, 1H, *J* = 4.9, 7.5 Hz), 7.30 – 7.37 (m, 1H), 8.24 (dd, 1H, *J* = 1.5, 4.9 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 27.03, 29.01, 34.32, 36.31, 72.17, 122.08, 135.67, 137.20, 144.35, 160.93.

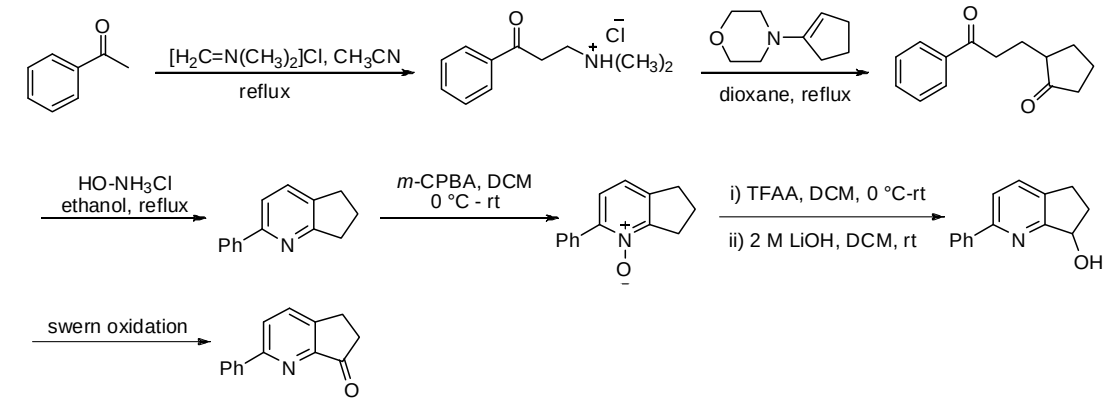


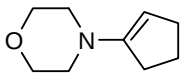
6, 7, 8, 9-tetrahydro-5H-cycloheptapyridine-9-one:

To a stirred solution of oxalyl chloride (0.056 mL, 0.652 mmol) in dichloromethane (1.4mL) was slowly added DMSO (0.093 mL, 1.304 mmol) at -78 °C, and the resulting mixture was stirred for 30 min at this temperature. A solution of 9-hydroxy-6, 7, 8, 9-tetrahydro-5H-cycloheptapyridine (95 mg, 0.582mmol) in dichloromethane (1 mL) was added to this mixture slowly, and then triethylamine (0.4mL, 2.62 mmol) was added drop wise. The reaction mixture was allowed to warm to rt and then quenched with water. After extraction with dichloromethane, the organic layer was washed with HCl, sat. Na_2CO_3 solution. The organic layer was dried over Na_2SO_4 and concentrated under pressure to afford the crude product. The crude product was purified by column chromatography to obtain desired product (56 mg, 60 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.73 – 1.92(m, 4H), 2.64 – 2.77 (m, 2H), 2.80 – 2.90 (m, 2H), 7.20 – 7.31 (m, 1H), 7.52 (dd, 1H, *J* = 0.6, 7.7 Hz), 8.5 – 8.6 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.17, 24.99, 30.96, 40.38, 125.76, 136.42, 138.08, 148.31, 154.84, 204.7.

General scheme for the synthesis of five membered pyridyl ketones :

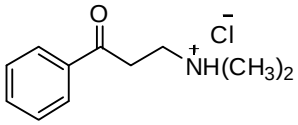




Cyclopentanone morpholine enamine:

The solution of cyclopentanone (12.5 g, 0.15 mol), morpholine (19.5 mL, 0.23 mol) in toluene (38 mL) was refluxed using dean-stark trap until water formation stopped. The solvent was removed under vacuum and crude product was purified by distillation (16 gm, 70 %).

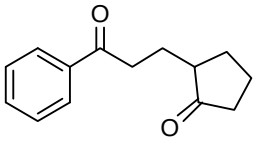
^{1}H-NMR (300 MHz; $CDCl_3$): δ 4.40 (s, 1H), 3.68 (t, *J* = 4.9 Hz, 4H), 2.83 (t, *J* = 4.9 Hz, 4H), 2.33-2.25 (m, 4H), 1.88-1.78 (m, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 151.71, 98.28, 66.64, 49.04, 31.33, 30.29, 22.50.



3-dimethylamino-1-phenyl-propan-1-one hydrochloride:

A mixture of N, N-Dimethyleneiminium chloride (2 g, 22 mmol) and acetophenone (4.2 mL, 22 mmol) in acetonitrile (11 mL) was refluxed for 1 h. After cooling to rt the product was recrystallized immediately (82 %).

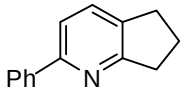
^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.79(s, 6H), 3.4(m, 2H), 3.65 (t, 2H, *J* = 7.1 Hz), 7.52 – 7.61(m, 2H), 7.64- 7.73 (m, 1H), 7.98 – 8.05 (m, 2H), 10.95 (s, 1H). ^{13}C-NMR (75.5 MHz; DMSO-d_6): δ 196.65, 135.83, 133.65, 128.74, 127.94, 51.61, 42.04, 33.07. IR (Neat): 3487, 3398, 2949, 2666, 2570, 2471, 1674, 1628, 1597, 1467, 1426, 1385, 1334, 1223, 1137, 1078, 1037, 1003, 958,754, 688, 652.



2-(3-oxo-3-phenyl-propyl)-cyclopentanone:

3-dimethylamino-1-phenyl-propan-1-one hydrochloride (2.5 g, 11.7 mmol) was suspended dioxane (15 mL). After addition of cyclopentanone morpholine enamine (1.79 g, 11.7 mmol) the reaction mixture was refluxed for 16 h. After cooling to rt, water was added and refluxed for additional one hour. The water phase was extracted with dichloromethane and the combined organic layers were washed with diluted HCl, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (1.06 mg, 42 %).

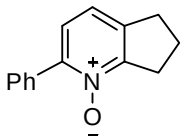
^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.94 (dd, *J* = 7.1, 1.5 Hz, 2H), 7.55-7.50 (m, 1H), 7.46-7.40 (m, 2H), 3.09 (m, 2H), 2.27-1.92 (m, 6H), 1.83-1.68 (m, 2H), 1.61-1.48 (m, 1H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 220.96, 199.86, 136.82, 133.07, 128.62, 128.08, 48.23, 38.15, 36.20, 29.94, 24.28, 20.70.



2-phenyl-6, 7-dihydro-*5H*-[1]pyridine:

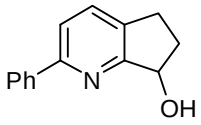
The solution of 2-(3-oxo-3-phenyl-propyl)-cyclopentanone (1.0 g, 4.63 mmol) and hydroxylamine hydrochloride (0.321 g, 4.63 mmol) in ethanol (20 mL) was refluxed for 3 h. After 3 h, the reaction mixture was neutralized by sodium carbonate solution and water and the water phase was extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4 and concentrated to yield crude brown oil, which was purified by column chromatography (787 mg, 87 %).

^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.92 (d, *J* = 6.9 Hz, 2H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.45-7.32 (m, 4H), 3.06 (t, *J* = 7.7 Hz, 2H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.13 (quintet, *J* = 7.5 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 165.90, 155.92, 140.07, 135.47, 132.62, 128.69, 128.40, 126.96, 118.29, 34.51, 30.57, 23.32.



2-phenyl-6, 7-dihydro-*5H*-[1]pyridine-N-oxide:

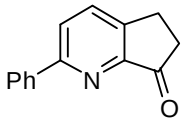
To the cold solution of *m*-CPBA (1.2 equiv.) in dichloromethane (10 mL), 2-phenyl-6, 7-dihydro-*5H*-[1]pyridine (0.5 g, 2.56 mmol) in dichloromethane was added drop wise. After removing the ice bath the reaction mixture was stirred at rt overnight. An additional 0.6 equiv. *m*-CPBA was added and stirred for 5 h. The organic layer was washed with dilutes NaOH to remove remaining peroxides. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was used for next step without further purification.



7-hydroxy- 6, 7-dihydro-5H-cyclopentapyridine:

Trifluoroacetic anhydride (0.7 mL) was added slowly to cold solution of crude 2-phenyl-6, 7-dihydro-5*H*-[1]pyridine-N-oxide in dichloromethane (20 mL). The reaction mixture was allowed to warm up to rt and was stirred overnight. The volatile compounds were removed under pressure and remaining organic phase was dissolved in dichloromethane and 2M LiOH solution was added to it. The combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (454 mg, 84 %).

^{1}H-NMR (300 MHz; $CDCl_3$): δ 7.94-7.90 (m, 2H), 7.54 (q, *J* = 7.6 Hz, 2H), 7.46-7.35 (m, 3H), 5.25 (t, *J* = 6.7 Hz, 1H), 4.80-4.72 (m, 1H), 3.04-2.94 (m, 1H), 2.82-2.71 (m, 1H), 2.50 (m, 1H), 2.05 (m, 1H). ^{13}C-NMR (75.5 MHz; $CDCl_3$): δ 164.96, 156.51, 139.48, 134.98, 133.83, 128.67, 127.12, 120.13, 74.58, 33.13, 27.29.

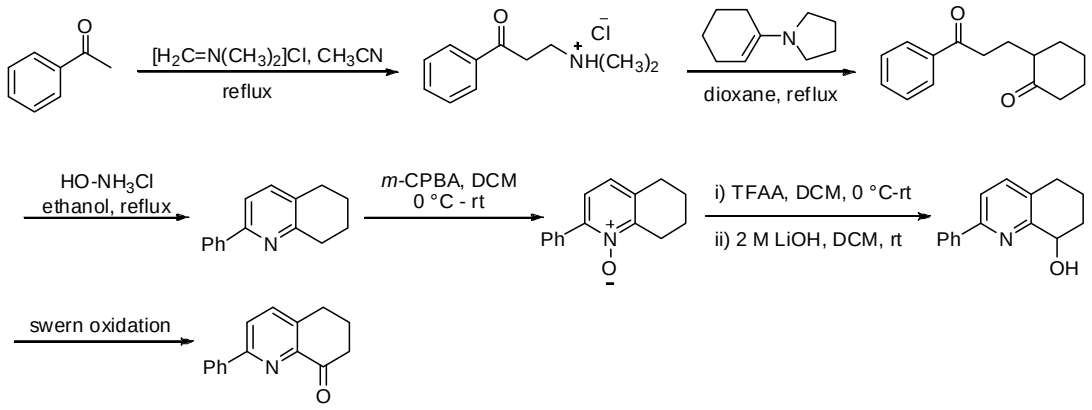


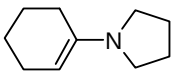
2-phenyl-6, 7-dihydro-5H-cyclopentapyridine-7-one:

To a stirred solution of oxalyl chloride (0.073 mL, 0.85 mmol) in dichloromethane (1.8mL) was slowly added DMSO (0.129 mL, 1.81 mmol) at -78 °C, and the resulting mixture was stirred for 30 min at this temperature. A solution of 7-hydroxy- 6, 7-dihydro-5H-cyclopentapyridine (160 mg, 0.76mmol) in dichloromethane (1.3 mL) was added to this mixture slowly, and then triethylamine (0.5mL, 3.42 mmol) was added drop wise. The reaction mixture was allowed to warm to rt and then quenched with water. After extraction with dichloromethane, the organic layer was washed with HCl, sat. Na_2CO_3 solution. The organic layer was dried over Na_2SO_4 and concentrated under pressure to afford the crude product. The crude product was purified by column chromatography to obtain desired product (124 mg, 78 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.78 – 2.85(m, 2H), 3.15 – 3.22 (m, 2H), 7.40 – 7.52 (m, 3H), 7.925 (q, 2H, *J* = 8.3, 11.2 Hz), 8.09 (dd, 2H, *J* = 1.9, 8.3 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.28, 35.34, 124.7, 127.4, 128.8, 129.6, 135.9, 138.2, 148.24, 158.7, 205.7.

General scheme for the synthesis of phenyl substituted six membered pyridyl ketones:

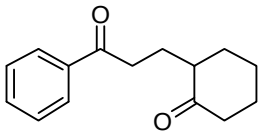




Cyclohexanone pyrrolidine enamine:

The solution of cyclohexanone (26 mL, 0.25 mol), pyrrolidine (32 mL, 0.38 mol) in toluene (75 mL) was refluxed using dean-stark trap until waster formation stopped. The solvent was removed under vacuum and crude product was purified by distillation in quantitative yield.

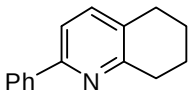
^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.47 – 1.58(m, 2H), 1.6 – 1.73(m, 2H), 1.811 (q, 4H, *J* = 6.6 Hz), 2.02 – 2.12 (m, 2H), 2.13 – 2.21 (m, 2H), 2.97 (t, 4H, J = 6.3 Hz), 4.26 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.00, 23.35, 24.52, 27.02, 27.52, 41.96, 47.40, 51.22, 93.51, 143.36.



2-(3-oxo-3-phenyl-propyl)-cyclohexanone:

3-dimethylamino-1-phenyl-prpan-1-one hydrochloride (4 g, 16.4 mmol) was suspended dioxane (40 mL). After addition of cyclohexanone pyrrolidine enamine (2.5 g, 16.4 mL) the reaction mixture was refluxed for 16 h. After cooling to rt, water was added and refluxed for additional one hour. The water phase was extracted with dichloromethane and the combined organic layers were washed with diluted HCl, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (1.2 gm, 31 %).

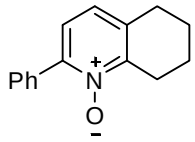
^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.34 – 1.52(m, 1H), 1.59 – 1.76(m, 3H), 1.78 – 1.92 (m, 1H), 1.98 – 2.20 (m, 3H), 2.22 – 2.50 (m, 3H), 2.88 – 3.03 (m, 1H), 3.04 – 3.19 (m, 1H), 7.38 – 7.48 (m, 2H), 7.49 – 7.57 (m, 1H), 7.92 – 8.00(m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 24.51, 25.13, 28.19, 34.68, 36.36, 42.32, 49.9, 128.1, 128.6, 133.0, 136.8, 200.4, 213.4.



2-phenyl-5, 6, 7, 8-tetrahydroquinoline:

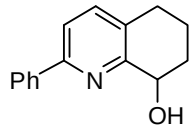
The solution of 2-(3-oxo-3-phenyl-propyl)-cyclohexanone (2.6 g, 11 mmol) and hydroxylamine hydrochloride (0.8 g, 11 mmol) in ethanol (20 mL) was refluxed for 3 h. After 3 h, the reaction mixture was neutralized by sodium carbonate solution and water and the water phase was extracted with dichloromethane. The combined organic layers were dried over Na_2SO_4 and concentrated to yield crude brown oil which was purified by column chromatography (0.898 gm, 38 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.79 – 2.01(m, 4H), 2.80(t, 2H, J = 6.3 Hz), 3.03 (t, 2H, J = 6.4 Hz), 7.35 – 7.51 (m, 5H), 7.94 – 8.00 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.86, 23.27, 28.60, 32.92, 117.94, 126.86, 128.30, 128.67, 130.75, 137.47, 139.95, 154.68, 157.26.



2-phenyl-5, 6, 7, 8-tetrahydroquinoline-N-oxide:

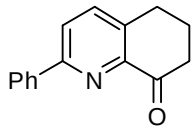
To the cold solution of *m*-CPBA (2.47 gm, 14.3 mmol) in dichloromethane (10 mL), 2-phenyl-5, 6, 7, 8-tetrahydroquinoline (2.50 g, 12 mmol) in dichloromethane was added drop wise. After removing the ice bath the reaction mixture was stirred at rt overnight. An additional 0.6 equiv. *m*-CPBA was added and stirred for 5 h. The organic layer was washed with dilutes NaOH to remove remaining peroxides. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was used for next step without further purification.



8-hydroxy-2-phenyl-5, 6, 7, 8-tetrahydroquinoline:

Trifluoroacetic anhydride was added slowly to cold solution of 2-phenyl-5, 6, 7, 8-tetrahydroquinoline-N-oxide (1.4 gm, 6.2 mmol) in dichloromethane (20 mL). The reaction mixture was allowed to warm up to rt and was stirred overnight. The volatile compounds were removed under pressure and remaining organic phase was dissolved in dichloromethane and 2M LiOH solution was added to it. The combined organic layers were washed with water, dried over Na_2SO_4 and concentrated. The crude product was purified by column chromatography (1.2 gm, 87 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.72 – 1.93(m, 2H), 1.95 – 2.11(m, 1H), 2.30 – 2.45 (m, 1H), 2.76 – 2.94 (m, 2H), 4.37 (s, 1H), 4.73 (dd, 1H, *J* = 5.3, 9.2 Hz), 7.37 – 7.52 (m, 4H), 7.57 (d, 1H, *J* = 8.0 Hz), 7.97 – 8.03 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 19.72, 28.02, 30.67, 69.20, 119.19, 126.69, 128.74, 128.88, 137.76, 138.92, 154.22, 157.65.

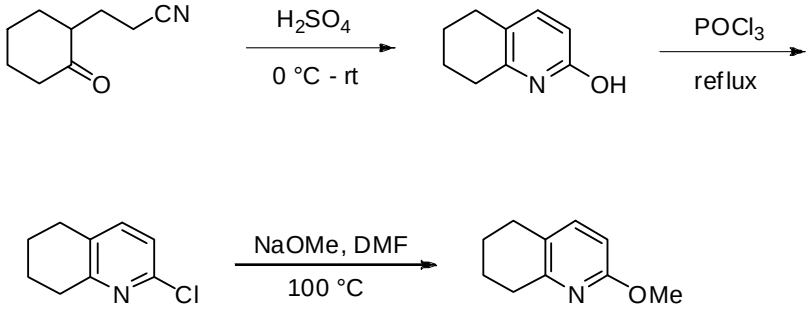


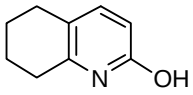
2-phenyl-5, 6, 7, 8-tetrahydroquinoine-8-one:

To a stirred solution of oxalyl chloride (0.2 mL, 2.5 mmol) in dichloromethane (5mL) was slowly added DMSO (0.4 mL, 5.3 mmol) at -78 °C, and the resulting mixture was stirred for 30 min at this temperature. A solution of 8-hydroxy-2-phenyl-5, 6, 7, 8-tetrahydroquinoline (500 mg, 2.22 mmol) in dichloromethane (4 mL) was added to this mixture slowly, and then triethylamine (1.4 mL, 10 mmol) was added drop wise. The reaction mixture was allowed to warm to rt and then quenched with water. After extraction with dichloromethane, the organic layer was washed with HCl, sat. Na_2CO_3 solution. The organic layer was dried over Na_2SO_4 and concentrated under pressure to afford the crude product. The crude product was purified by column chromatography to obtain desired product (461 mg, 93 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.22(q, 2H, *J* = 6.6 Hz), 2.84 (t, 2H, *J* = 6.03 Hz), 3.06 (t, 2H, *J* = 6.03 Hz), 7.38 – 7.51 (m, 3H), 7.72 (d, 1H, *J* = 8 Hz), 7.83(d, 1H, *J* = 8 Hz), 8.02 – 8.09 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.77, 29.04, 39.96, 124.0, 127.22, 128.77, 129.32, 138.52, 139.23, 147.92, 156.74, 196.86.

General scheme for the synthesis of chloro substituted six membered pyridyl ketones:

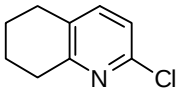




5, 6, 7, 8-tetrahydro-2-quinolone:

To a cold 97 % suphuric acid (20 mL) was added dropwise 3-(2-oxocyclohexyl)propanenitrile (3 gm, 19.4 mmol). After the addition, the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was poured into cold water and extracted with chloroform to remove polymeric impurities and unaromatized material. The resulting aqueous solution was neutralized with aqueous ammonia. A white solid precipitated which was extracted with chloroform. The organic layers were dried over Na_2SO_4 and concentrated under vacuum to obtain white solid product. The pure product was obtained after column chromatography (1.4 gm, 49 %).

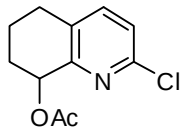
^{1}H-NMR (300 MHz; $CDCl_3$): δ 13.33 (s, 1H), 7.10 (d, *J* = 9.1 Hz, 1H), 6.29 (d, *J* = 9.1 Hz, 1H), 2.62 (t, *J* = 5.7 Hz, 2H), 2.39 (t, *J* = 5.5 Hz, 2H), 1.71-1.64 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.07, 143.73, 143.21, 116.64, 114.44, 26.67, 26.05, 22.51, 21.55.



2-chloro-5, 6, 7, 8-tetrahydro-2-quionoline:

A mixture of $POCl_3$ (6.6 mL, 19.8 mmol) and 5, 6, 7, 8-tetrahydro-2-quinolone (1 gm, 6.6 mmol) was refluxed under nitrogen overnight. The mixture was cooled, poured into 2M cold NaOH and extracted with dichloromethane. The organic layer was dried over Na_2SO_4 and concentrate under pressure. The crude product was purified by column chromatography in quantitative yield.

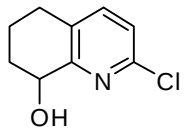
^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.6 – 1.85 (m, 4H), 2.62 (t, 2H, *J* = 6.1 Hz), 2.77 (t, 2H, *J* = 6.2 Hz), 6.92 (d, 1H, *J* = 8 Hz), 7.20 (d, 1H, *J* = 8 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.34, 22.62, 27.98, 32.19, 121.1, 131.0, 139.5, 147.6, 158.0.



2-chloro-5, 6, 7, 8-tetrahydro-2-quionoline-8-acetate:

To 2-chloro-5, 6, 7, 8-tetrahydro-2-quionoline (526 mg, 3.5 mmol) was added glacial acetic acid (2.5 mL) and the mixture was stirred at 82 °C. 30 % aqueous hydrogen peroxide (0.53 mL) was added slowly to the reaction mixture and stirred further for 5 h at 82 °C, after which additional hydrogen peroxide (0.09 mL) was added. The resulting mixture was stirred for 12 h at this temperature and then cooled to room temperature. The excess hydrogen peroxide was destroyed by adding catalytic manganese dioxide and stirred for one more hour at room temperature. Water and acetic acid were removed under pressure. The residue was poured into water and neutralized with Na_2CO_3 and then extracted with dichloromethane. The combined organic layers were washed with water, dried over Na_2SO_4 and concentrated in vacuum to afford corresponding pyridine N-oxide, which was used directly for the next step without further purification. The crude pyridine N-oxide was dissolved in acetic anhydride (4mL) and stirred at 85 °C for 5 h. The resulting reaction mixture was then cooled to room temperature and concentrated under vacuum to afford crude acetate product. Column chromatography afforded the desired compound colorless oil (545 mg, 77 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.68 – 1.98 (m, 3H), 1.99 - 2.04 (s, 3H), 2.05 – 2.18 (m, 1H), 2.56 – 2.83 (m, 2H), 5.76 (t, 1H, *J* = 3.6 Hz), 7.09 (d, 1H, *J* = 6.7 Hz), 7.34 (d, 1H, *J* = 6.5 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.05, 21.4, 27.7, 28.6, 70.4, 123.9, 132.5, 140.0, 148.8, 153.7, 170.2.

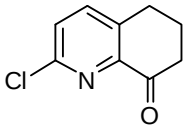


8-hydroxy-2-chloro-5, 6, 7, 8-tetrahydro-2-quionoline:

To a stirred solution of 2-chloro-5, 6, 7, 8-tetrahydro-2-quionoline-8-acetate (153 mg, 0.67 mmol) in ethanol (0.4 mL), a solution of KOF (54 mg) in ethanol (1 mL) was added. The resulting mixture was stirred at rt for 30 min and then the solvent was removed under vacuum to yield dark solid, which was treated with water and extracted with dichloromethane. The

combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography to obtain 8-hydroxy-2-chloro-5, 6, 7, 8-tetrahydro-2-quionoline (116 mg, 93 %).

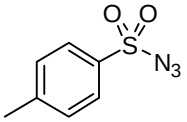
^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.6 – 1.84 (m, 2H), 1.85 – 2.01 (m, 1H), 2.05 – 2.2 (m, 1H), 2.57 – 2.8 (m, 2H), 3.8 (s, 1H), 4.62 (dd, 1H, *J* = 4.0, 16.3 Hz), 7.05 (d, 1H, *J* = 8.0 Hz), 7.31 (d, 1H, *J* = 8.0 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 18.03, 16.8, 29.3, 67.4, 75.7, 121.9, 129.6, 138.9, 147.3, 157.6.



2-chloro-5, 6, 7, 8-tetrahydro-2-quionoine-8-one:

To a stirred solution of oxalyl chloride (0.19 mL, 2.3 mmol) in dichloromethane (4.6 mL) was slowly added DMSO (0.35 mL, 4.90 mmol) at -78 °C, and the resulting mixture was stirred for 30 min at this temperature. A solution of 8-hydroxy-2-chloro-5, 6, 7, 8-tetrahydro-2-quionoline (375 mg, 2.04 mmol) in dichloromethane (3.7 mL) was added to this mixture slowly, and then triethylamine (1.43mL, 9.18 mmol) was added drop wise. The reaction mixture was allowed to warm to rt and then quenched with water. After extraction with dichloromethane, the organic layer was washed with HCl, sat. Na_2CO_3 solution. The organic layer was dried over Na_2SO_4 and concentrated under pressure to afford the crude product. The crude product was purified by column chromatography to obtain desired product 2-chloro-5, 6, 7, 8-tetrahydro-2-quionolone. (363 mg, 98%).

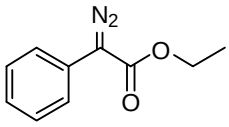
^{1}H NMR (CDCl3, 300 MHz): δ 2.19(q, 2H, *J* = 6.3 Hz), 2.78 (t, 2H, *J* = 6.03 Hz), 7.40 (d, 1H, *J* = 8.0 Hz), 7.63 (d, 1H, *J* = 7.99 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.5, 28.5, 39.3, 128.2, 139.6, 140.6, 148.1, 150.9, 195.0.



***p*-toluolsulfonyl azide:**

To an ice cooled solution of *p*-toluolsulfonyl chloride (5.0 g, 26 mol) in acetone/water (1/1, 149 mL, 6 mL/mmol) was added sodium azide (1.7 g, 26 mol). The reaction mixture was stirred for 2 h at 0°C and the acetone was then evaporated. The phases were separated and the aqueous layer was extracted with diethyl ether. The combined phases were dried and concentrated to afford *p*-toluolsulfonyl azide (2.24 g, 43 %) pale yellow oil which was stored in deep freeze.

(R_f 0.76 hexanes/ethyl acetate 1/1). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.74 (s, 3H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.84 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 21.7, 128, 130, 136, 146.



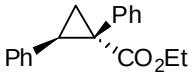
Ethyl phenyldiazoacetates:

To an ice cooled solution of *p*-toluolsulfonyl azide (2.24 g, 11.33 mmol) and ethyl phenylacetate (1.8 mL, 11.33 mmol) in acetonitrile (24 mL) was added DBU (2.24 mL, 15 mmol) and the reaction was warmed to room temperature and stirred overnight. The solvent was evaporated and was dissolved in dichloromethane followed by washing with NH_4Cl, water and brine. Desired product was obtained after purification by column chromatography in quantitative yield.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.35 (t, 3H), 4.34 (q, 2H), 7.18 (m, 1H), 7.39 (m, 2H), 7.50 (m, 2H). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ =14.53, 61, 123.97, 125.7, 128.9, 165.2.

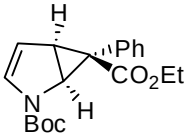
Typical procedure for cyclopropanation catalyzed by Cu(I)- ^{t}BuBINC complex:

A mixture of $CuPF_6$ $(CH_3CN)_4$ (4 mg, 0.011 mmol), ^{t}BuBINC (4 mg, 0.012 mmol), styrene (100 mg, 0.96 mmol) in ethylacetate (0.5 mL) was stirred at room temperature for 2 h. The resulting mixture was heated to 40 °C and then 4 Å MS (100 mg) was added. To this solution was injected ethyl phenyldiazoacetates (41 mg, 0.213 mmol) in 1 mL ethyl acetate via a syringe pump within 6 h. After the reaction was complete (monitored by TLC), the mixture was filtered through a small plug of silica gel and eluted with DCM. The filtrate was concentrated and the residue was purified by chromatography to afford the desired product.



(1S, 2R)-ethyl 1, 2-diphenylcyclopropanecarboxylate:

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.19 (t, 3H), 1.89 (dd, *J* = 7.3, 4.8 Hz, 1H), 2.15 (dd, *J* = 9.2, 4.72 Hz, 1H), 3.12 (dd, *J* = 9.2, 7.1 Hz, 1H), 4.06 - 4.24 (m, 2H), 6.74 - 6.82 (m, 2H), 7.03 - 7.16 (m, 8H). ^{13}C NMR (75.5 MHz): δ = 14.18, 20.28, 32.91, 37.59, 61.29, 126.25, 126.90, 127.59, 127.67, 128.05, 131.92, 134.84, 136.49, 173.78. Mass EI-MS (m/e) 266.2 ($M^{+\cdot}$)



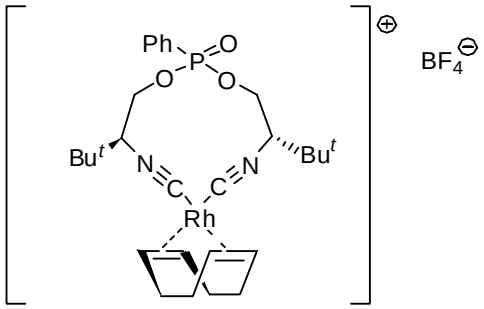
2-tert-butyl 6-ethyl 6-phenyl-2-azabicyclo[3.1.0]hex-3-ene-2,6-dicarboxylate.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.07-1.19 (m, 3 H), 1.44-1.58 (two singlet, 9 H), 3.26 -3.34 (m, 1 H), 4.0-4.15 (m, 2 H), 4.55-4.74 (m, 1 H), 5.07-5.21 (m, 1 H), 5.93-6.16 (m, 1 H), 7.05-7.16 (m, 2 H), 7.19-7.28 (m, 3 H). ^{13}C NMR (75.5 MHz): δ = 14.20, 28.27, 29.74, 38.04, 39.26, 49.13, 61.19, 81.69, 107.43, 127.22, 127.77, 130.6, 131.28, 132.56, 151.3, 173.44.

$[Rh(COD)_2]BF_4$:

To a dichloromethane solution (2 mL) of $[Rh(COD)Cl]_2$ (99 mg, 0.2 mmol) and 1,5-cyclooctadiene (0.5 mL, 4.07 mmol), $AgBF_4$ (92.5 mg, 2.37 mmol) was added. The resulting slurry was stirred in the dark for 2 h, subsequently filtered through celite and washed wth CH_2Cl_2 (2 mL). The solution was concentrated and anhydrous Et_2O (15 mL) was added to precipitate the complex. The red solid formed was filtered, washed with cold Et_2O (3 x 10 mL) and dried (73 mg, 90 %).

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.57 (m, 8H, CH_2), 5.35 (m, 4H, CH). ^{13}C NMR (75.5 MHz) 29.93 (s, CH_2), 107.7 (d, CH).

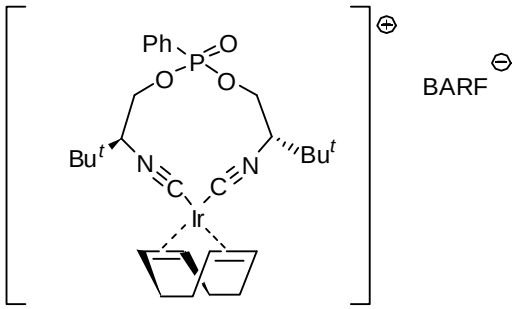


$[Rh(COD)(^t$Bu BINC$)]BF_4$ (120):

To a solution of $[Rh(COD)_2]BF_4$ (25 mg, 0.062 mmol) in dichloromethane (1 mL) ^{t}Bu-BINC (23 mg, 0.062 mmol) was added. The reaction mixture was left stirring for 4 h after which the solvent was evaporated under vacuum. The resulting bright red solid was washed twice with ether and dried (33.2 mg, 80 %).

IR (neat): υ: 2967, 2169, 1245, 993, 516 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1. 04 (s, 18 H), 2.46 (m, 8H), 3.99 (dd, 1H, *J* = 3.27 Hz, 8.5 Hz), 4.09- 4.21 (m, 2H), 4.31- 4.48 (m, 3 H), 5.38- 5.58 (m, 4H), 7.54- 7.66 (m, 3 H), 7.91-7.98 (m, 2H). ^{13}C NMR (151 MHz): δ = 26.29, 26.38, 30.38, 30.61, 33.21, 33.65, 64.33, 64.97, 67.16, 68.26, 99.29, 99.53, 99.68, 100.39, 125.59, 129.22, 132.03, 133.47. ^{31}P NMR (CDCl3, 121.5 MHz): δ = 19.27. MS (LSI-MS), m/z (rel. intensity): [M$^+$] 587.3.



[Ir (COD) (^{t}Bu BINC)]BARF (121):

Na(BARF) (118 mg, 0.133 mmol) was added to a solution of $[Ir(COD)Cl]_2$ (45 mg, 0.0665 mmol) in dichloromethane (4 ml) and stirred for 30 min followed by addition of ^{t}Bu-BINC (50 mg, 0.133 mmol) .The reaction mixture was stirred for 4 h after which the solvent was evaporated under vacuum. Crude complex was passed through a small plug of silica using dichloromethane. Quantitative yield was obtained.

IR (neat): υ: 2970, 2196, 1354, 1273, 1113 cm^{-1}. ^{1}H NMR (CDCl3, 300 MHz): δ = 0.987 (s, 9H), 1.03 (s, 9H), 2.25-2-47 (m, 8H), 3.89-4.0(m, 2H), 4.09-4.14 (m,2 H), 4.22-4.29 (m, 1H), 4.49 (quartet, 1 H, J = 10 Hz, 19.6 Hz), 5.02-5.21 (m, 4H), 7.46-7.56 (m, 6 H), 7.60- 7.83 (m, 11 H). ^{31}P NMR (CDCl3, 121.5 MHz): δ = 22.02. MS (LSI-MS), m/z (rel. intensity): $[M+H^+$- BARF] 677.2. HRMS: calcd. for $C_{28}H_{39}O_3N_2PIr^{193}$ $[M^{\cdot+}]$: 675, found: 675.233.

Na{B[3,5-$(CF_3)_2C_6H_3]_4$} Na(BARF):

Slow addition of a solution of 3,5-bis (trifluromethyl)bromobenzen (1 gm, 3.4 mmol) in ether (5 mL) to Mg turnings (99.4 mg, 4.09 mmol) in ether (3 mL), followed by refluxing for 30 min, gave a dark gray solution of aryl Grignard reagent. Upon addition of $NaBF_4$ (53 mg, 0.48 mmol), the heterogenous reaction mixture was stirred for 48 h, during which time the solution became brown and a fine precipitate formed. The reaction mixture was added to Na_2CO_3 (8.5 g) in water (100 ml), stirred for 30 min and filtered. The aqueous layer was extracted with ether (3 x 25 mL), and the combined organic layer was dried over sodium sulfate and treated with decolorizing charcoal. The mixture was filtered and the ether was removed under vacuum. The remaining oily solid was dissolved in 100 mL benzene, and water was removed with a stark trap by azeotropic distillation for 2 h. The solvent volume was reduced to 50 mL and solution was cooled to room temperature and the solvent was

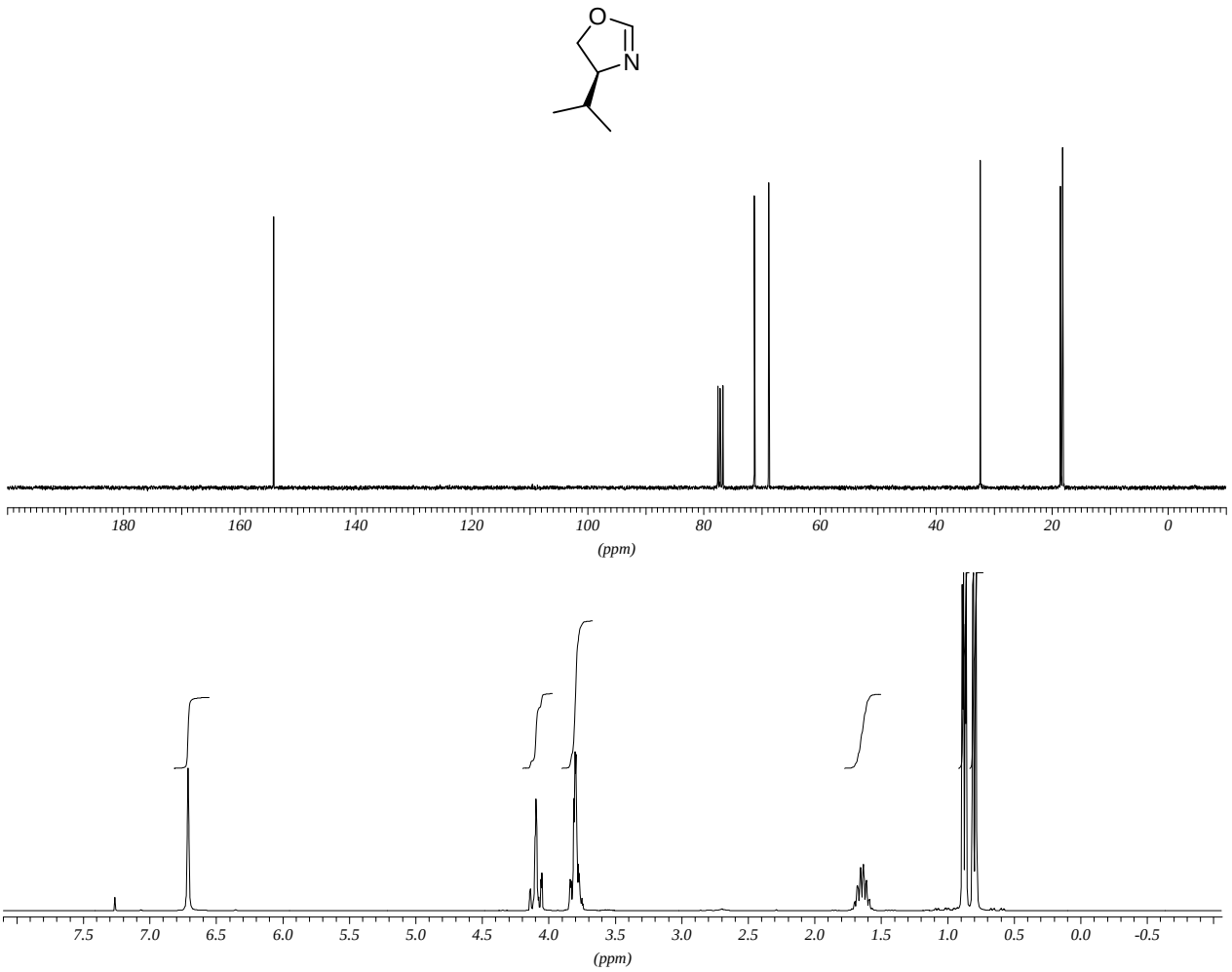
decanted to remove unreacted starting materials. The remaining off white solid was dried under vacuum (2.5 g, 84 %).

^{1}H NMR (acetone, 300 MHz): δ = 7.67 (s, 4H), 7.79 (br, 8H). Mass (ESMS): 863.1$(M\text{-}Na^{+})^{-}$.

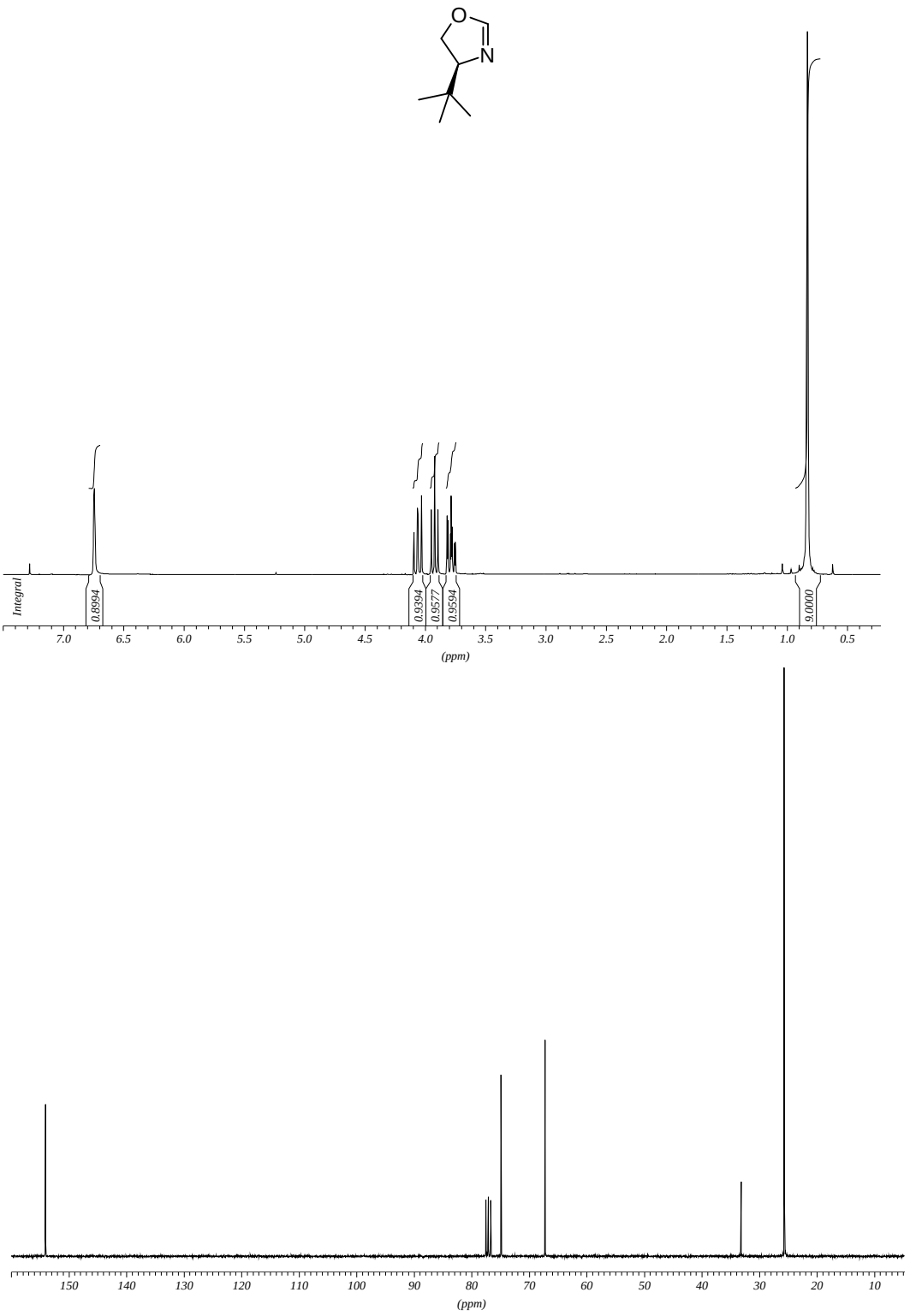
I. Appendix

^{1}H and ^{13}C NMR spectra

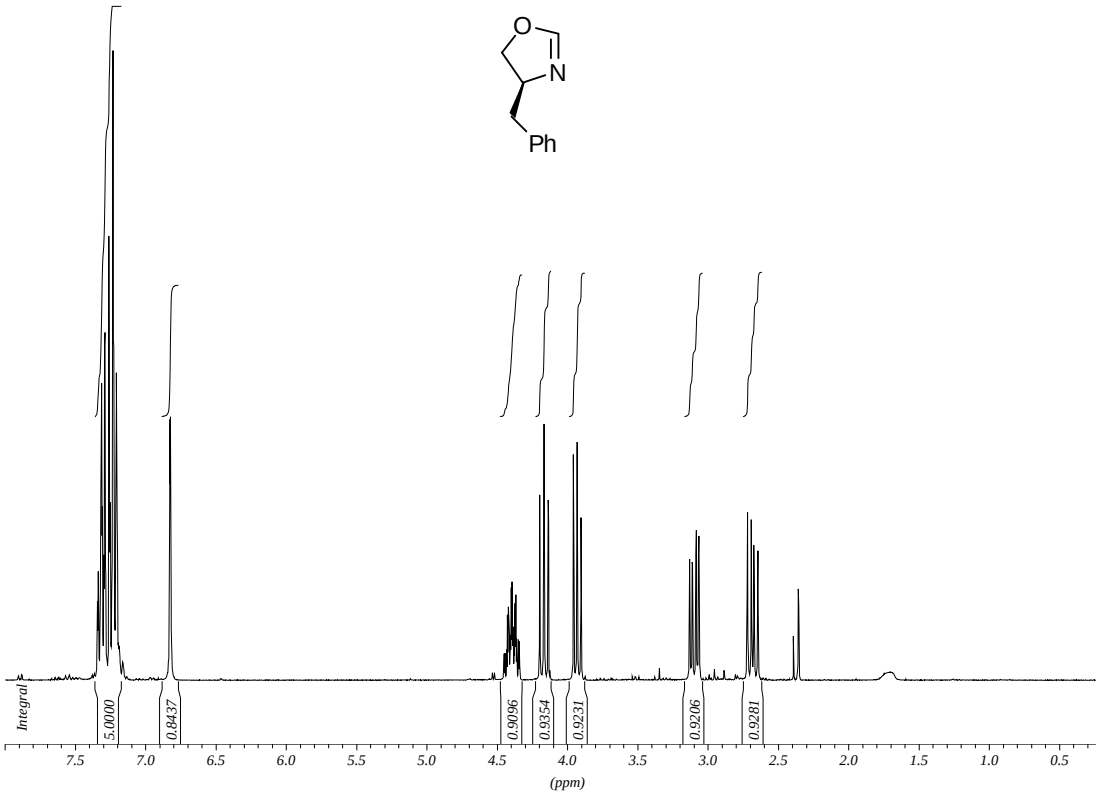
(*S*)-*i*-Propyl-2-oxazoline (71c)

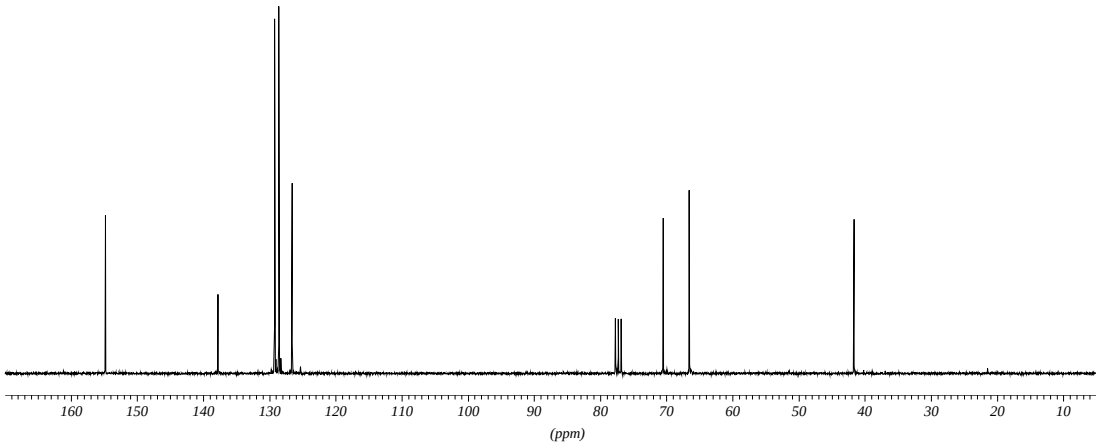


(*S*)-*t*-Butyl-2-oxazoline (71b)

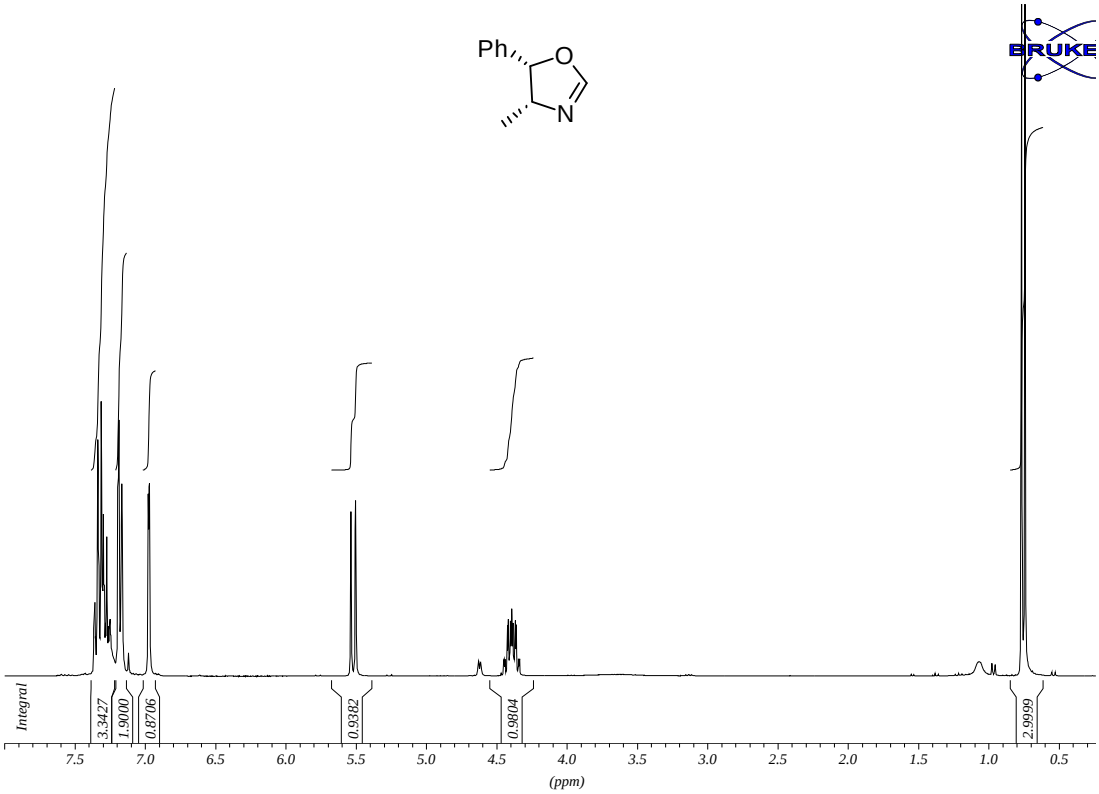


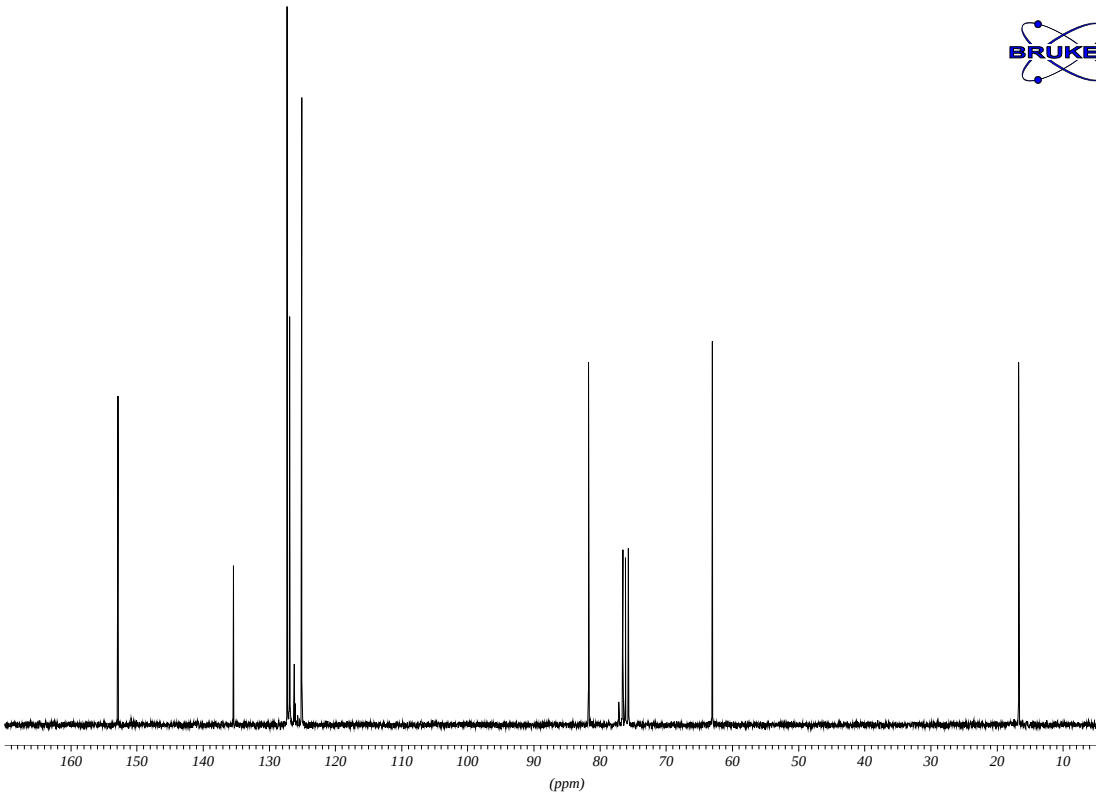
(*S*)-Benzyl-2-oxazoline (71a)



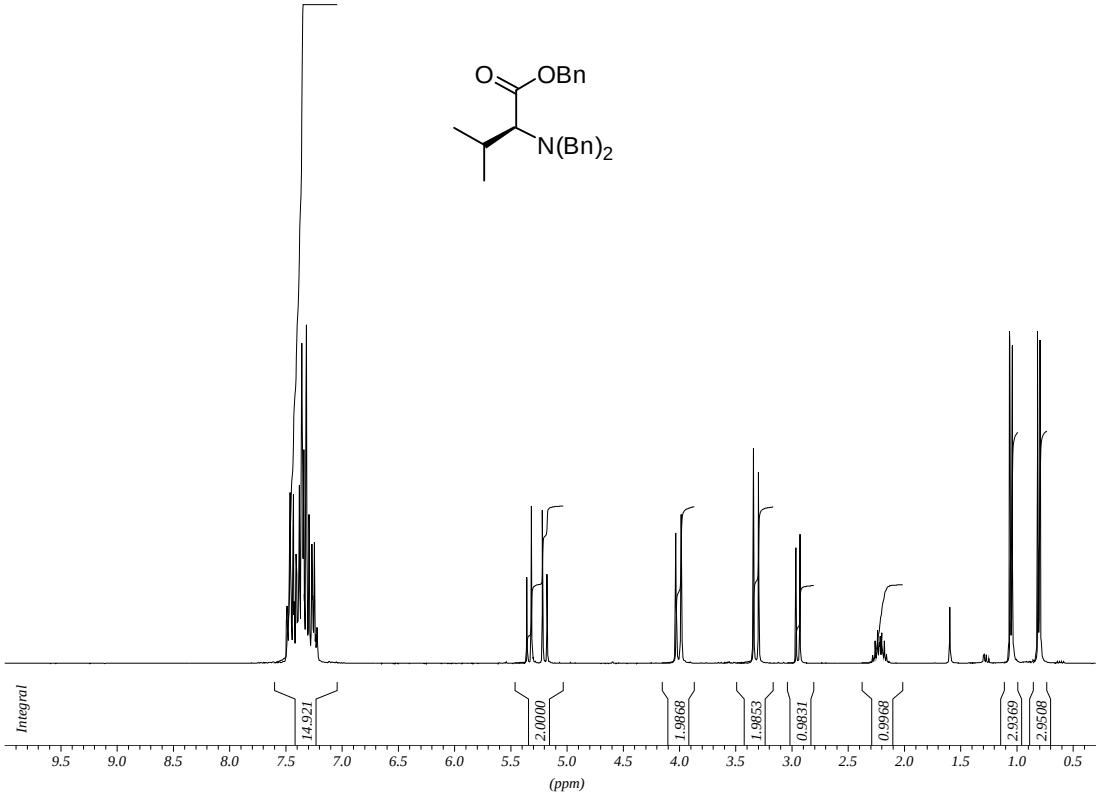


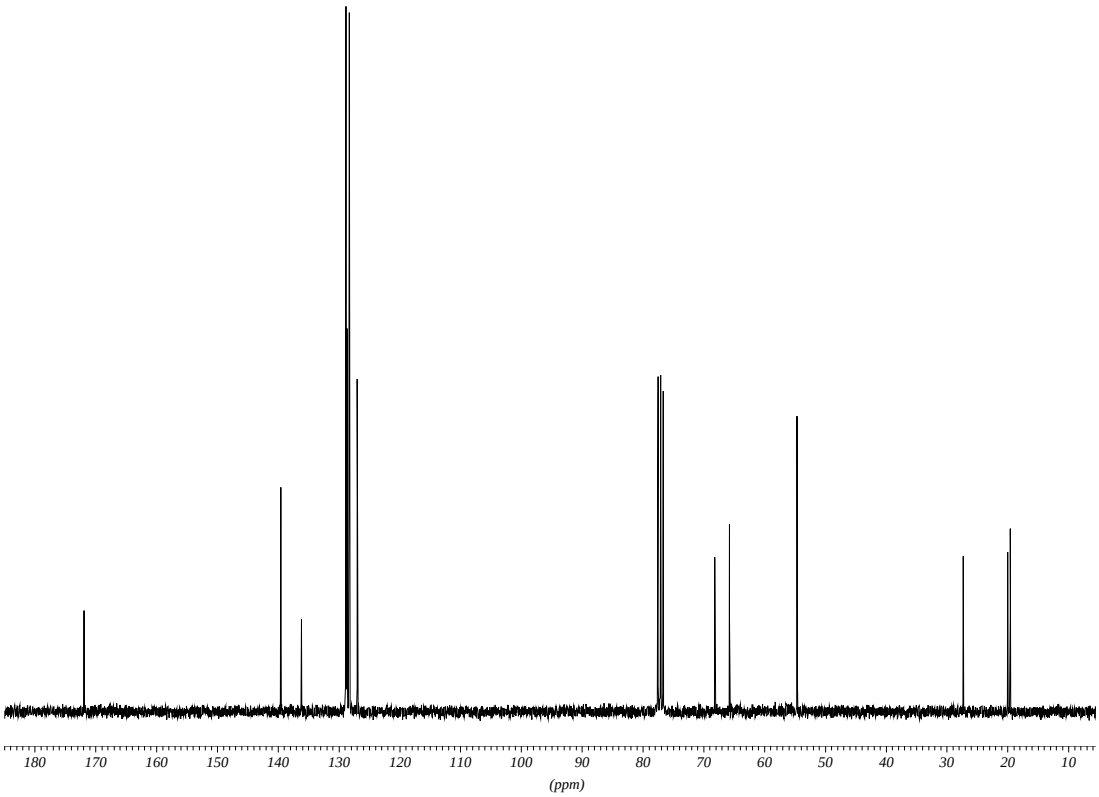
(4*S*,5*S*)-4-methyl-5-phenyl-4,5-dihydrooxazole (71d)



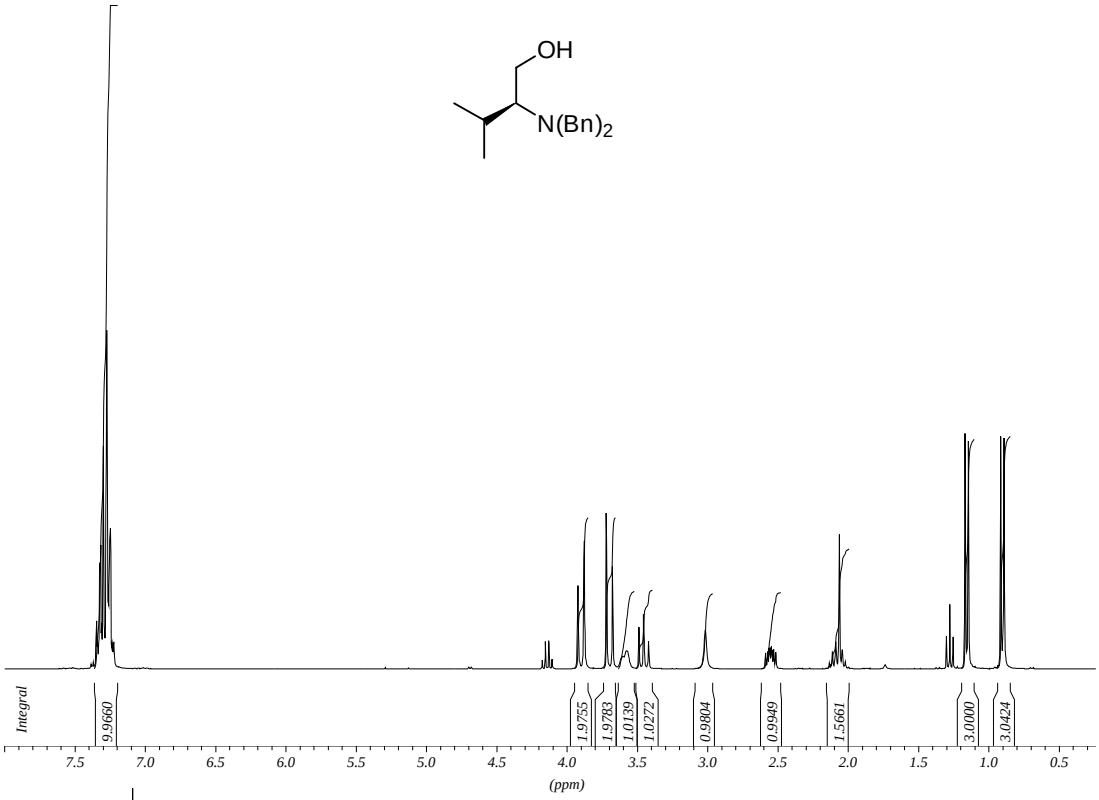


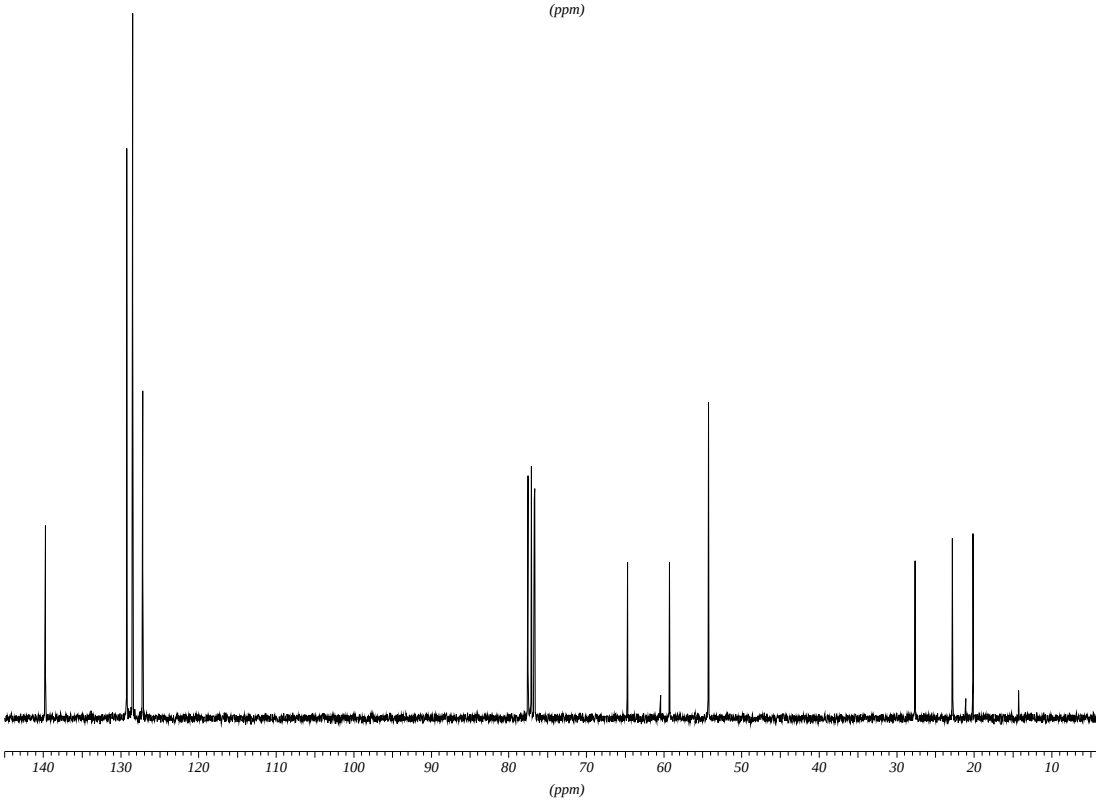
(*S*)-benzyl 2-(dibenzylamino)-3-methylbutanoate (76)



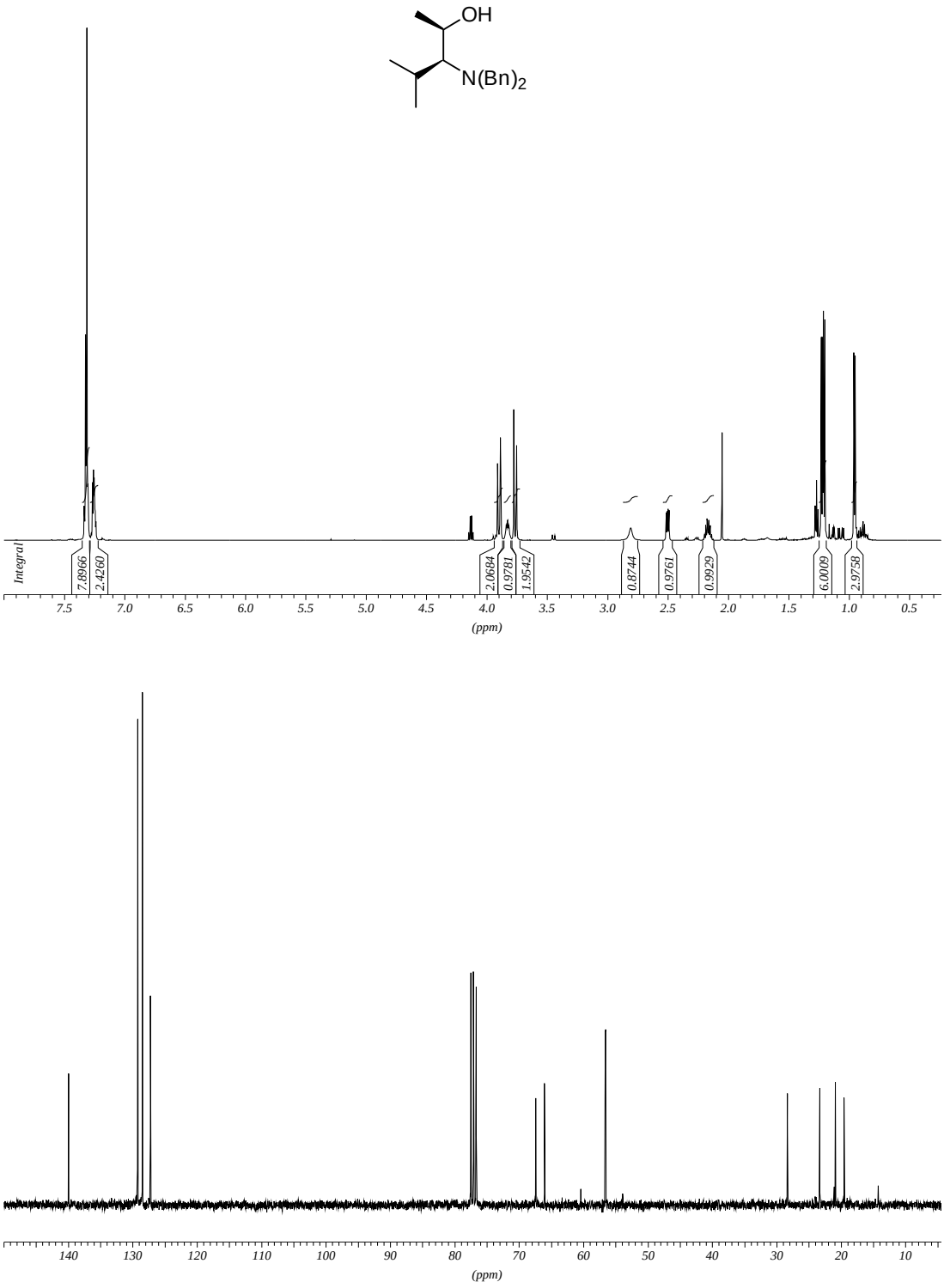


(*S*)-2-(dibenzylamino)-3-methylbutan-1-ol (77)

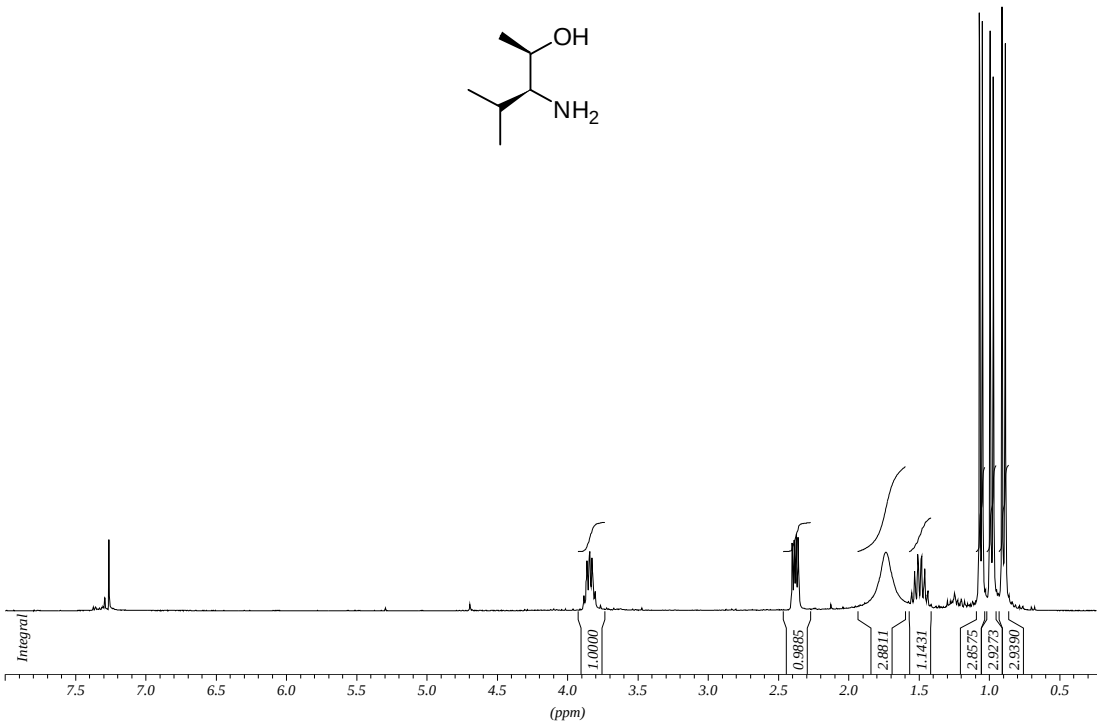


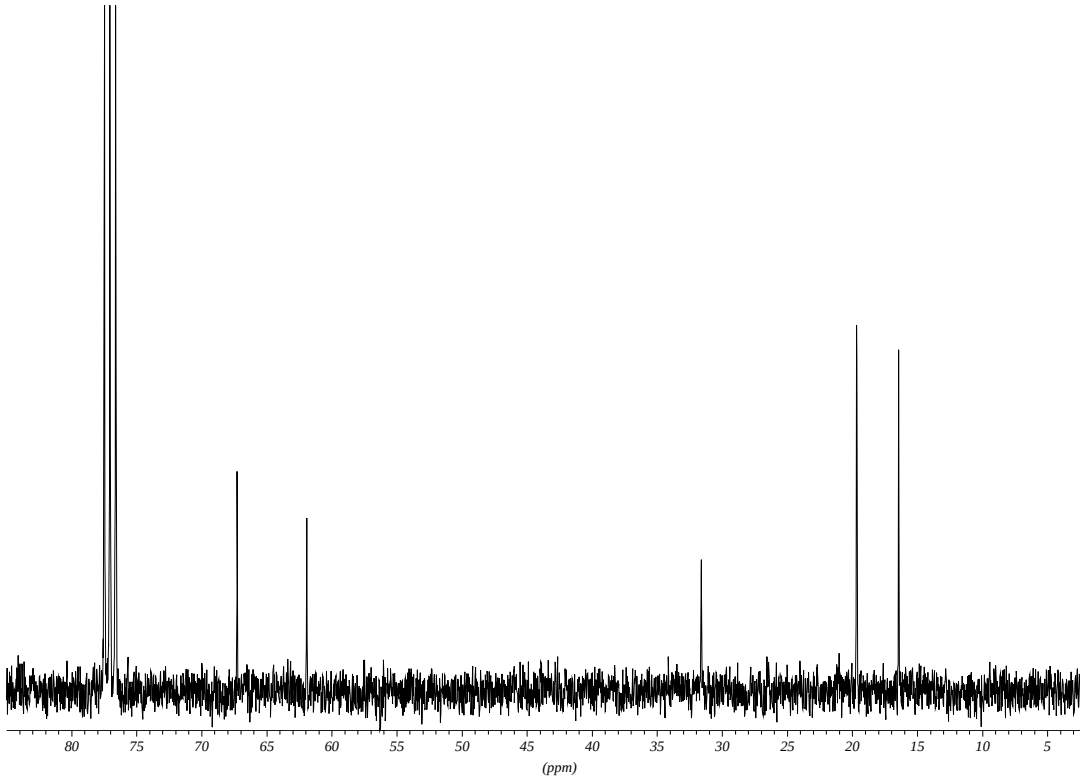


(2*R*,3*S*)-3-(dibenzylamino)-4-methylpentan-2-ol (78)

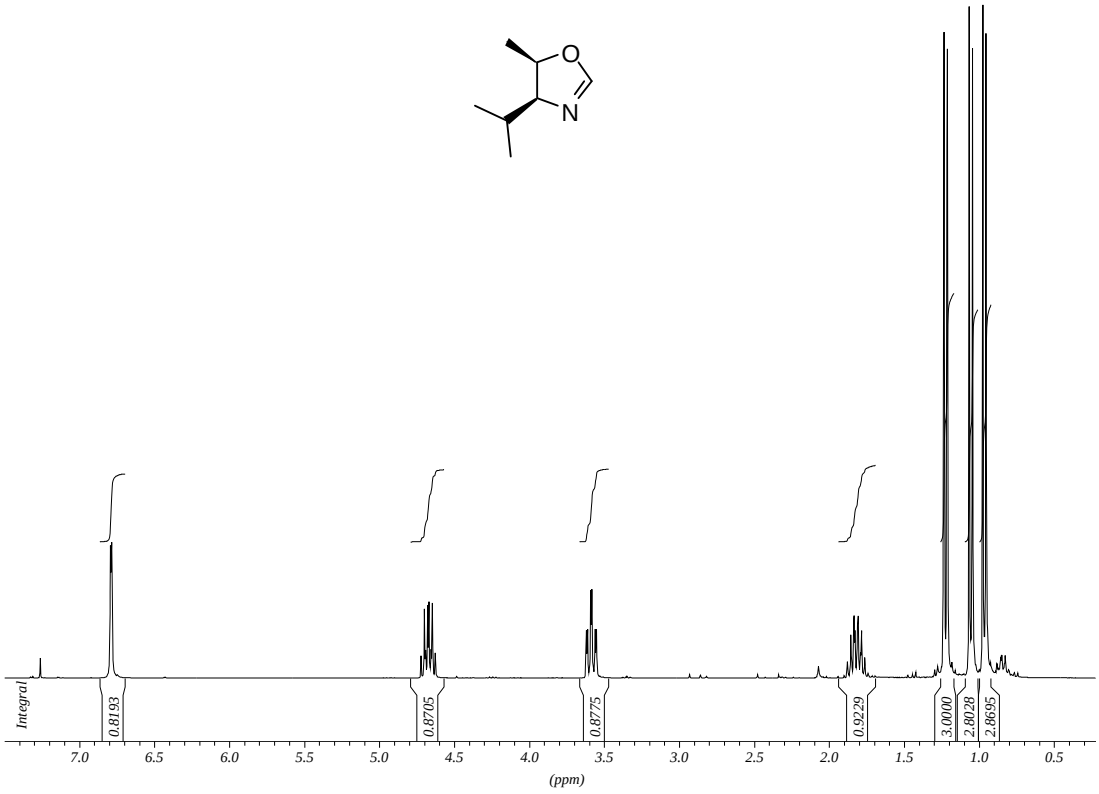


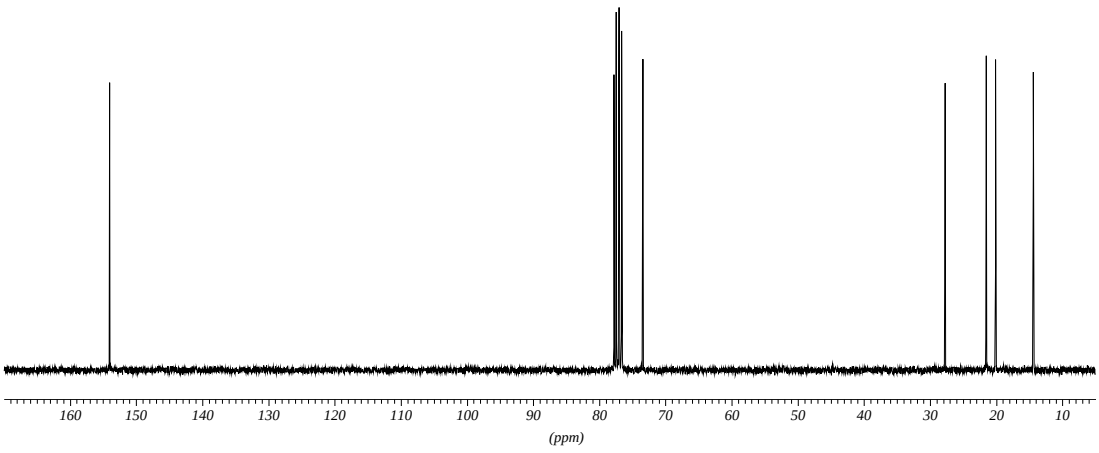
(2*R*,3*S*)-3-amino-4-methylpentan-2-ol (81)



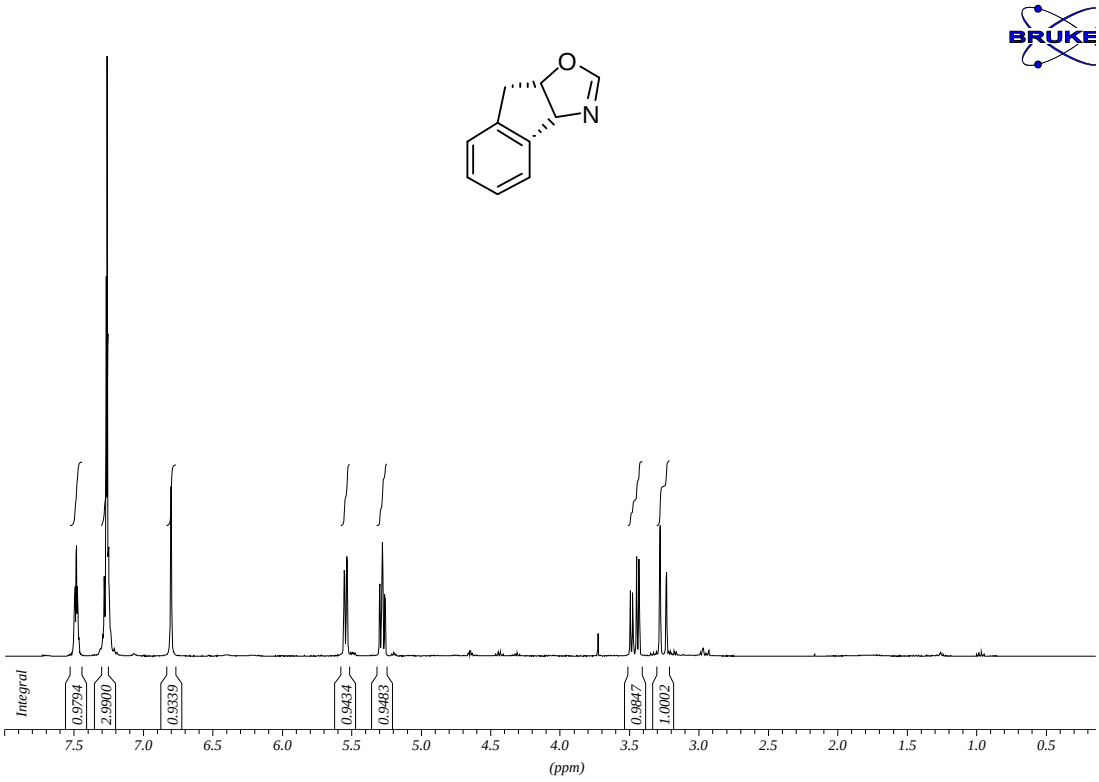


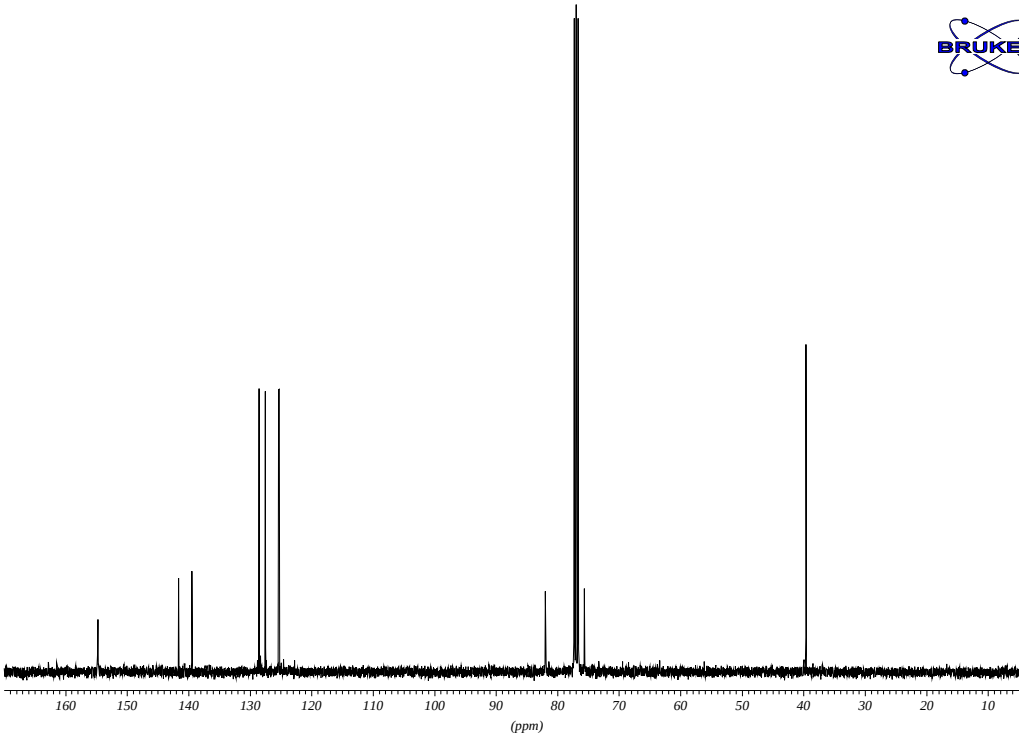
(4*S*,5*R*)-4-isopropyl-5-methyl-4,5-dihydrooxazole (71e)



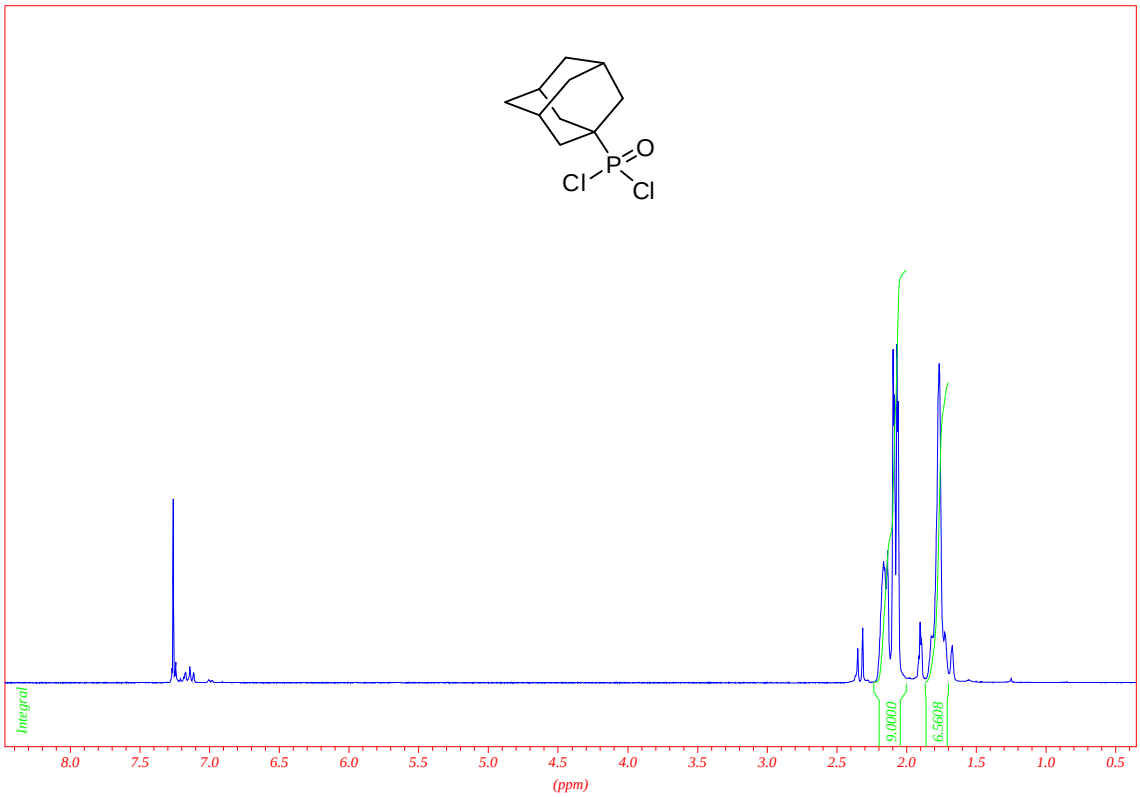


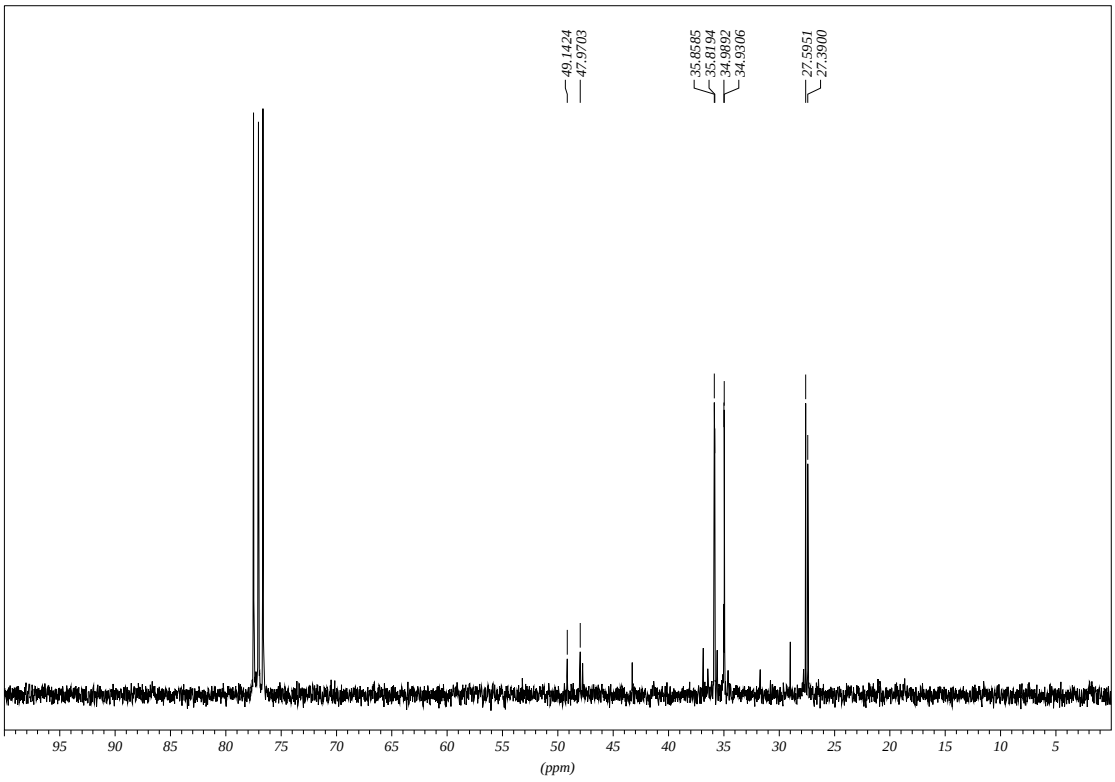
(3a*R*,8a*S*)-8,8a-dihydro-3aH-indeno[1,2-d]oxazole (71f)



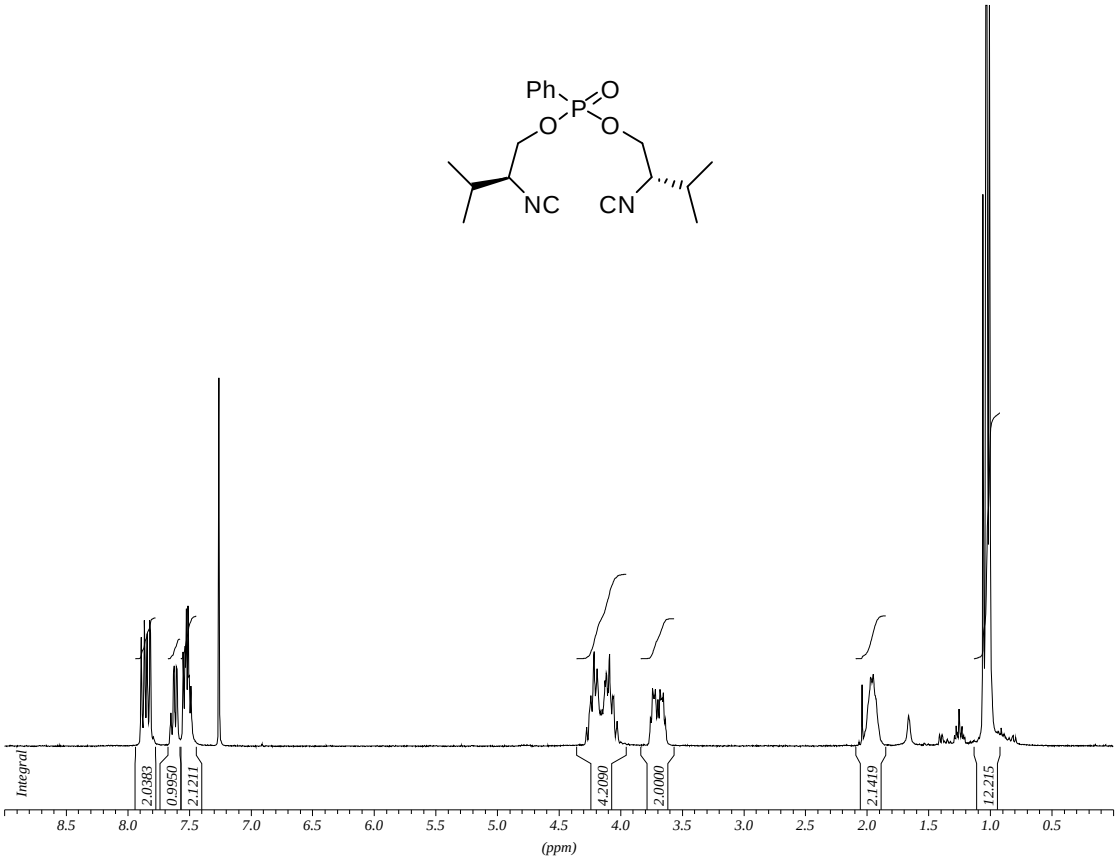


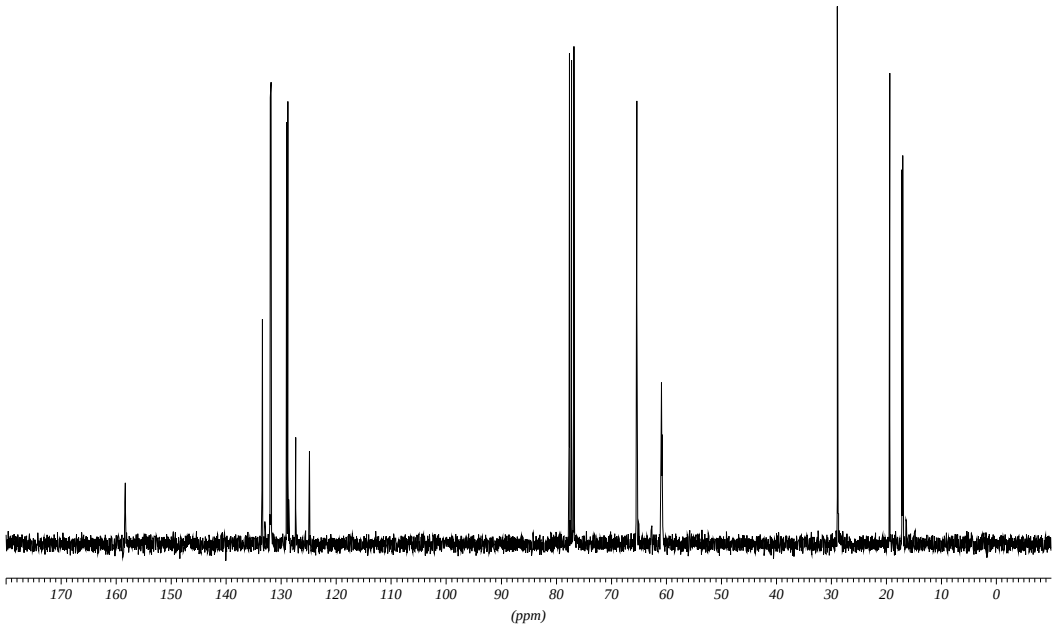
Adamantylphosphonic dichloride (74)



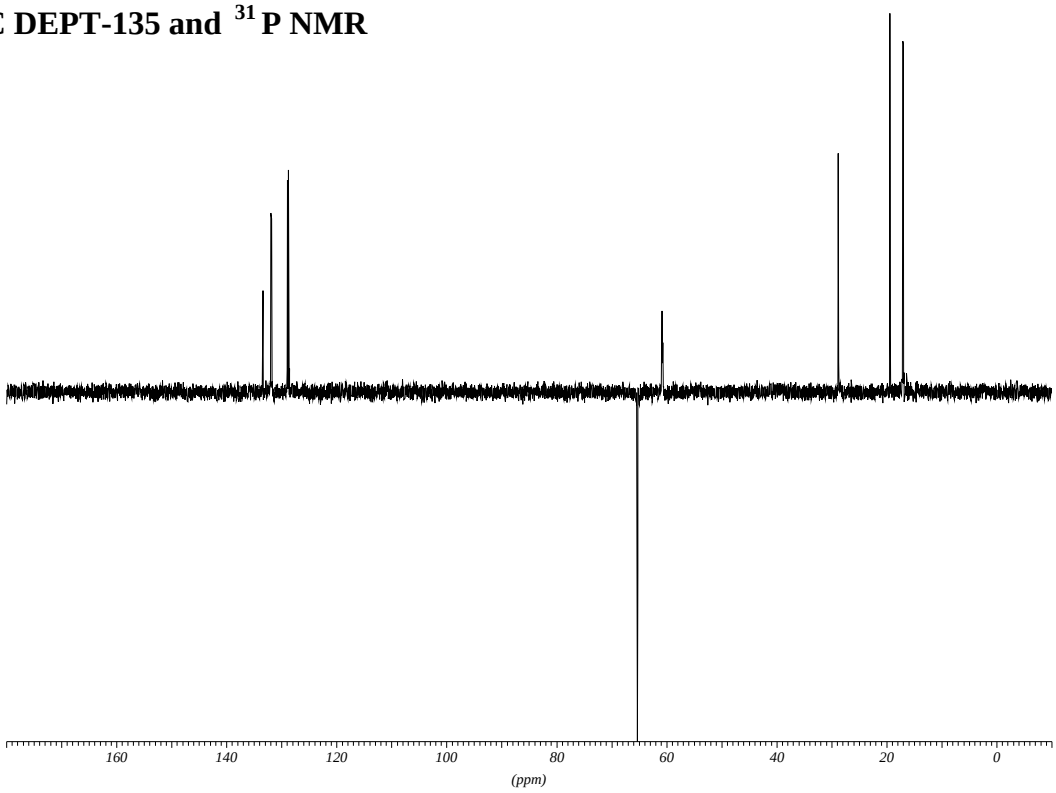


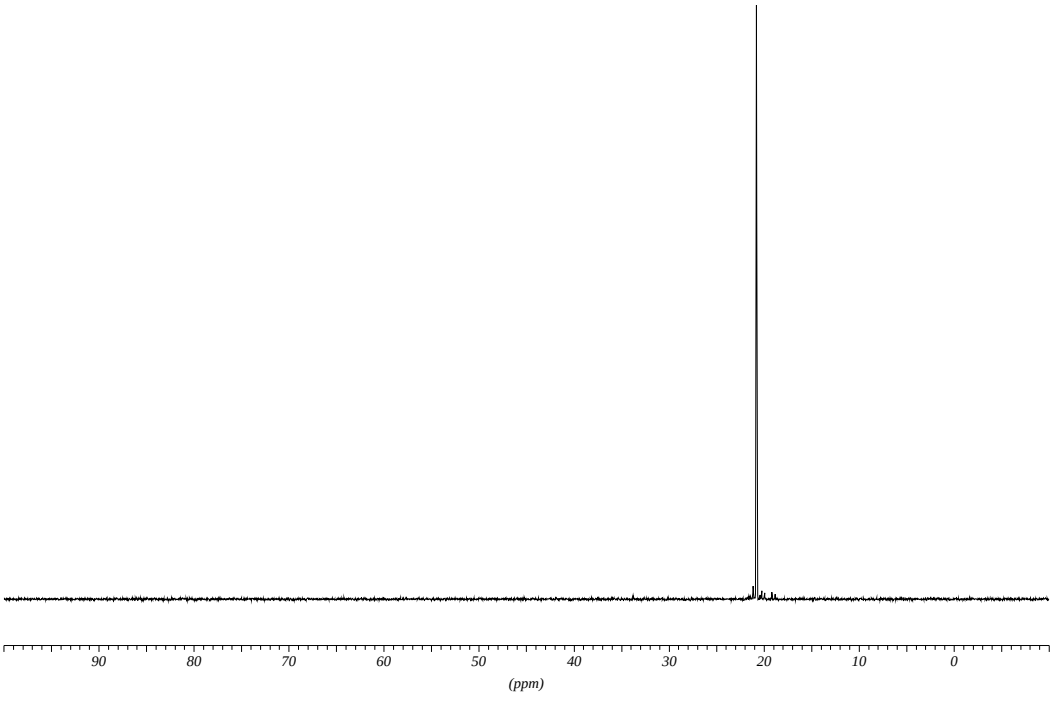
Bis((*S*)-2-isocyano-3-methylbutyl) phenylphosphonate (72c)



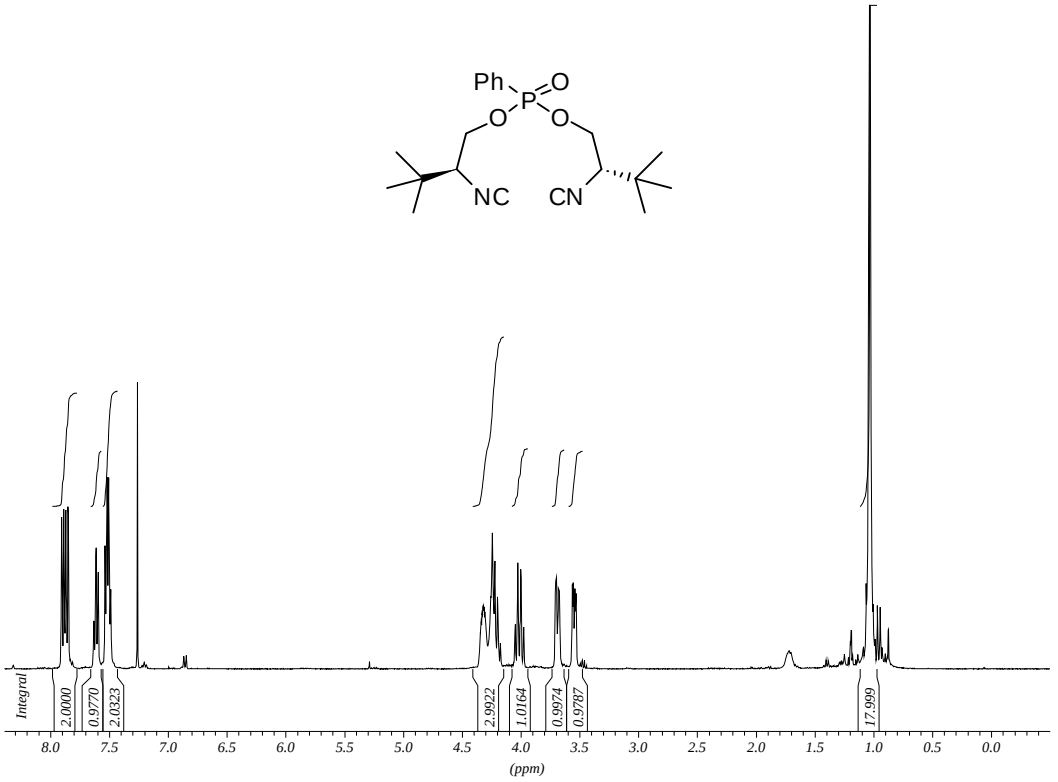


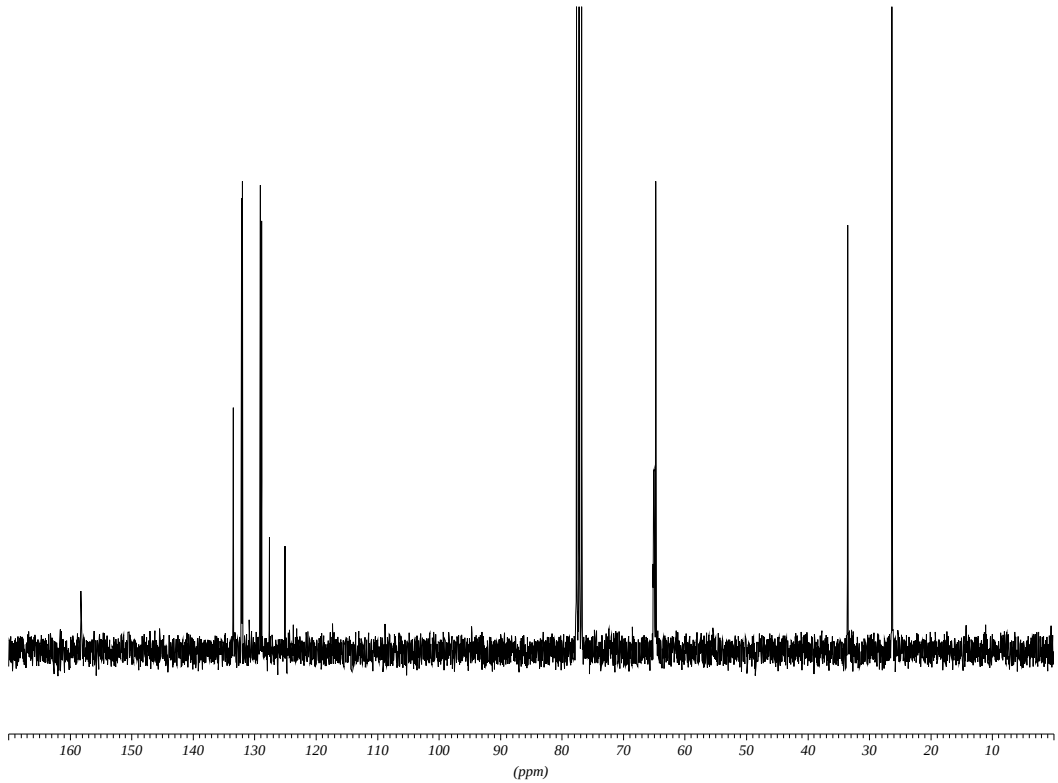
^{13}C DEPT-135 and ^{31}P NMR



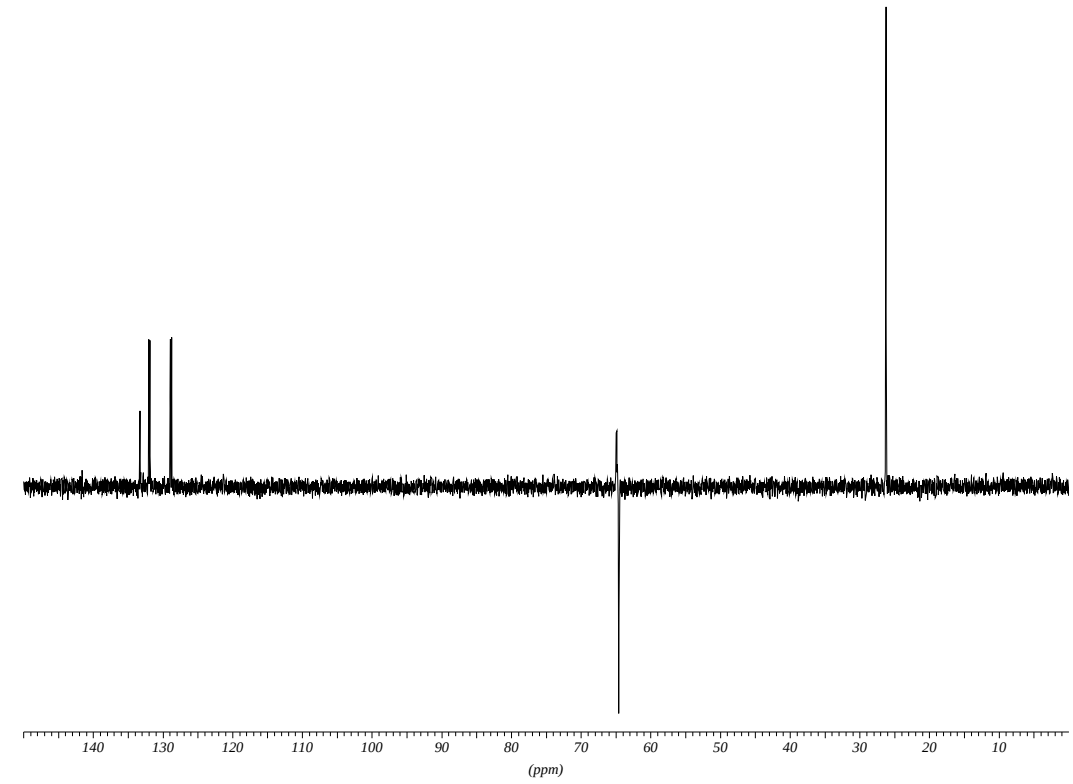


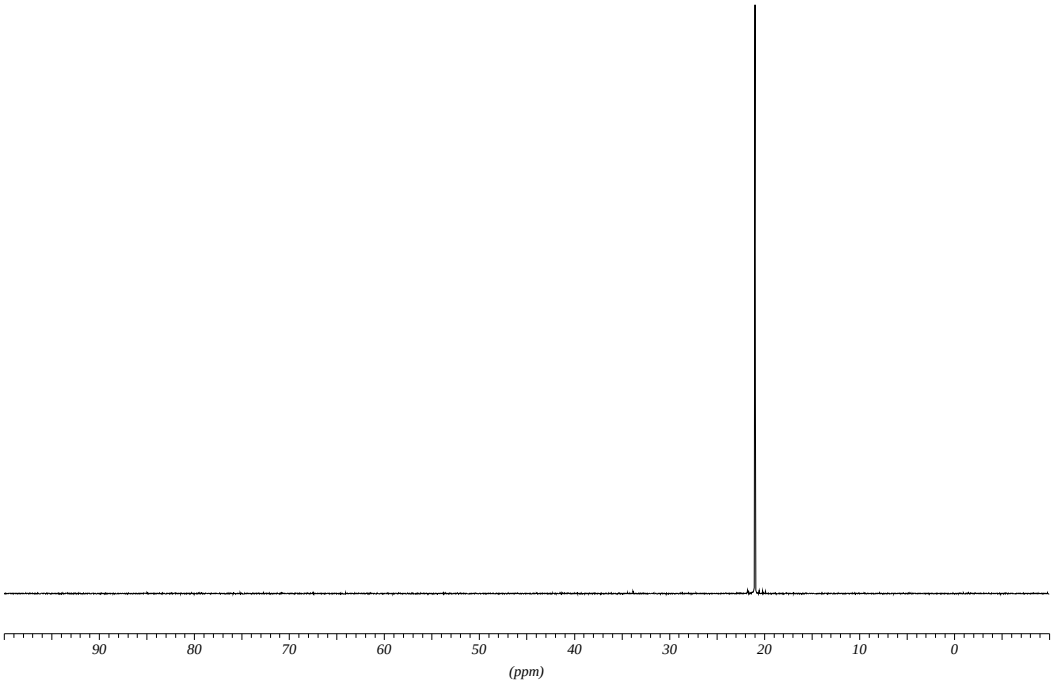
Bis((*S*)-2-isocyano-3,3-dimethylbutyl) phenylphosphonate (72b)



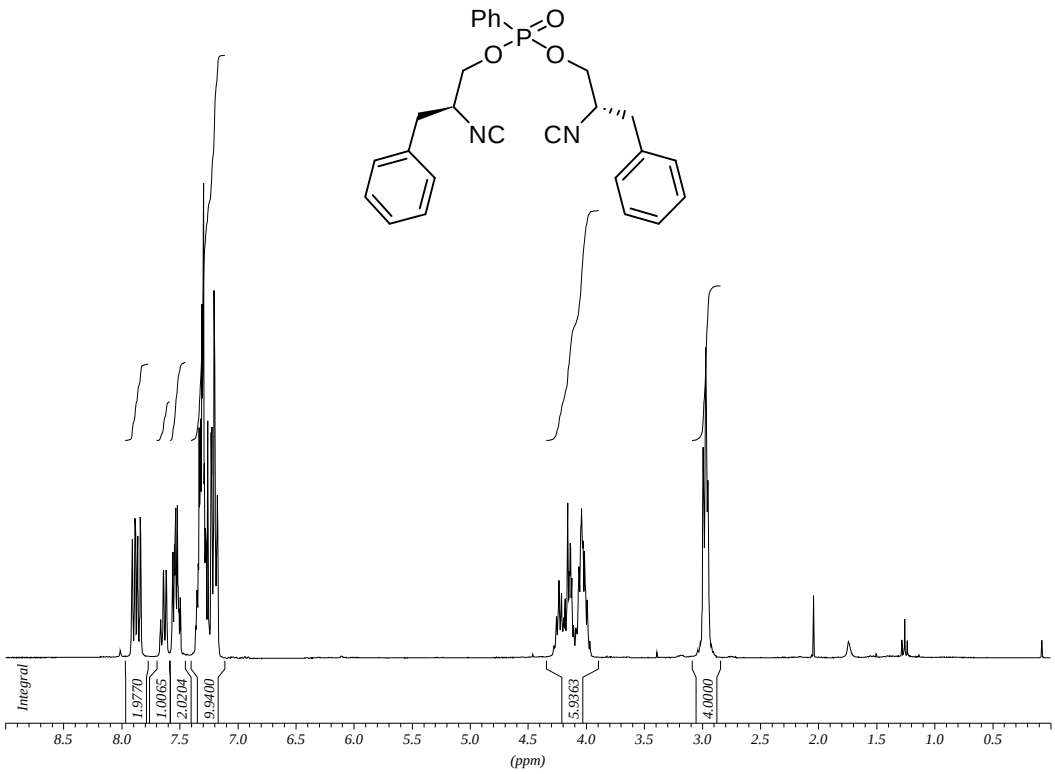


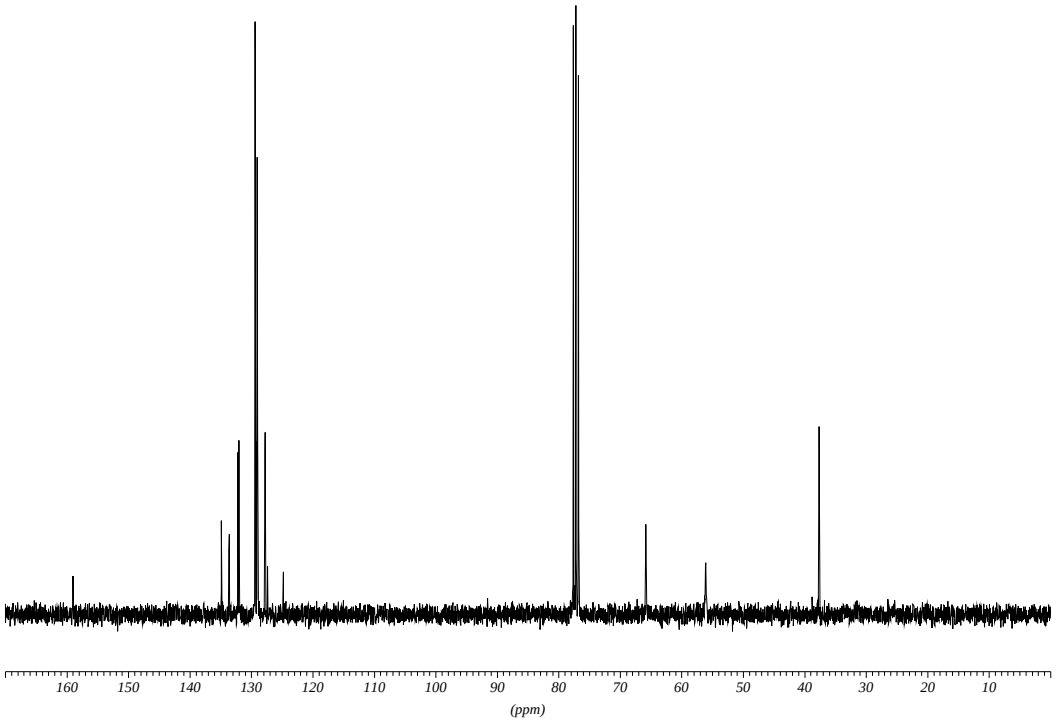
^{13}C DEPT-135 and ^{31}P NMR



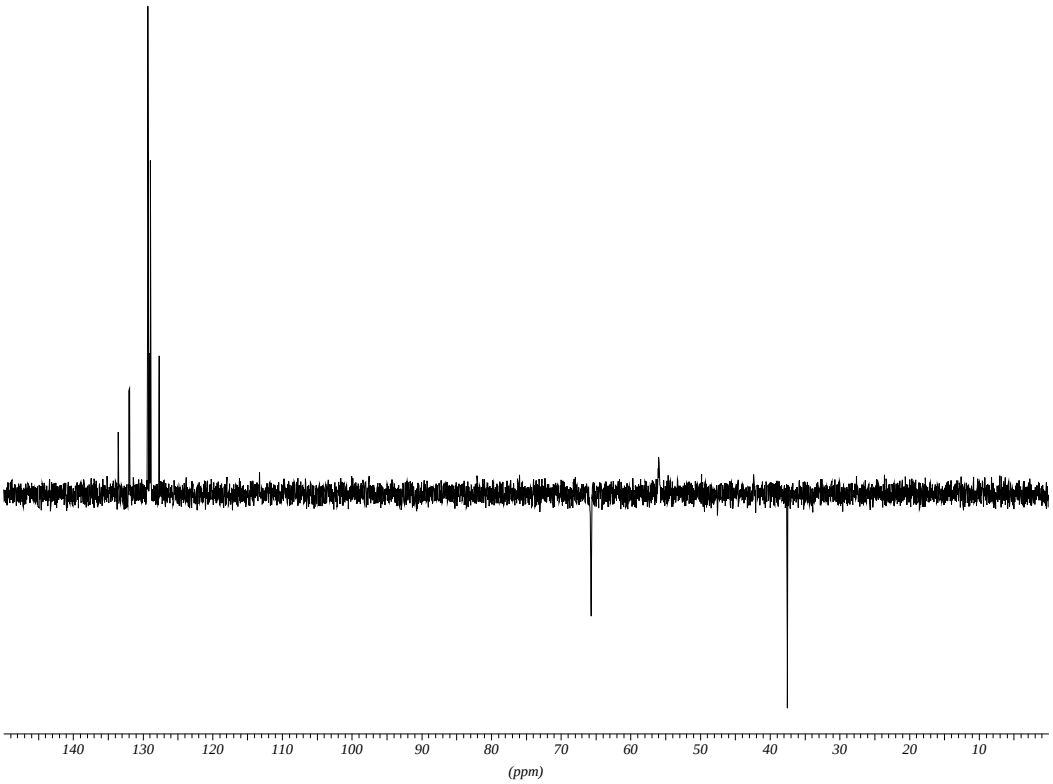


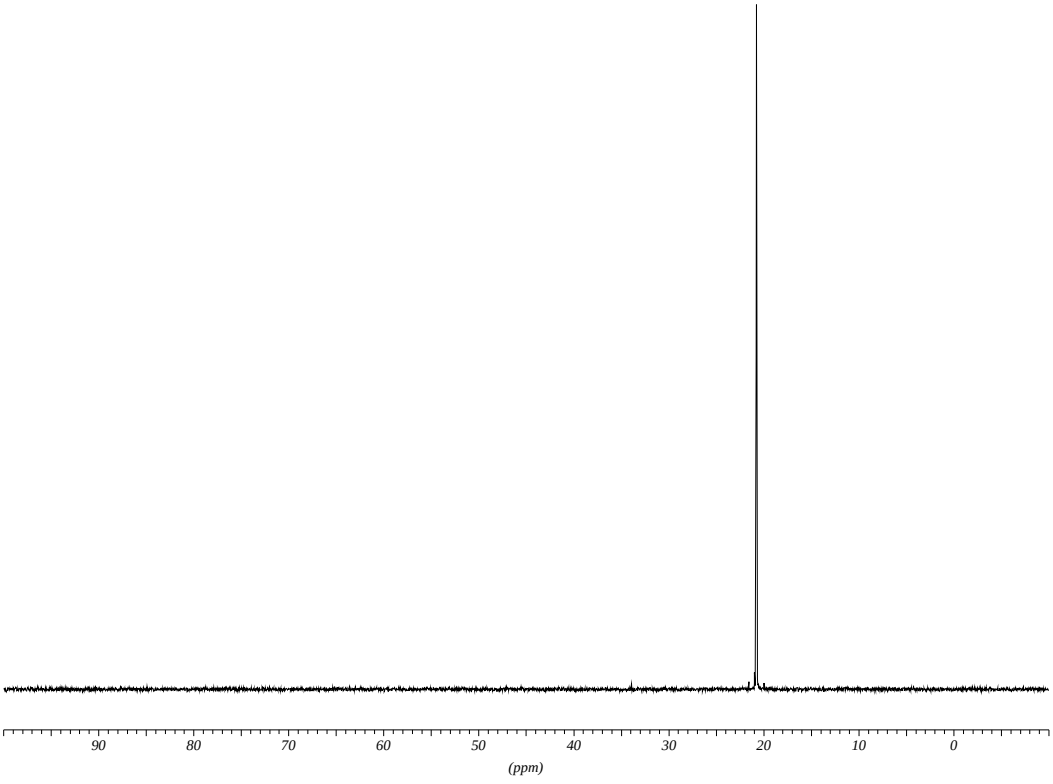
Bis((*S*)-2-isocyano-3-phenylpropyl) phenylphosphonate (72a)



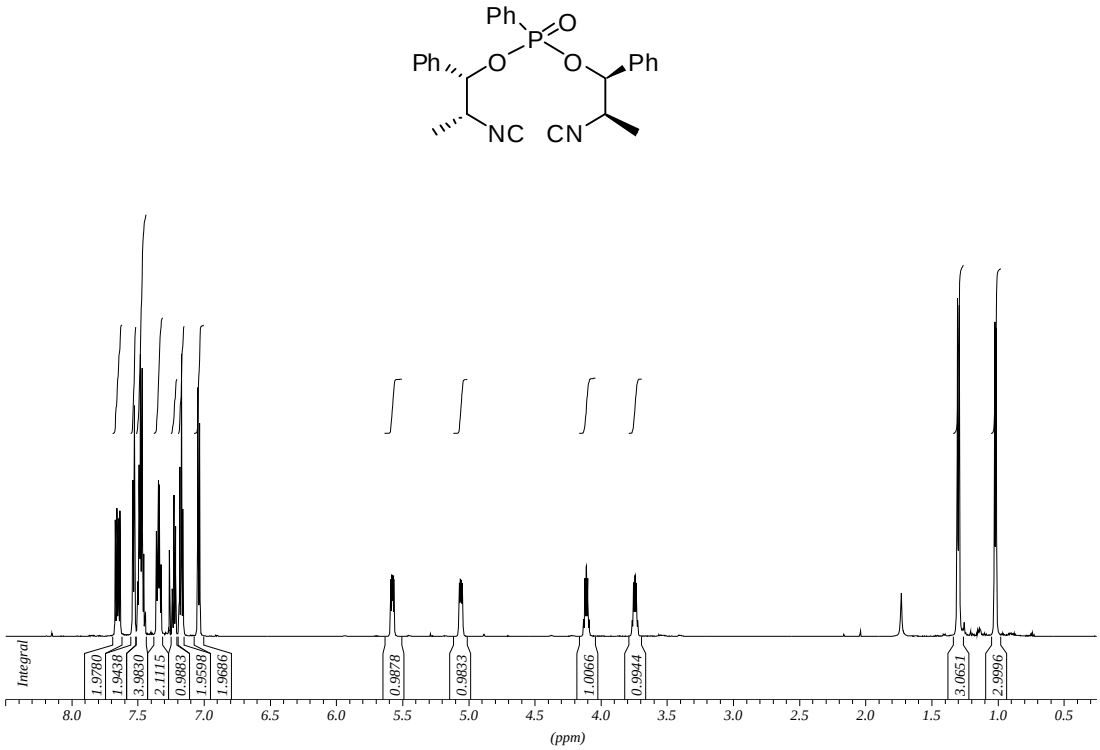


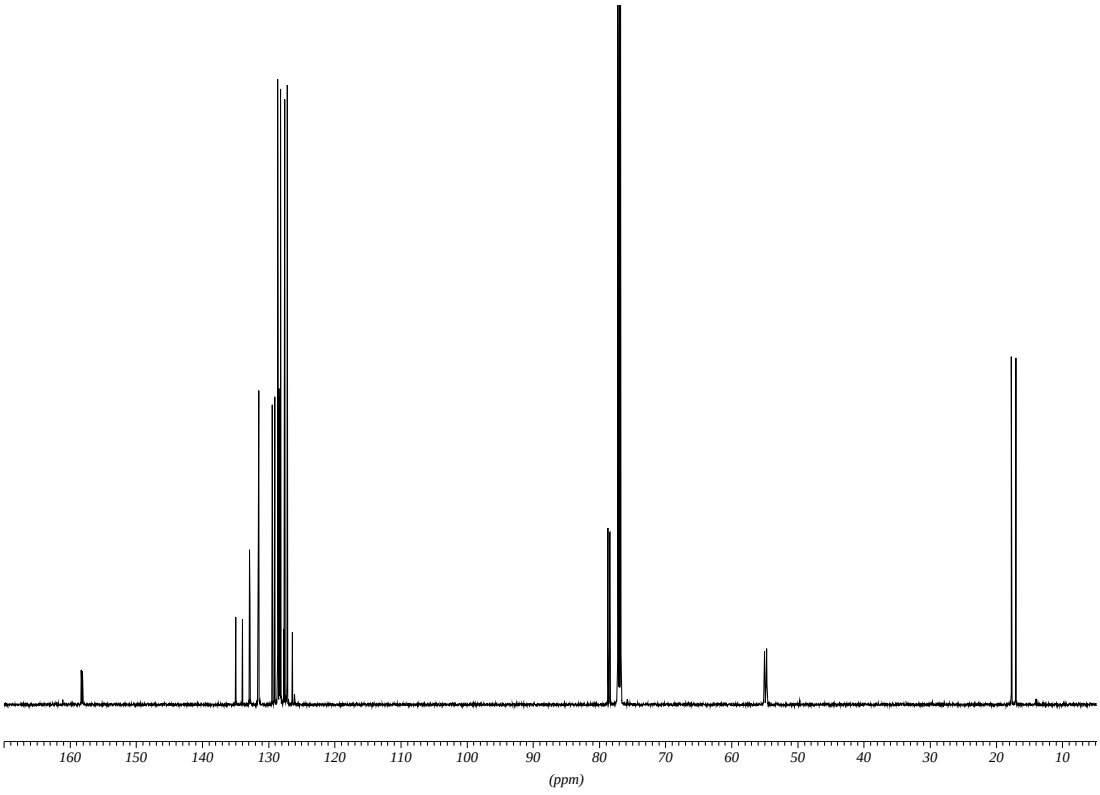
^{13}C DEPT-135 and ^{31}P NMR



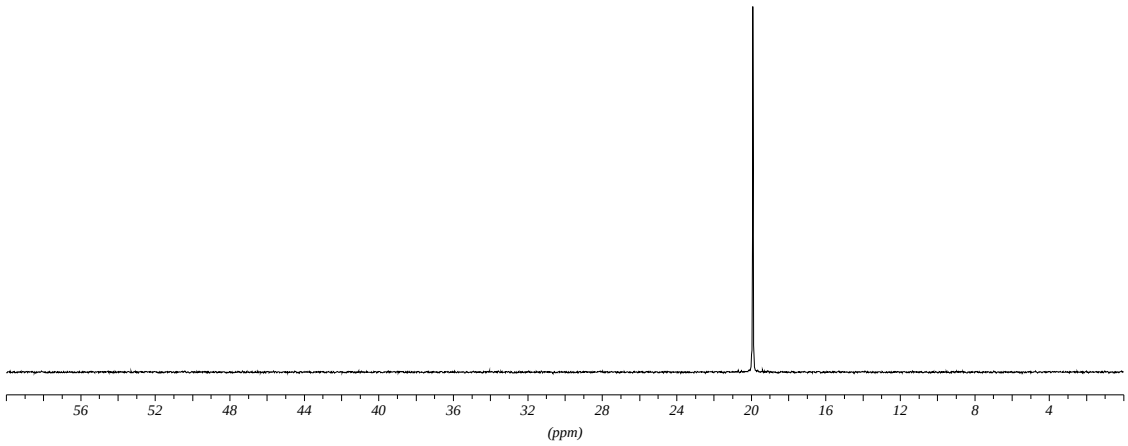


Bis((1*S*,2*S*)-2-isocyano-1-phenylpropyl) phenylphosphonate (72d)

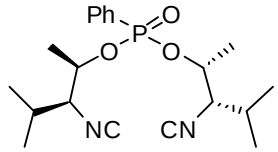


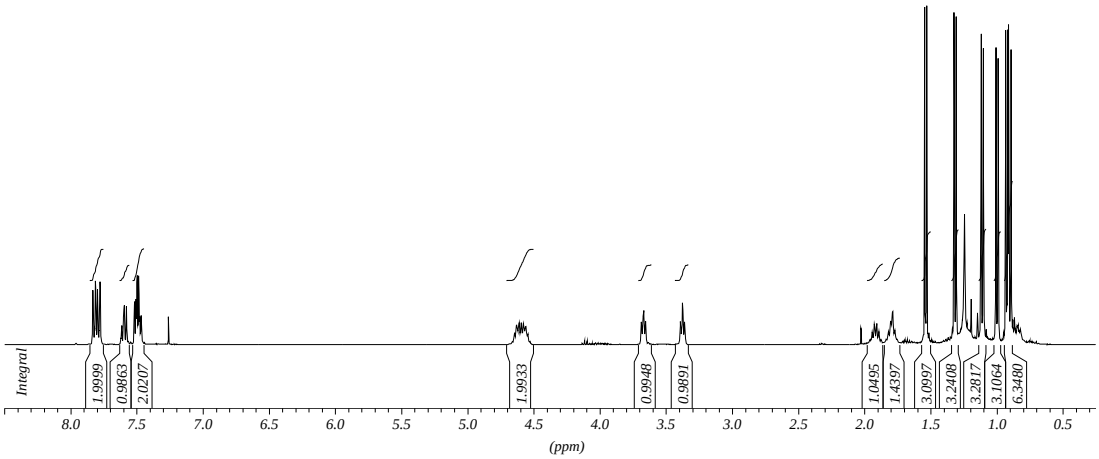


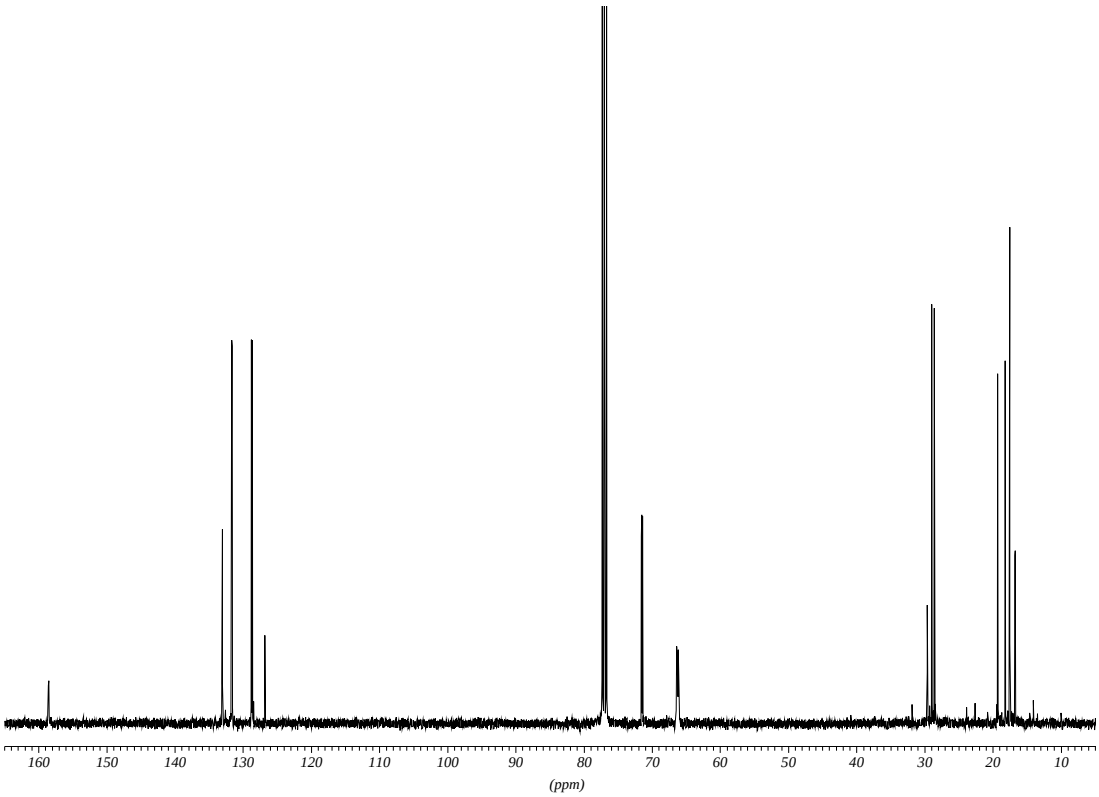
^{31}P NMR



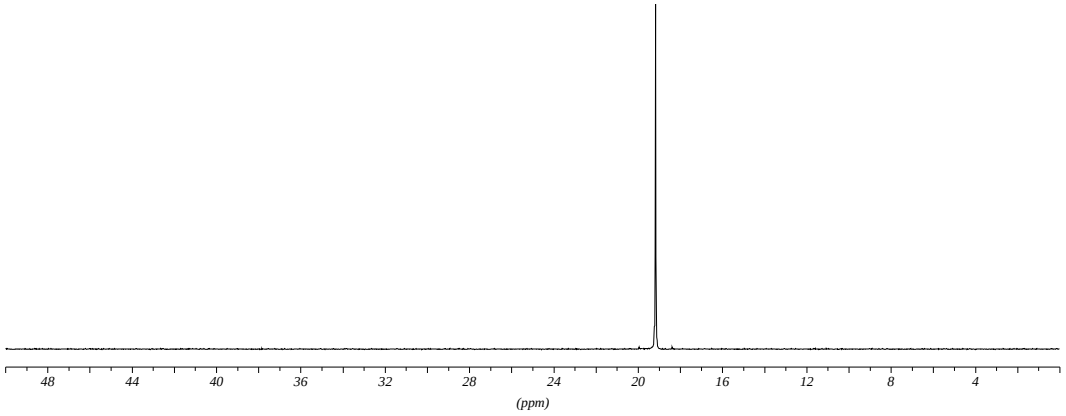
Bis((2*R*,3*S*)-3-isocyano-4-methylpentan-2-yl) phenylphosphonate (72e)



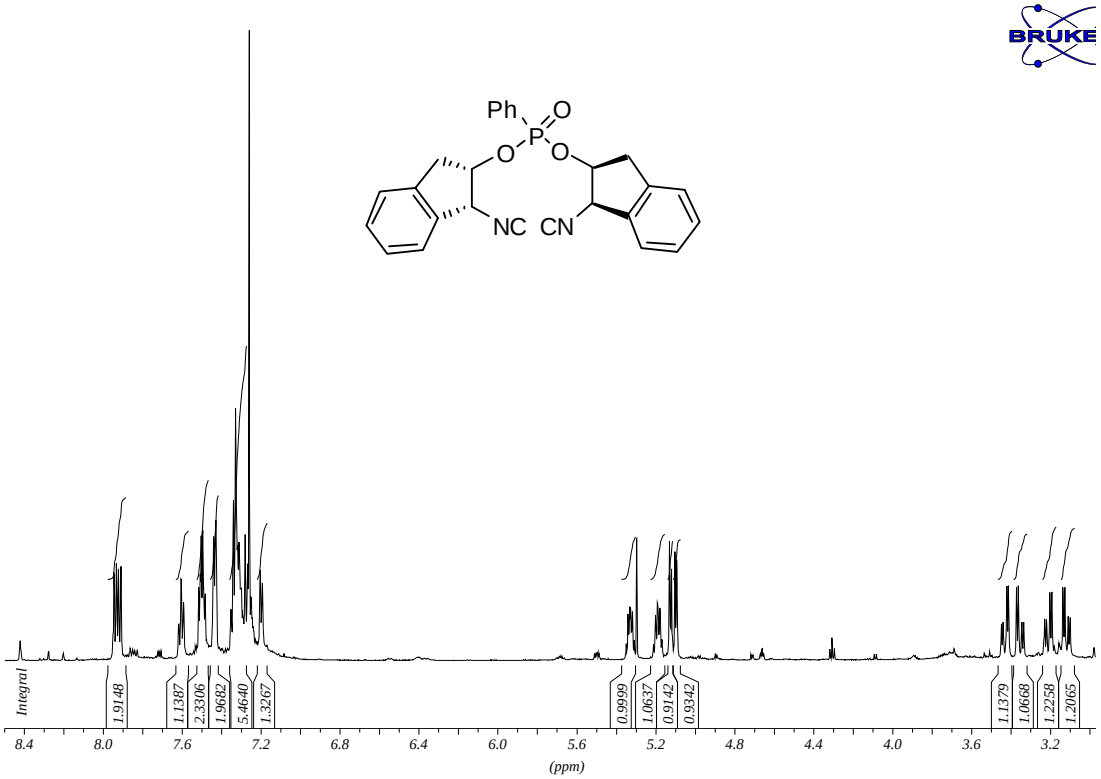


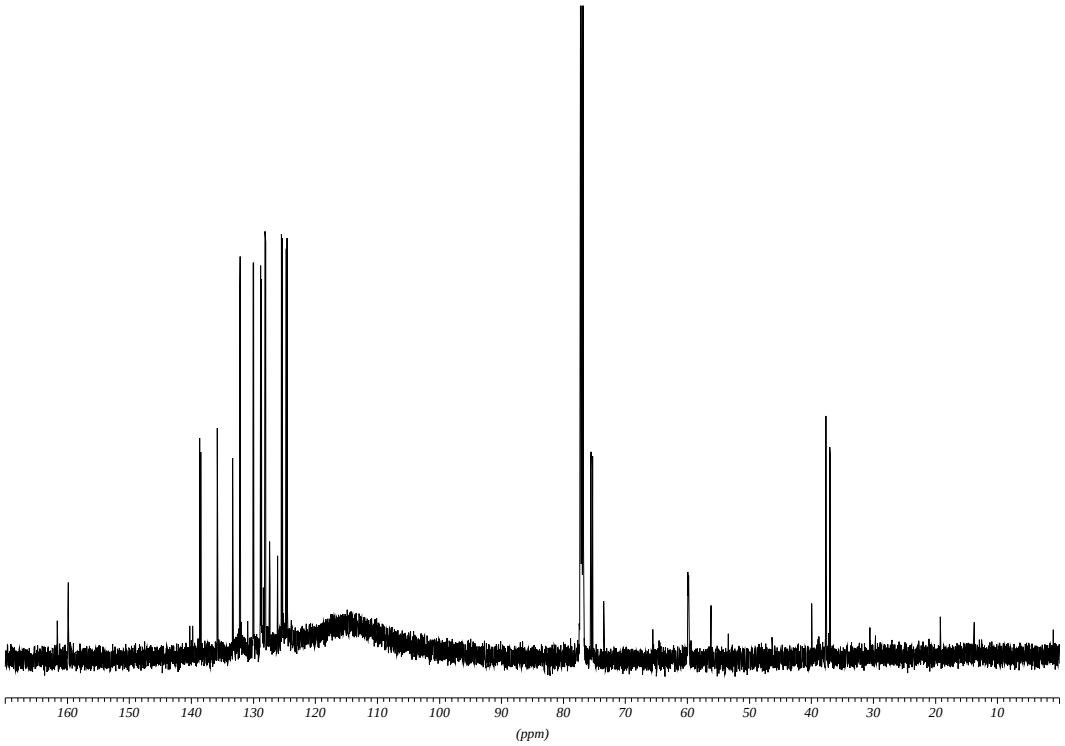


^{31}P NMR

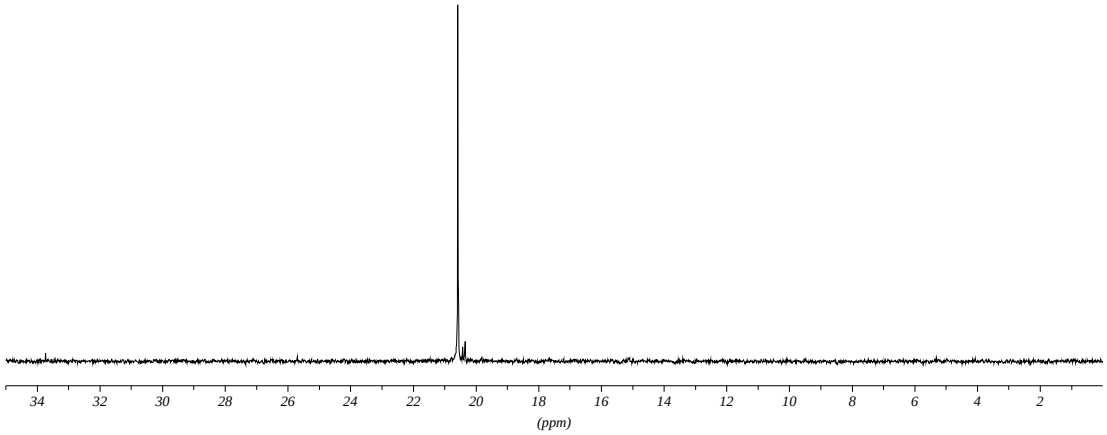


Bis((1*R*,2*S*)-1-isocyano-2,3-dihydro-1H-inden-2-yl) phenylphosphonate (72f)

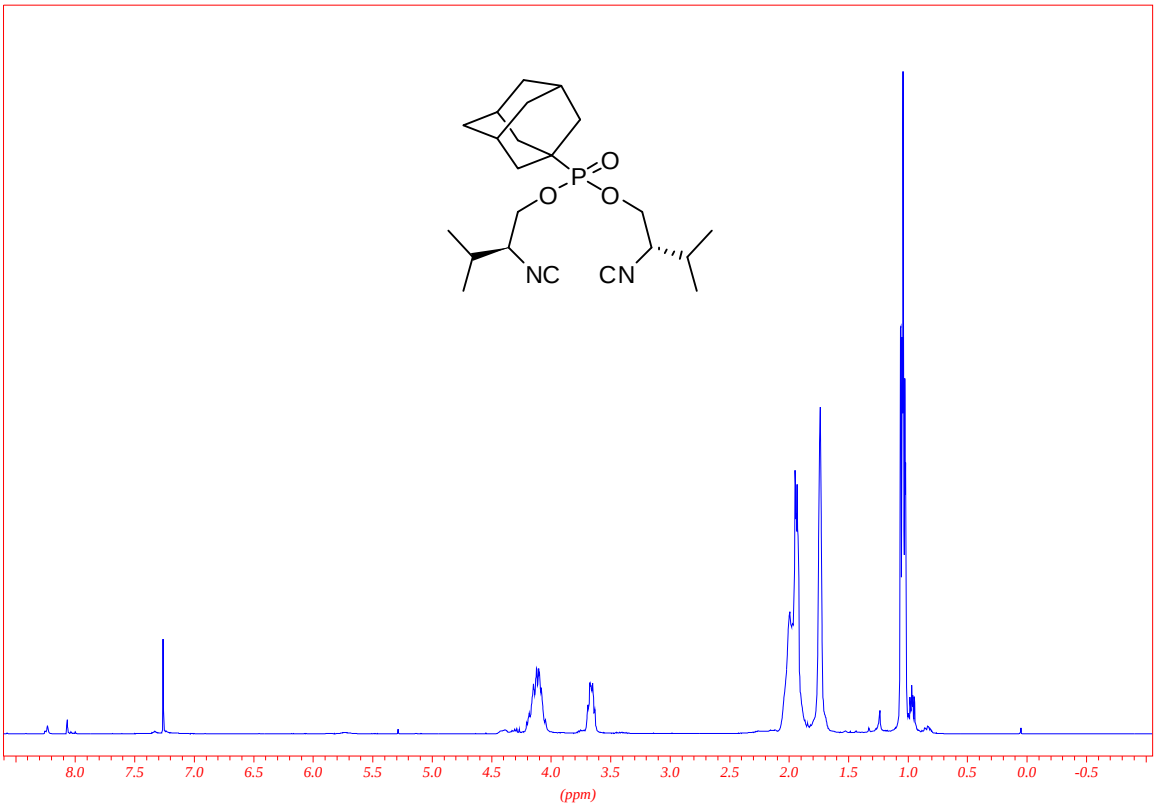


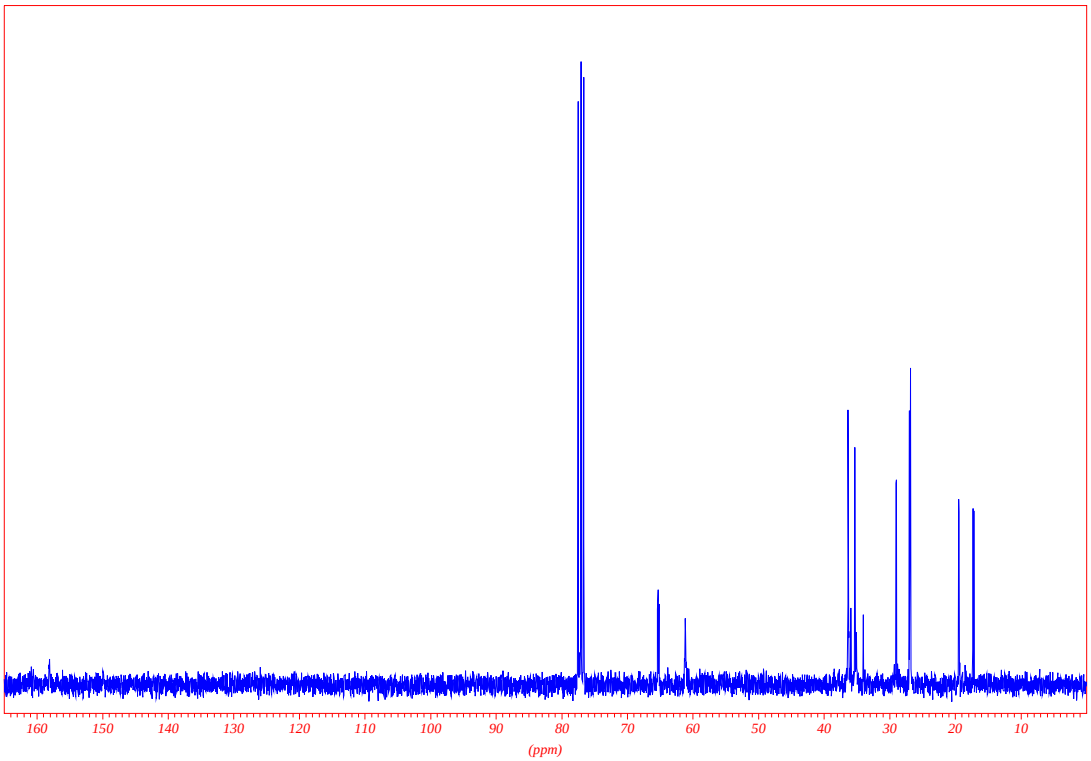


^{31}P NMR

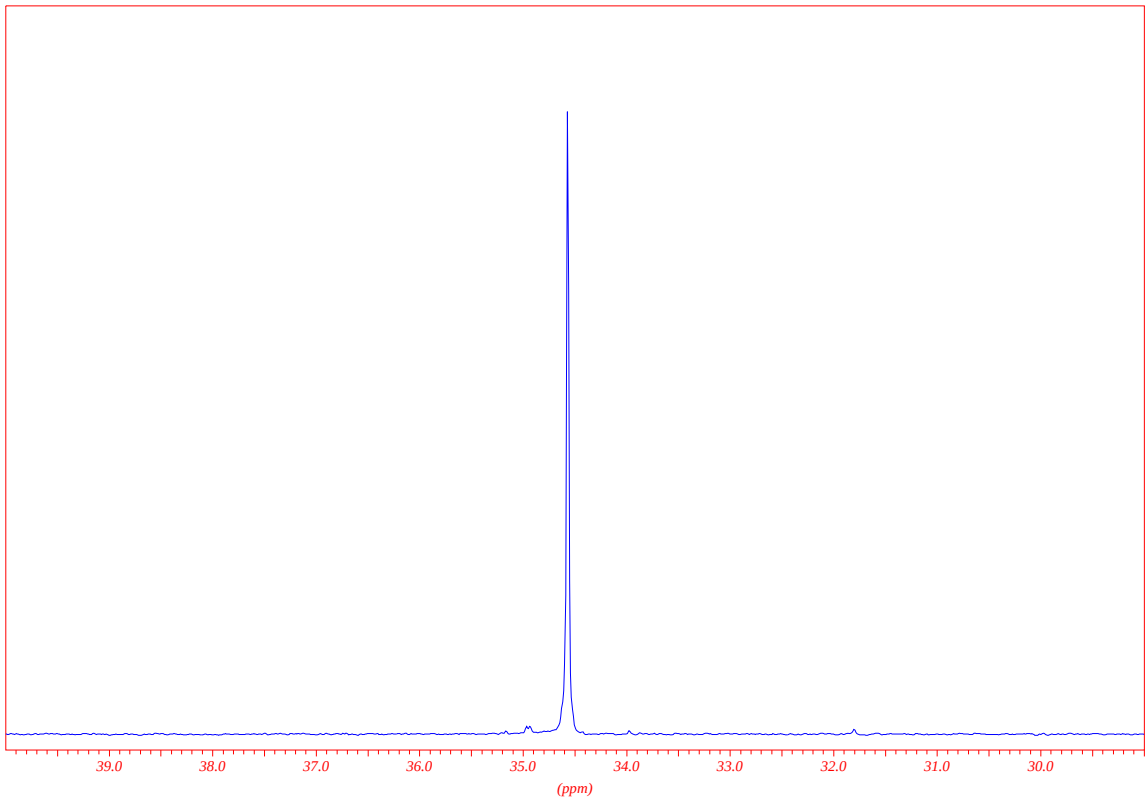


Bis((*S*)-2-isocyano-3-methylbutyl) admantylphosphonate (72g)

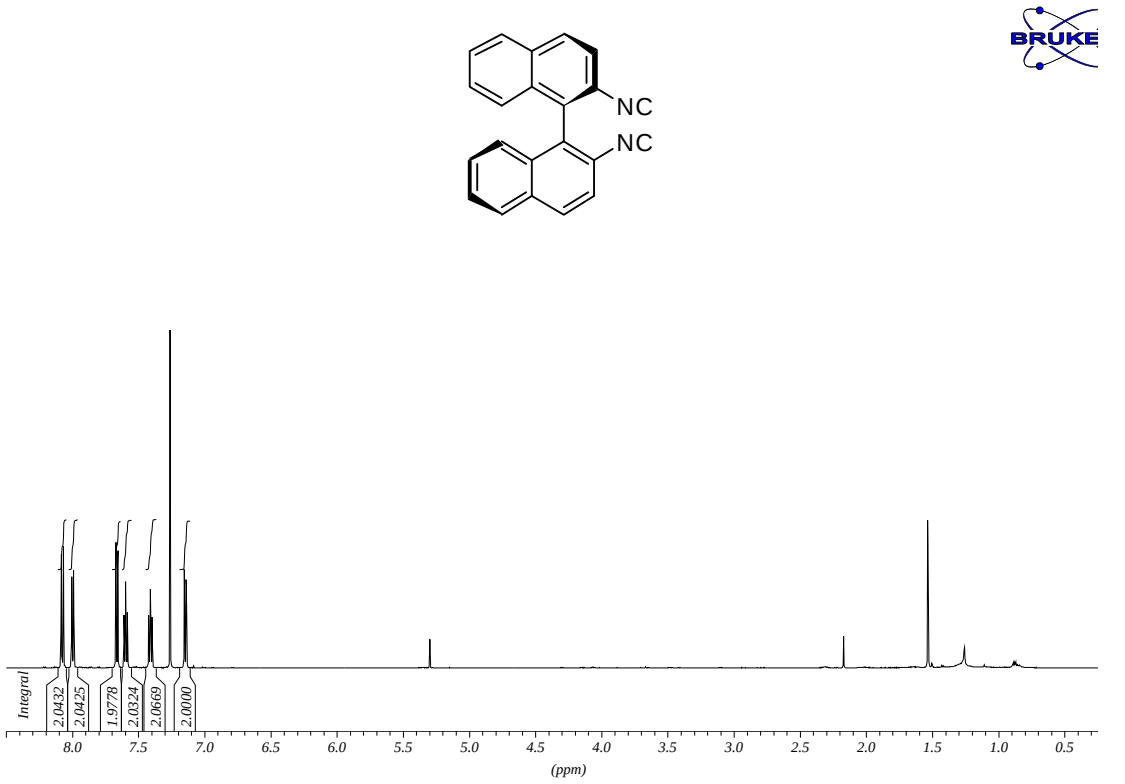


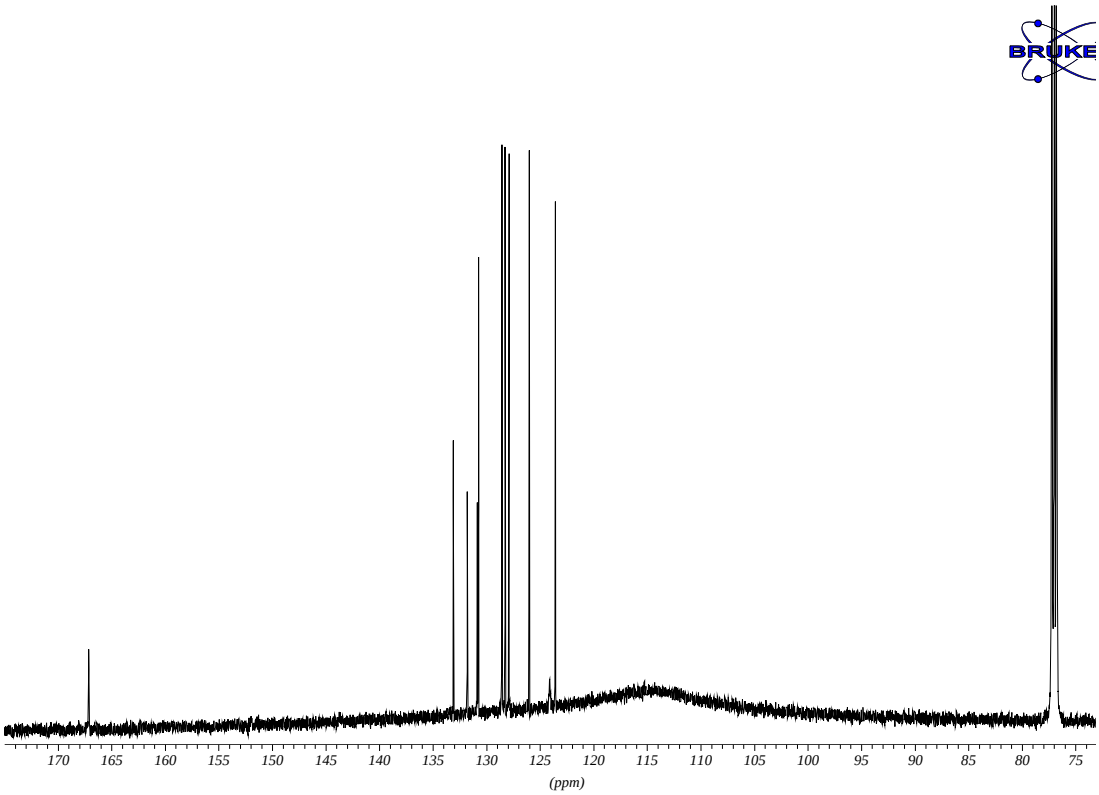


^{31}P NMR

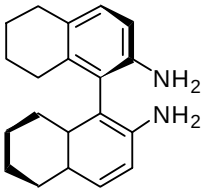


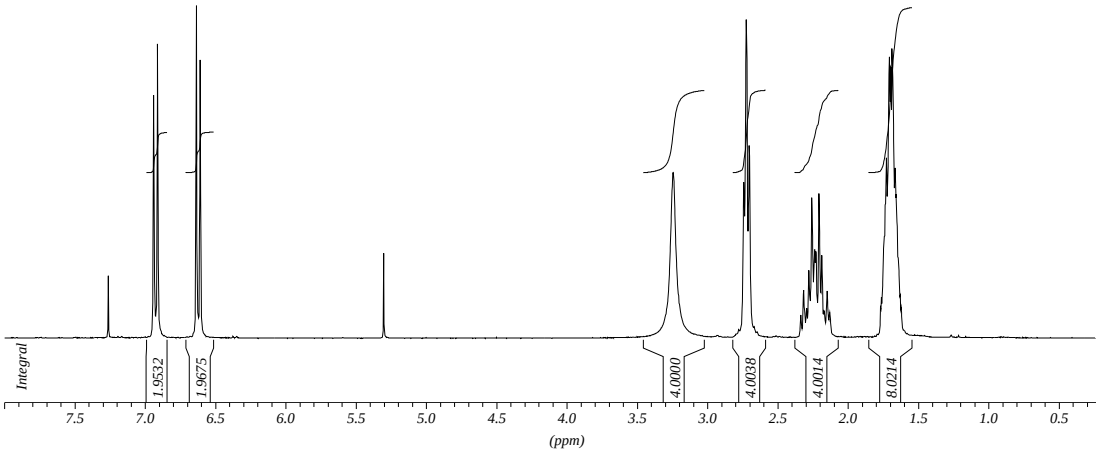
(*R*)-2,2'-diisocyano-1,1'-binaphthyl (87)

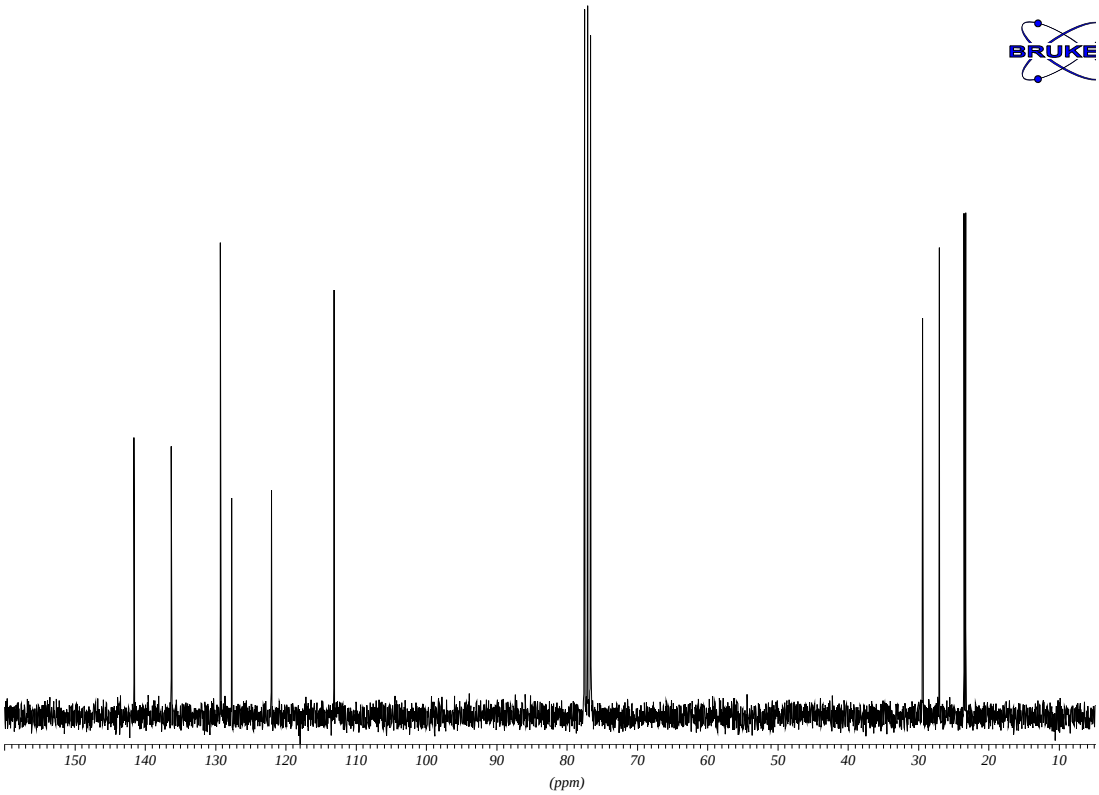




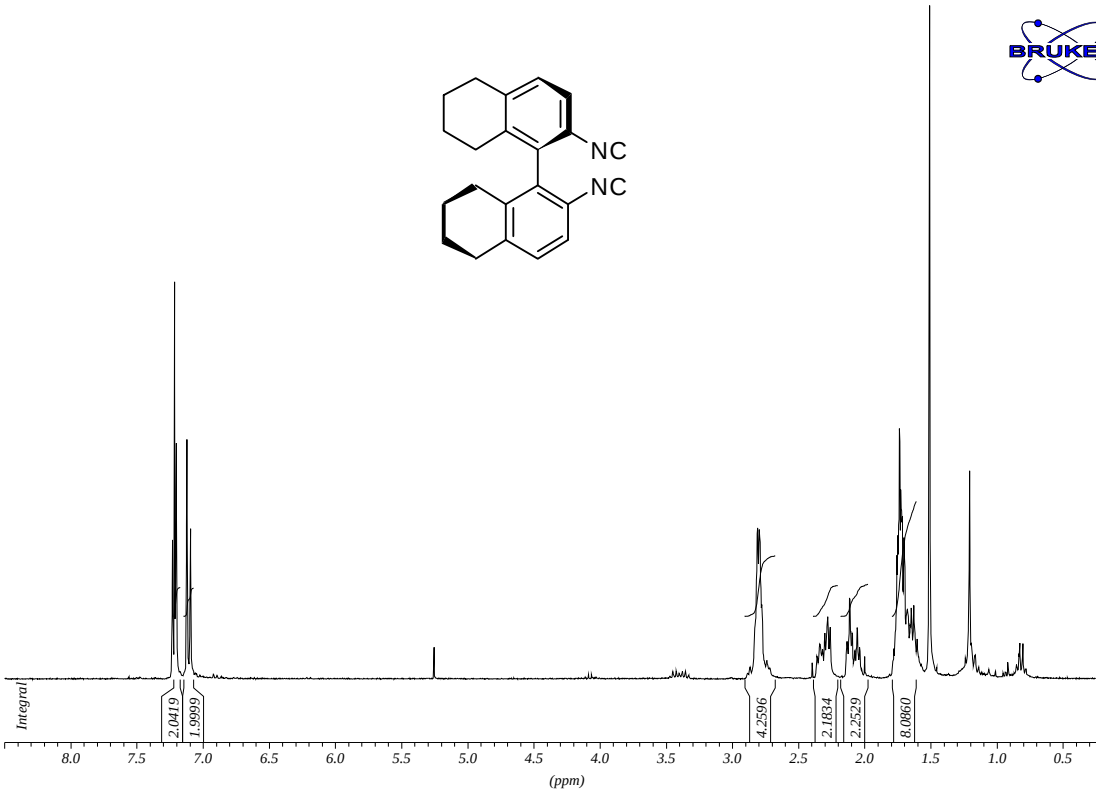
(*R*)-5,5',6,6',7,7',8,8'-Octahydro-1,1'-Binaphthyl-2,2'-diamine (84)

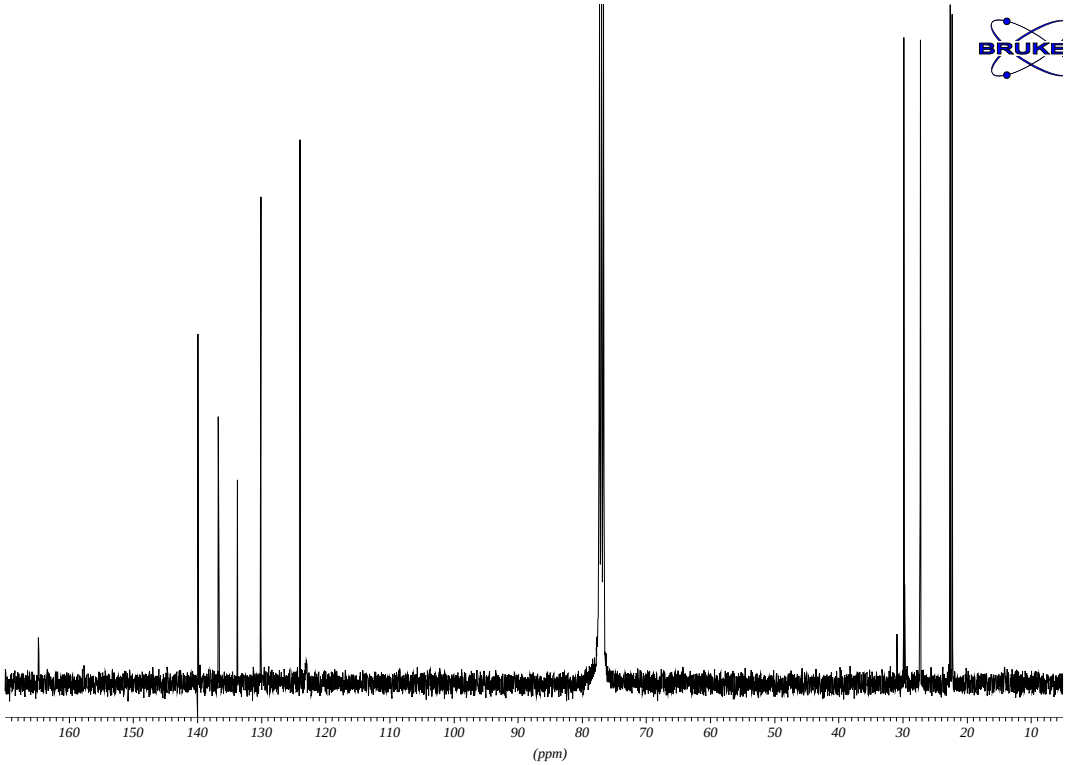




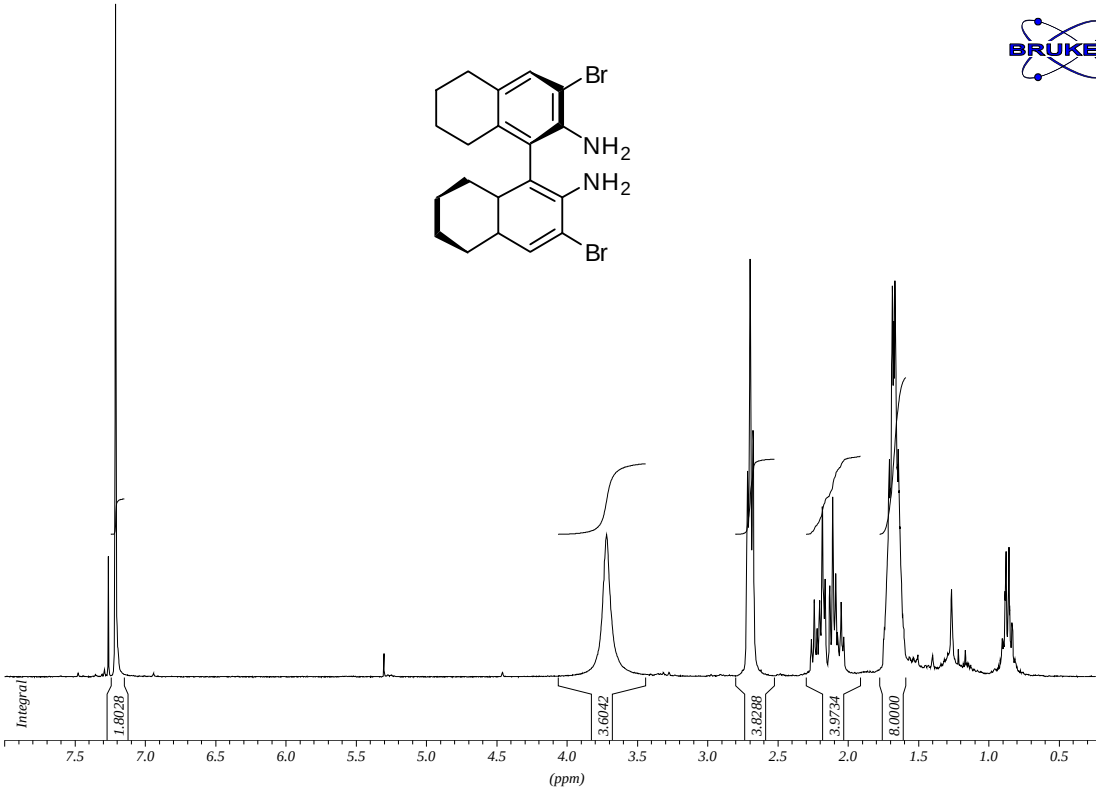


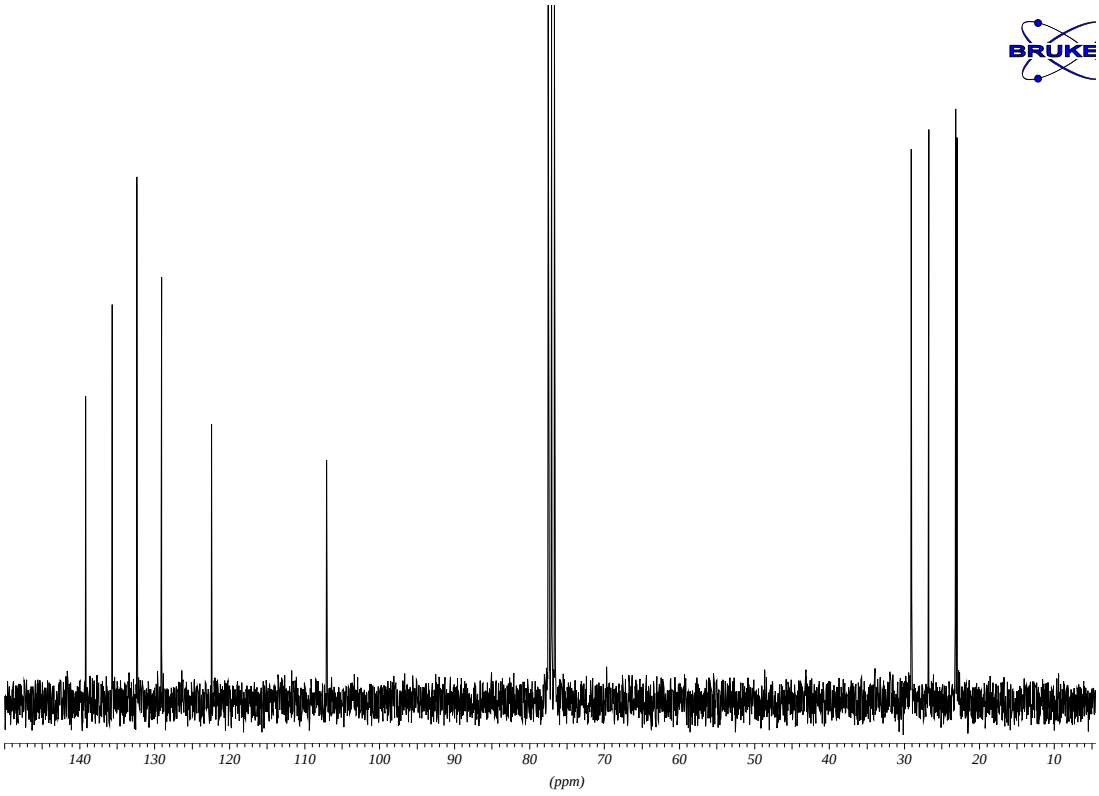
(*R*)-2,2'-diisocyano-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl (89)



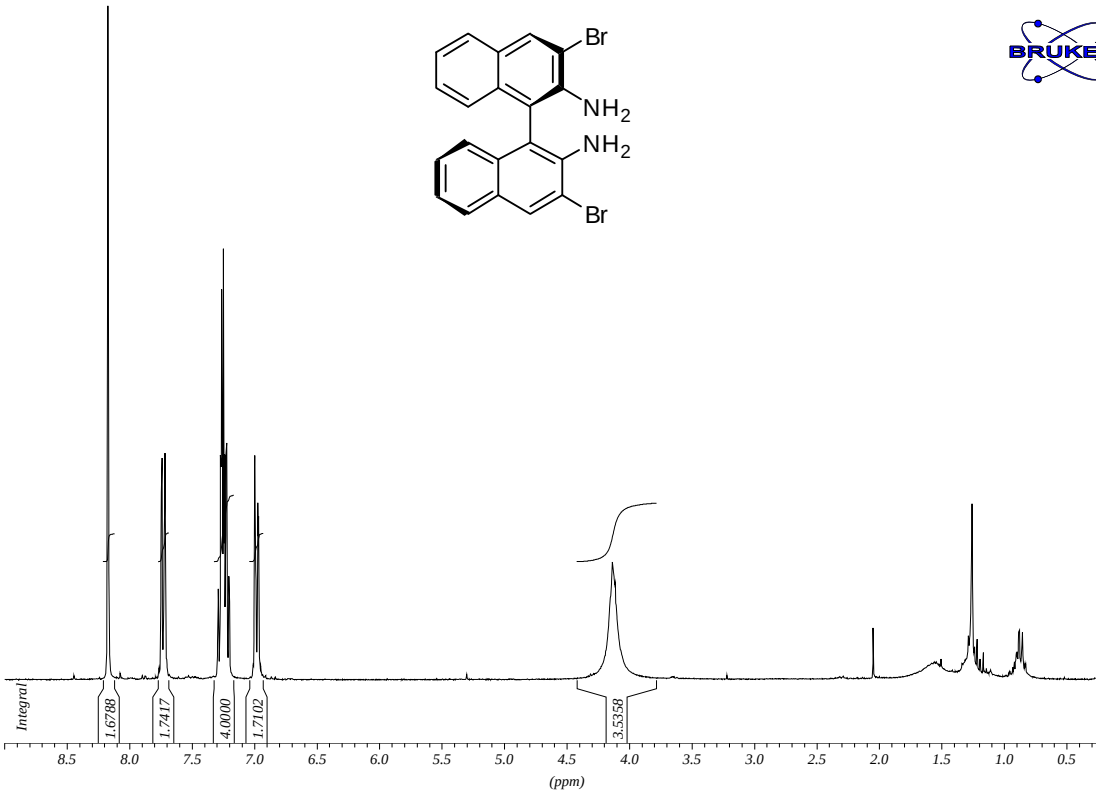


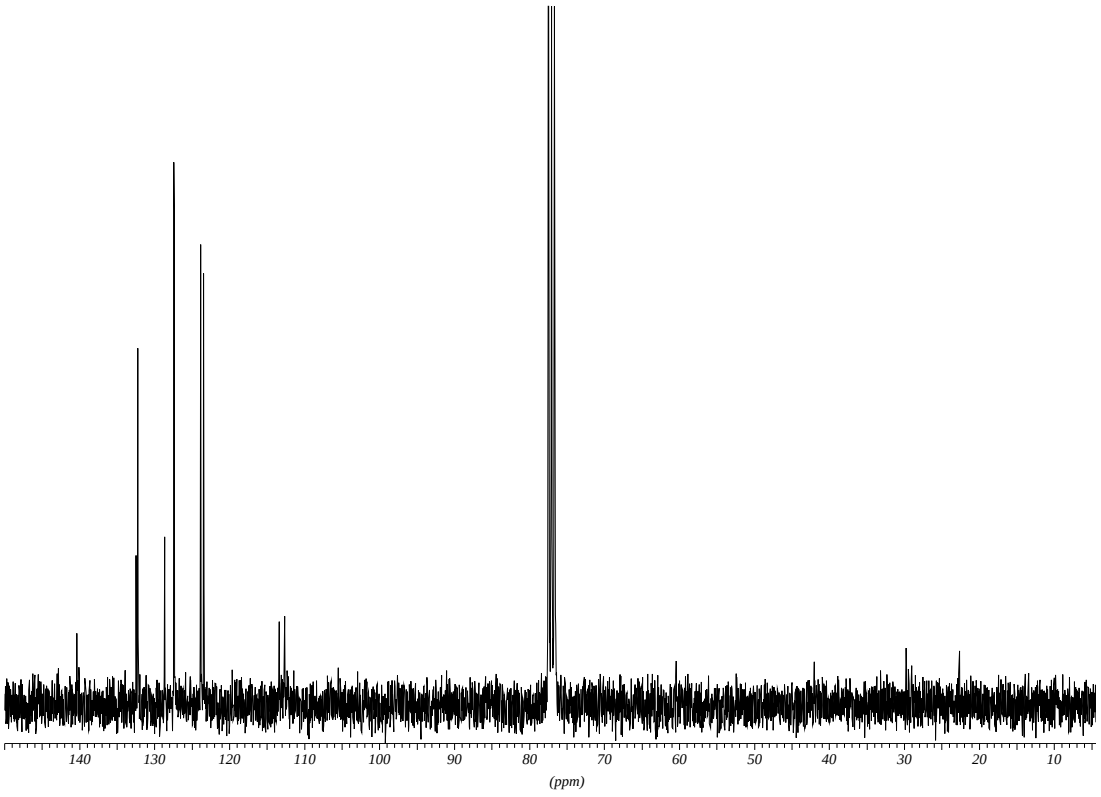
(*R*)-3,3'-Dibromo-5,5',6,6',7,7',8,8'-octahydro-1,1'-binaphthyl-2,2'-diamine (90)



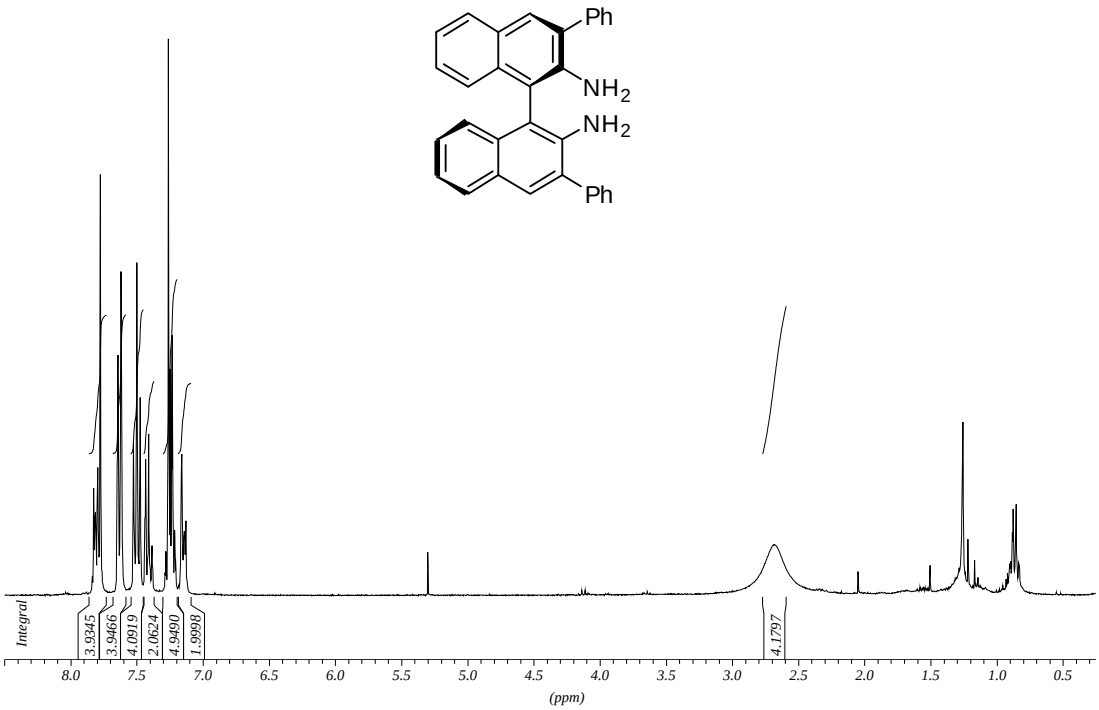


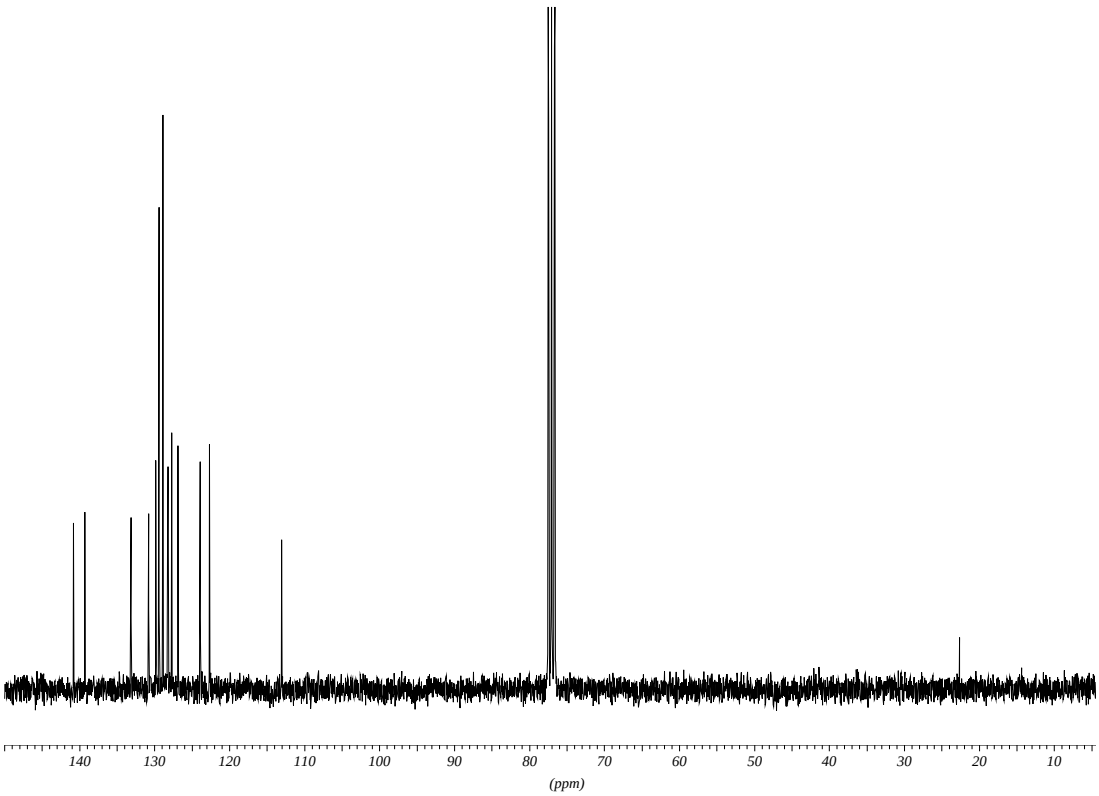
(*R*)-3,3'-Dibromo-1,1'-binaphthyl-2,2'-diamine (91)



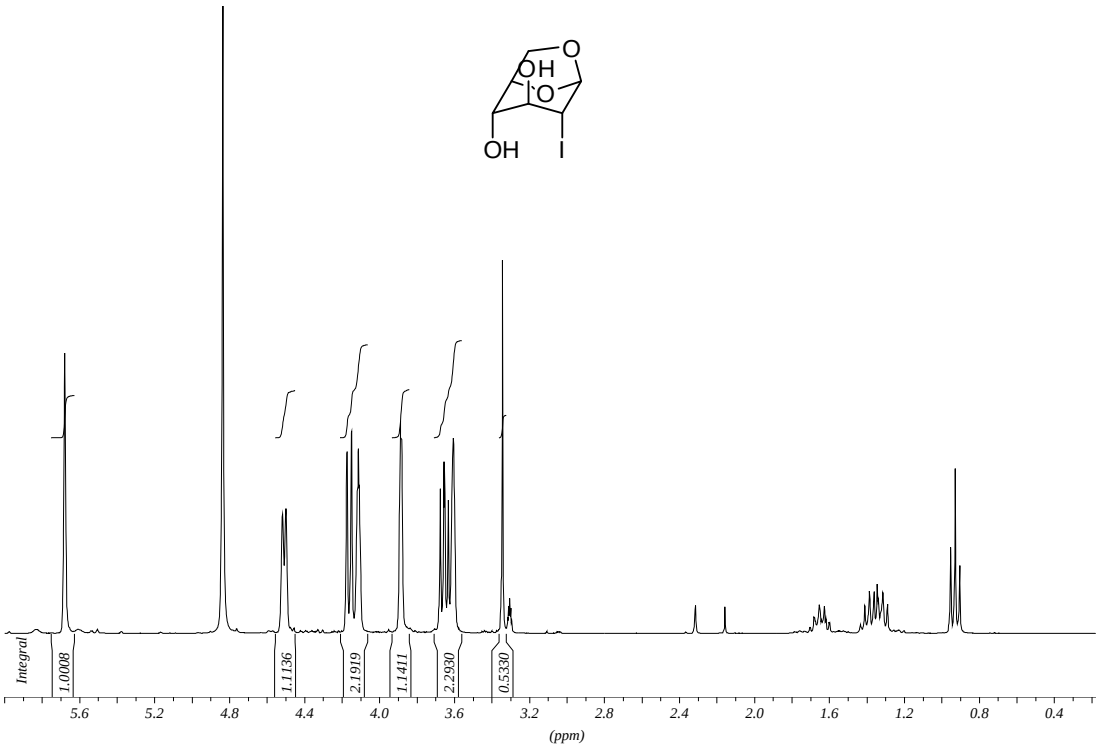


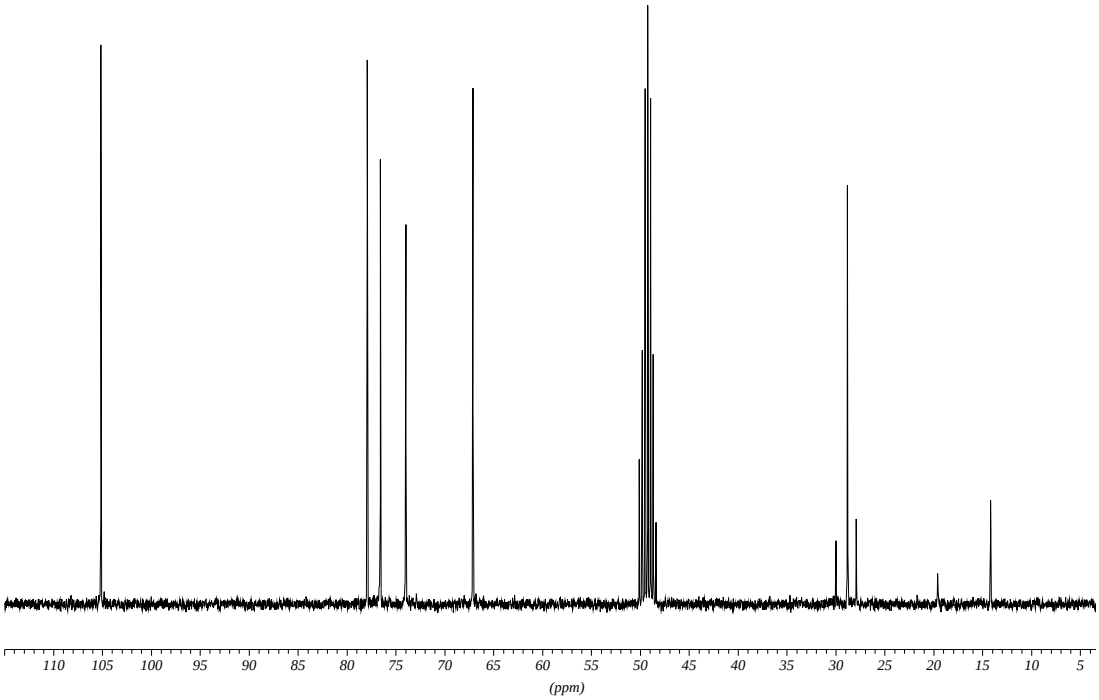
(*R*)-3,3'-Diphenyl-1,1'-binaphthyl-2,2'-diamine (92)



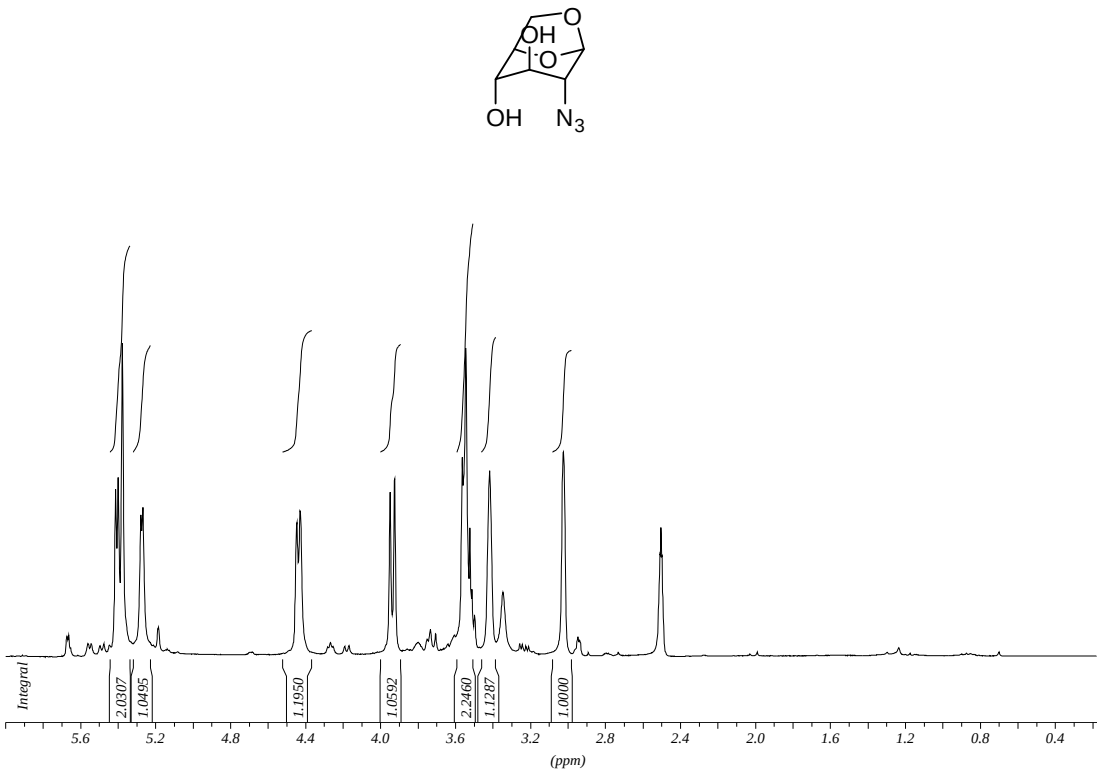


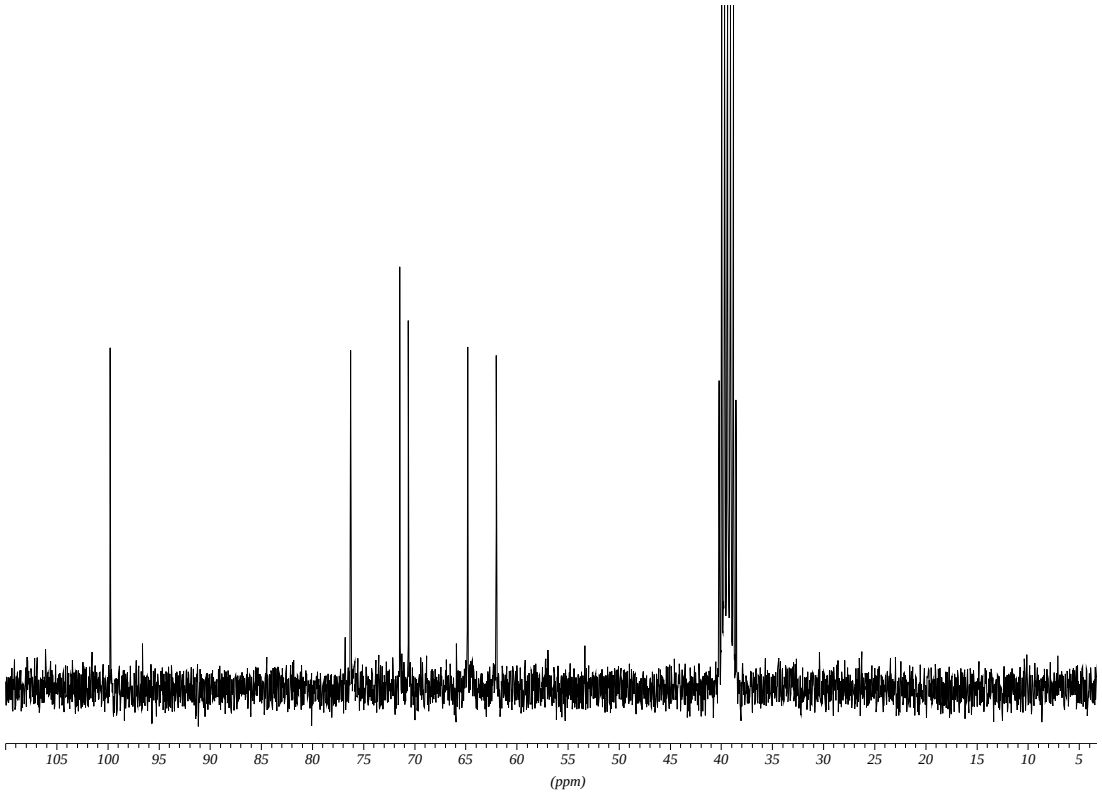
1,6-anhydro-2-deoxy-2-iodo-ß-D-glucopyranose (100)



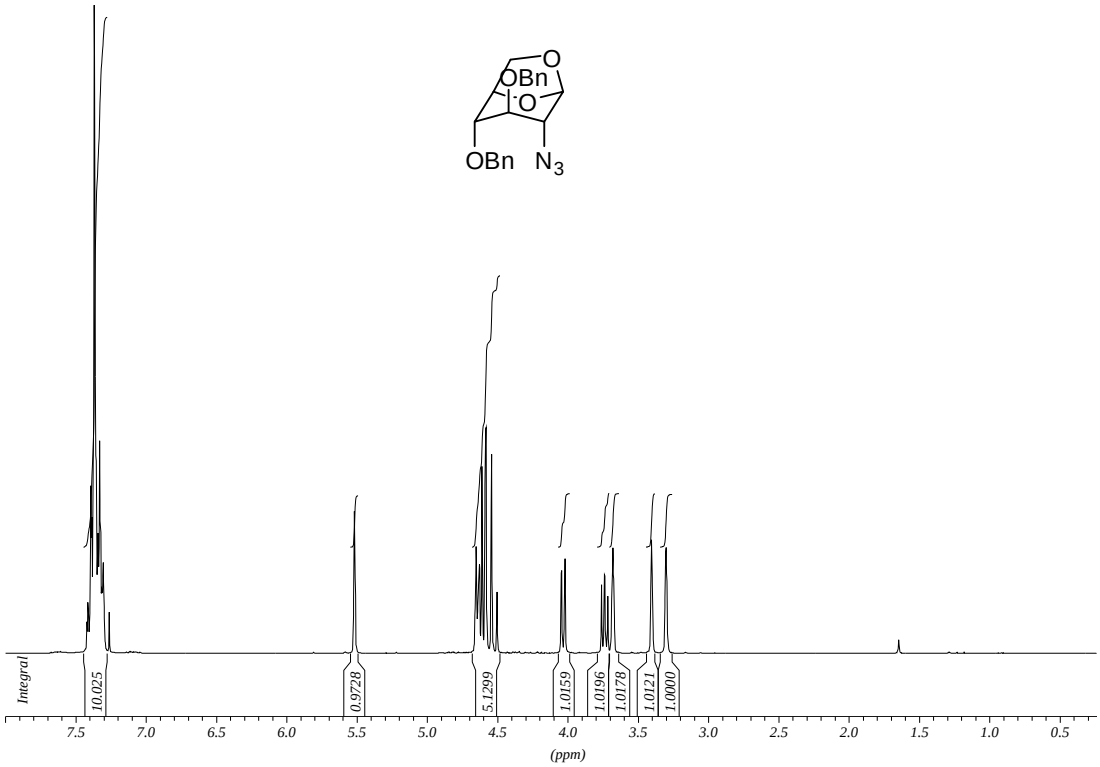


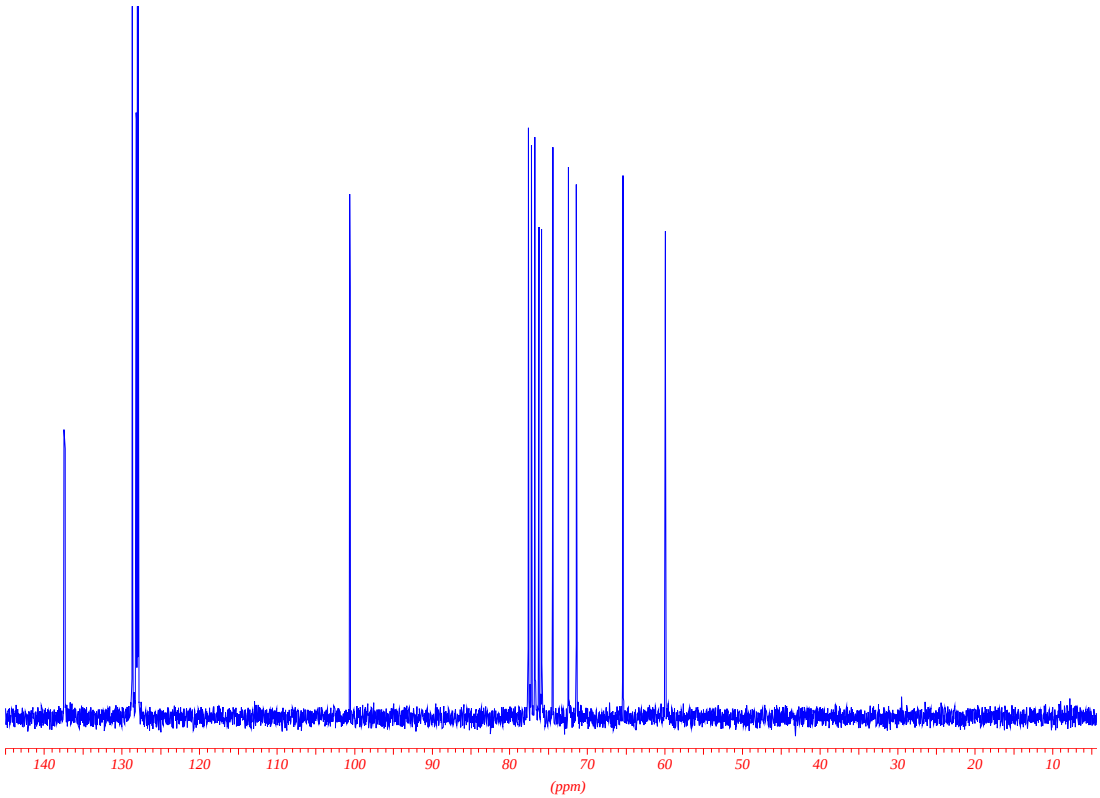
1,6-anhydro-2-deoxy-2-azido-ß-D-glucopyranose (101)



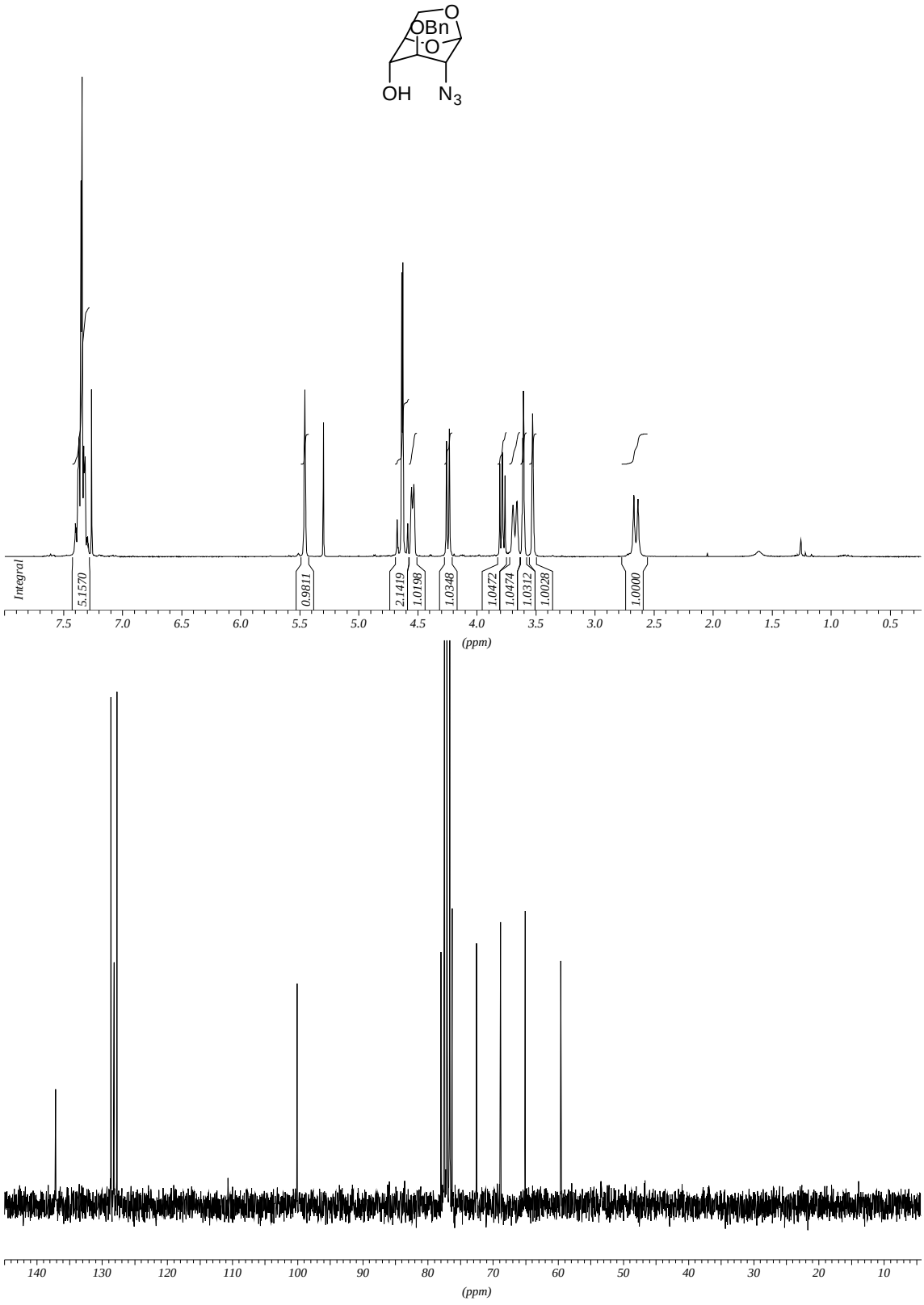


1, 6-anhydro-2-azido-3,4-di-O-benzyl-2-deoxy-ß-D-glucopyranose (102)

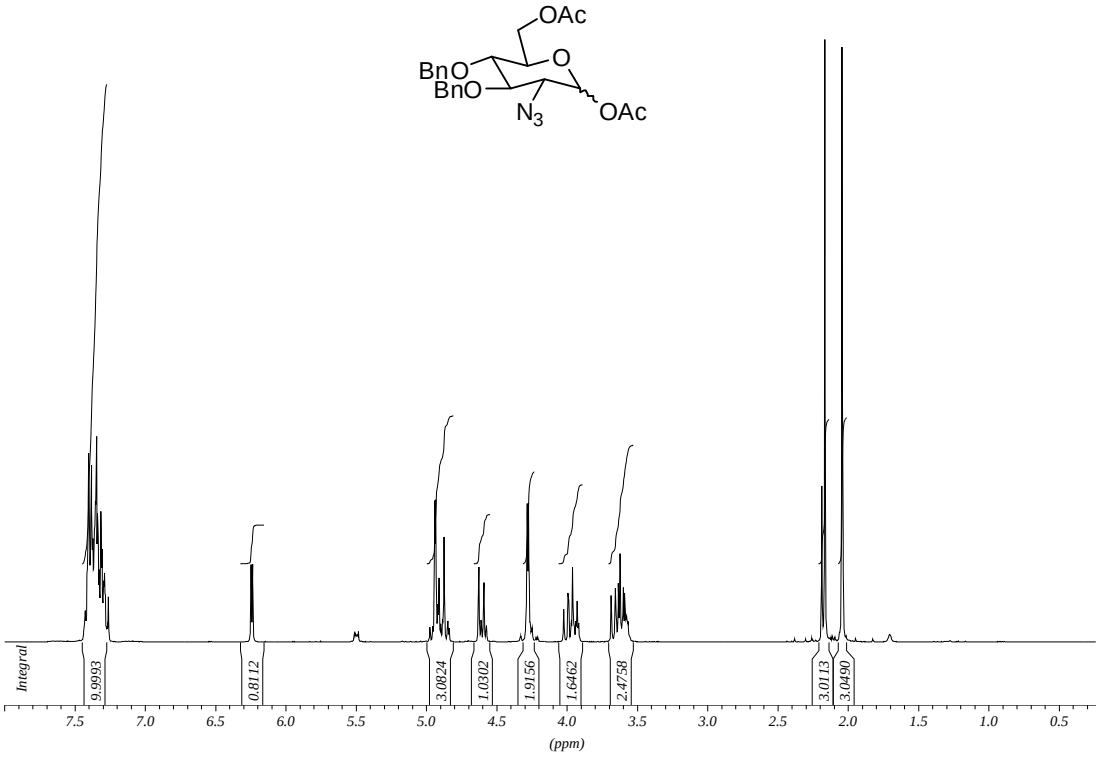


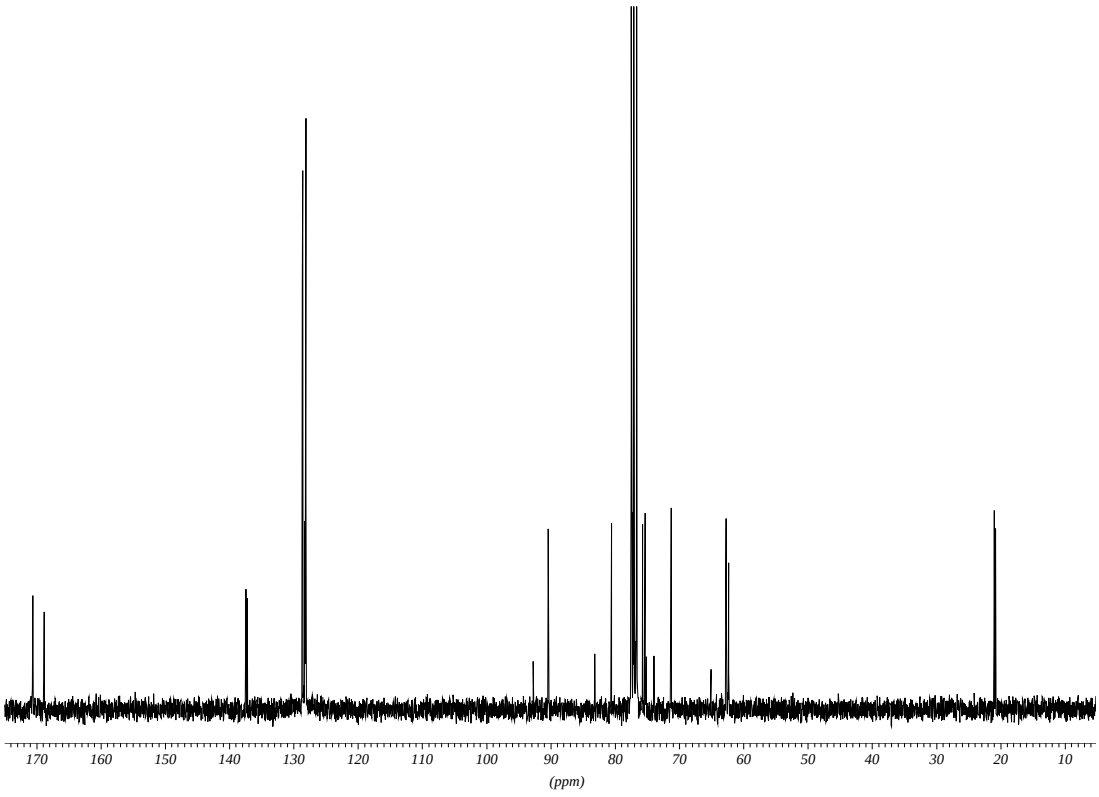


1, 6-anhydro-2-azido-3-O-benzyl-2-deoxy-ß-D-glucopyranose (103)

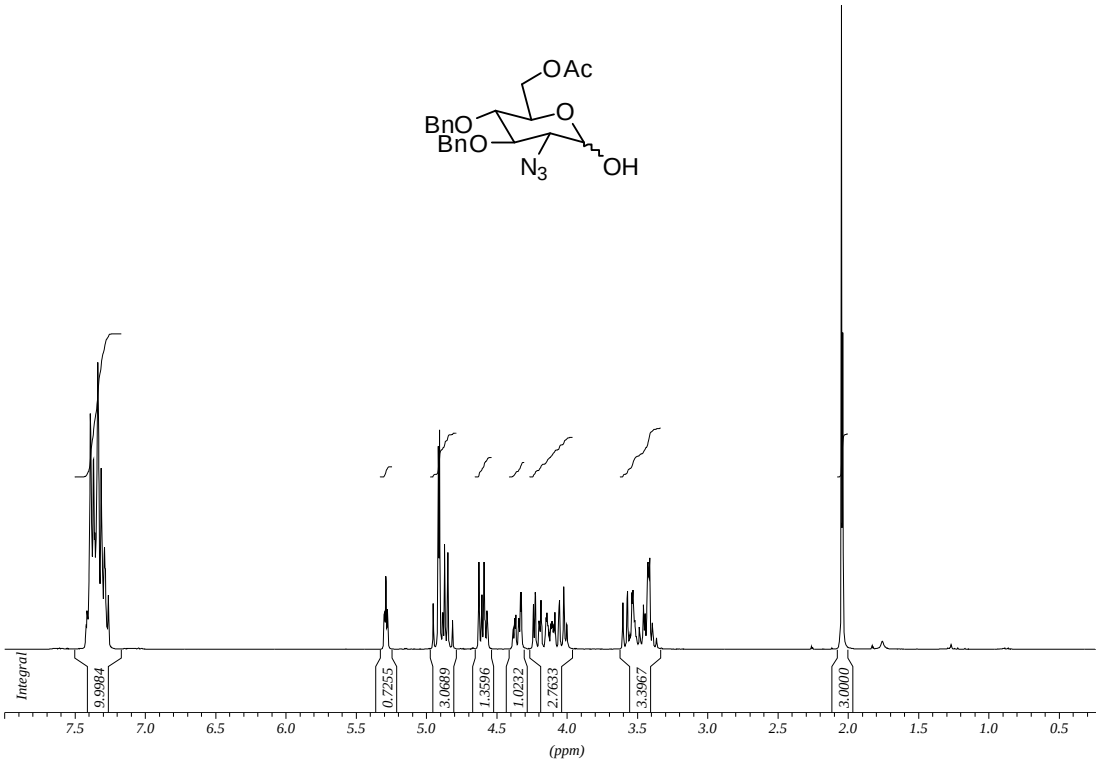


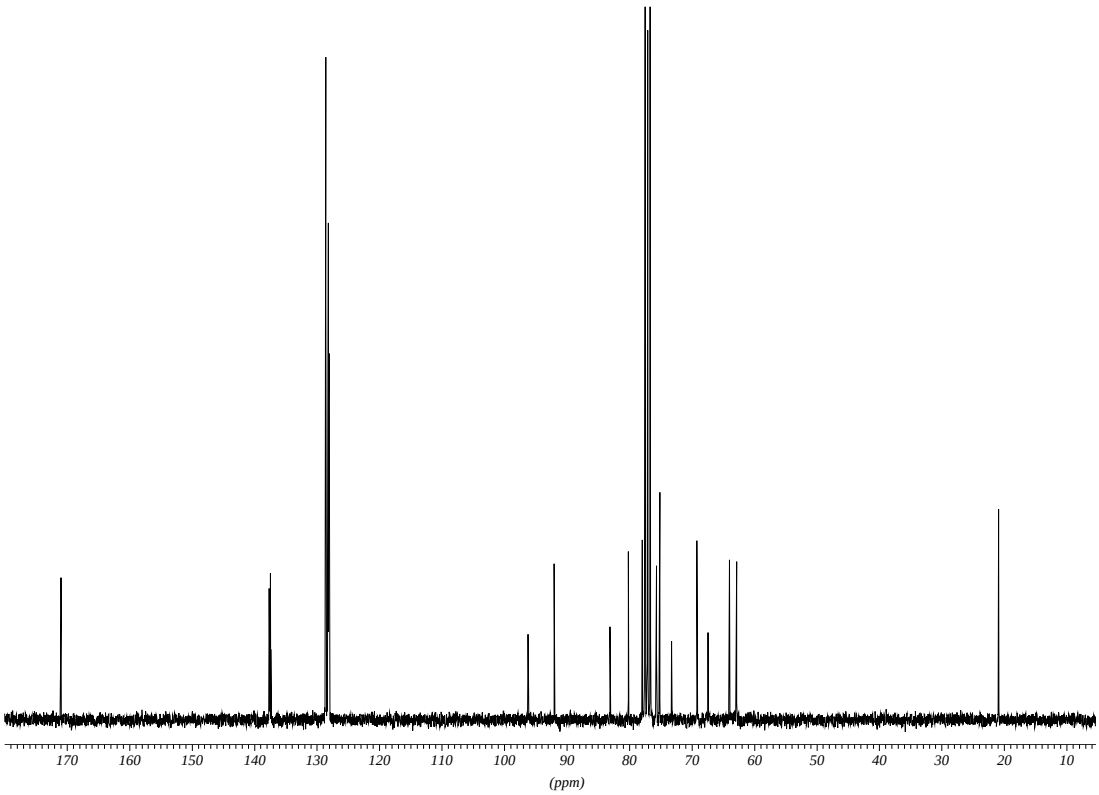
1, 6-diacetae-2-azido-3,4-di-O-benzyl-2-deoxy-ß-D-glucopyranose (104)



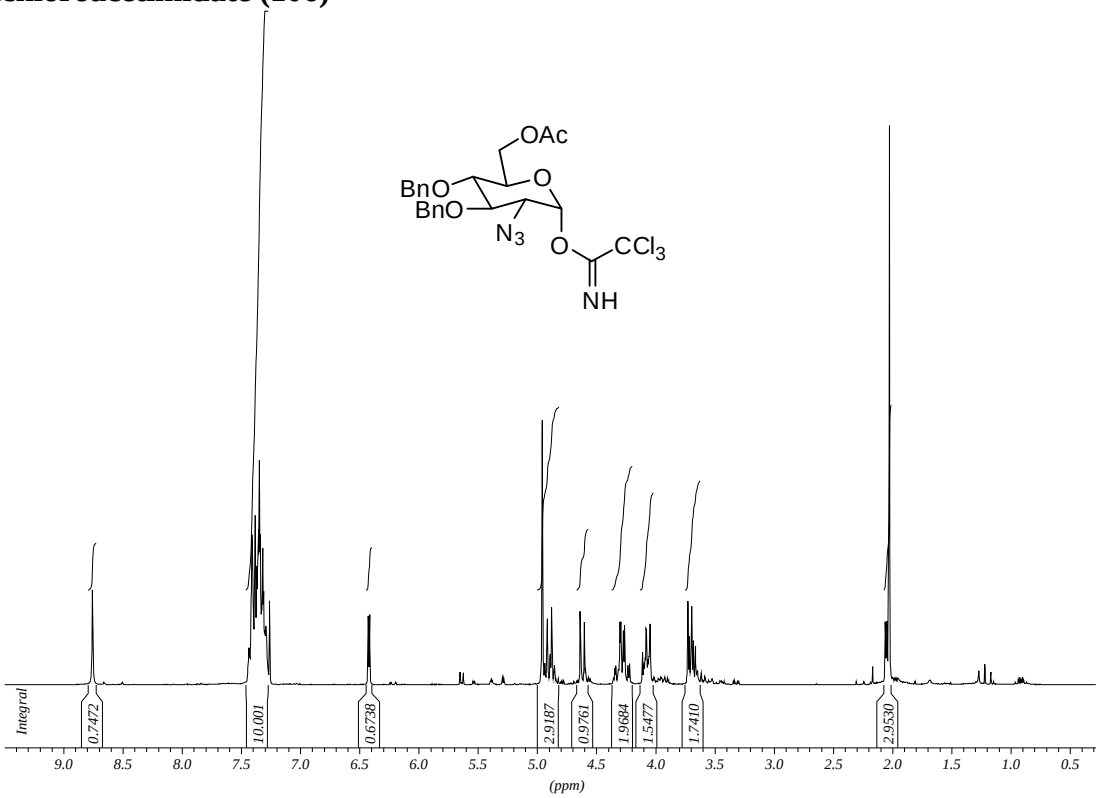


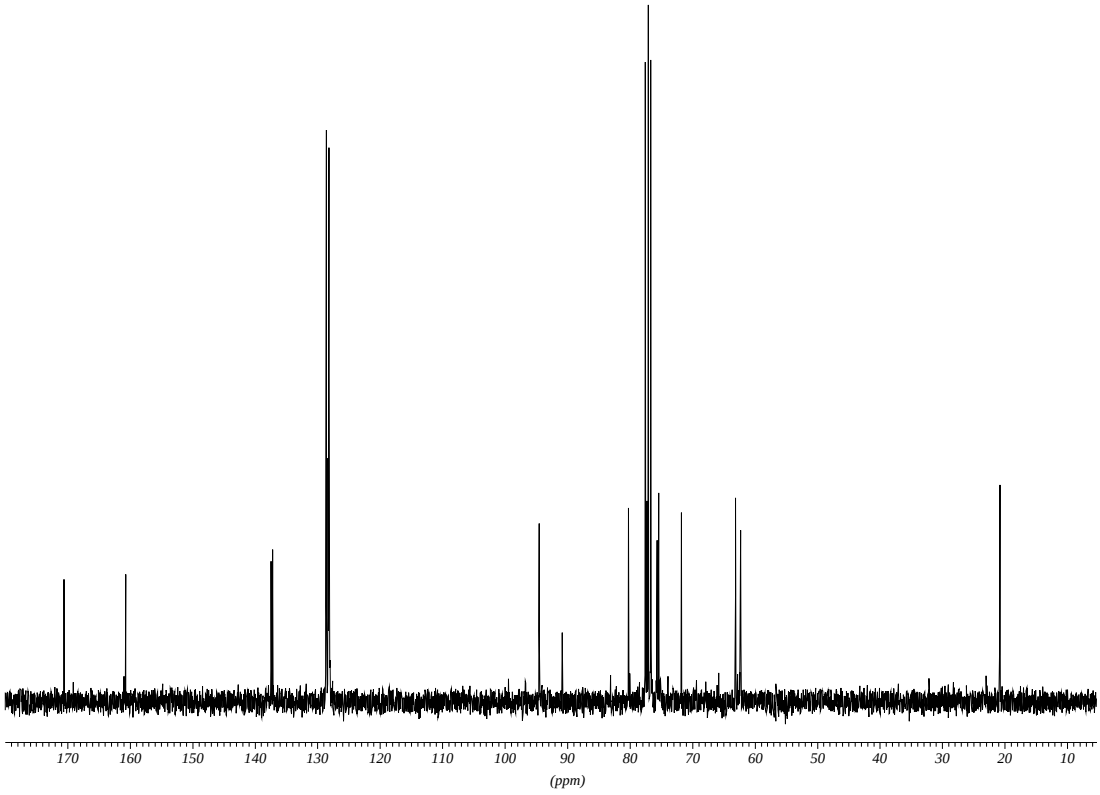
6-acetae-2-azido-3,4-di-O-benzyl-2-deoxy-ß-D-glucopyranose (105)



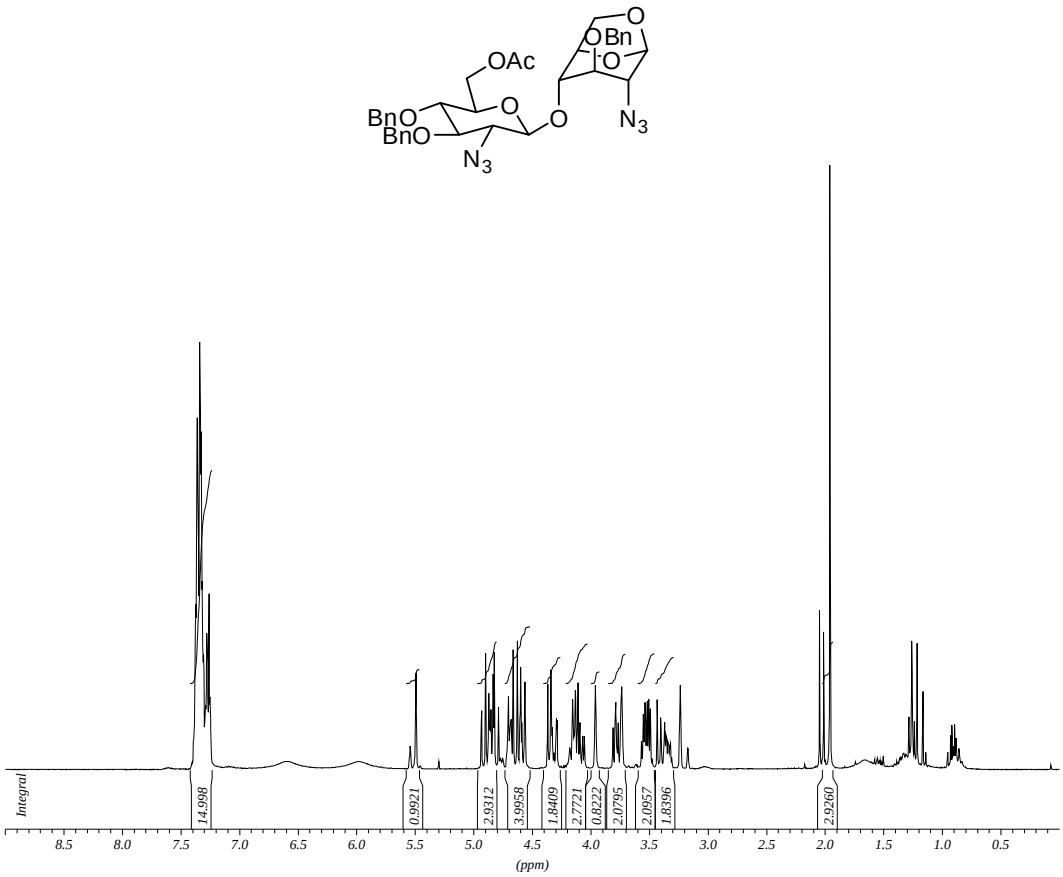


6-acetae-2-azido-3,4-di-O-benzyl-2-deoxy-ß-D-glucopyranose trichloroacetimidate (106)

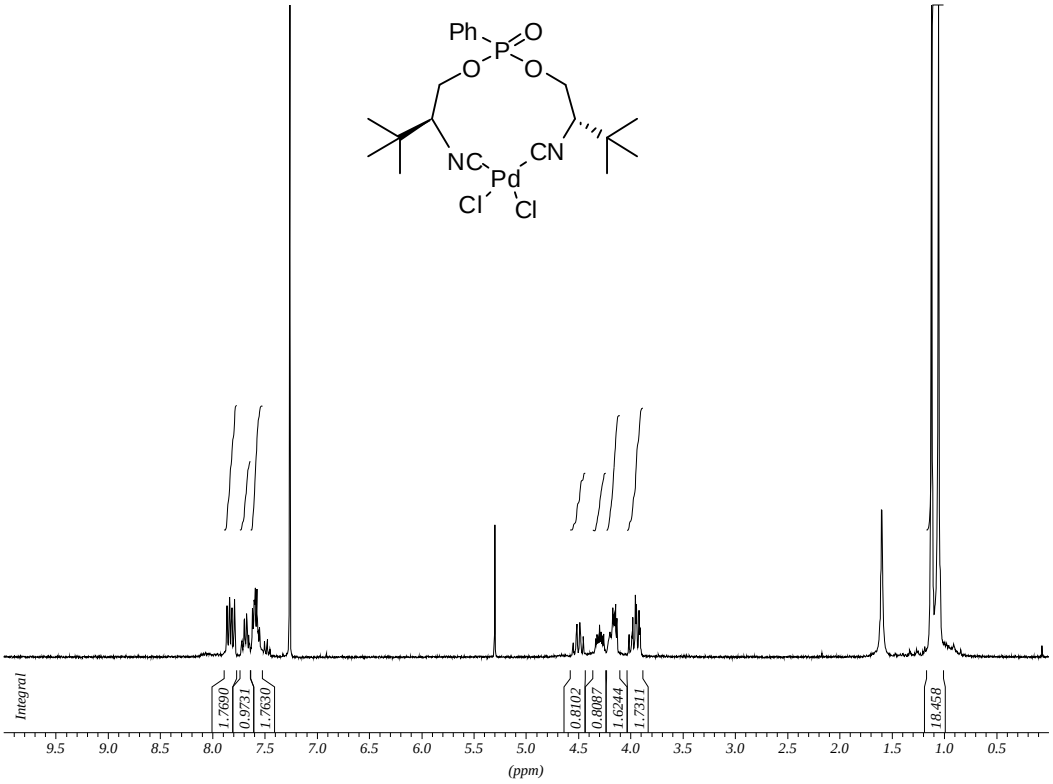


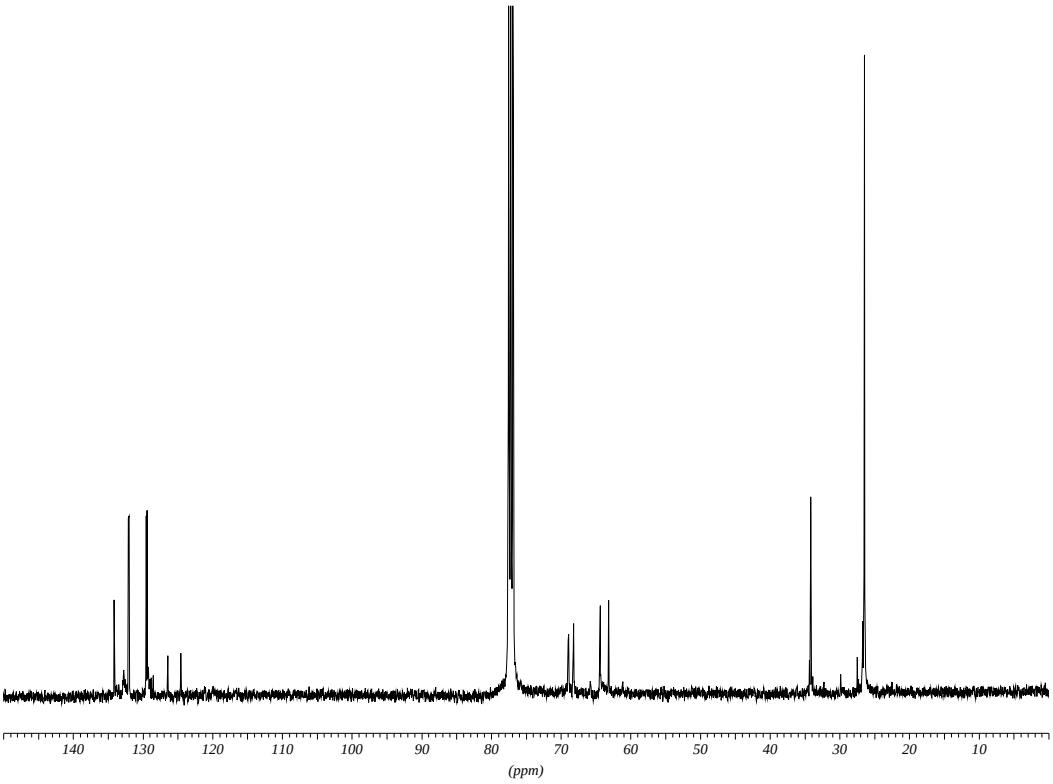


1,6-anhydro-2-azido-3-O-benzyl-4-O-(6-acetate-3,4-di-O-benzyl-2-deoxy-2-azido-ß-D-glucopyranosyl)-2-deoxy-ß-D-glucopyranose (95)

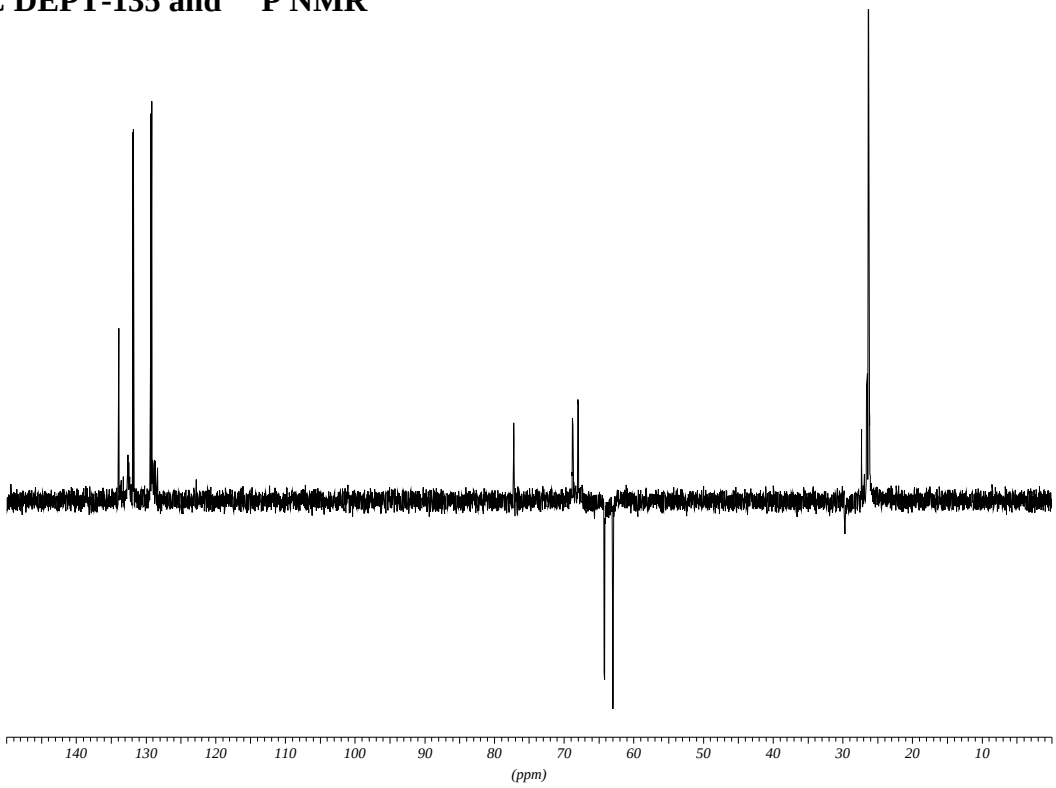


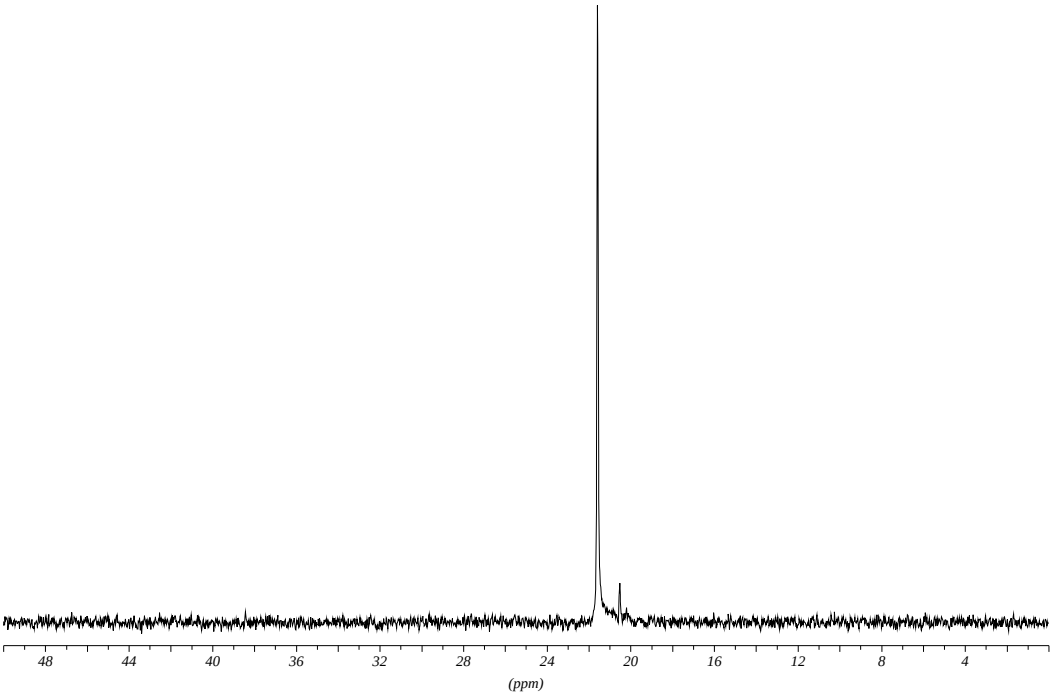
[$PdCl_2$(^{t}BuBINC)] (105b)



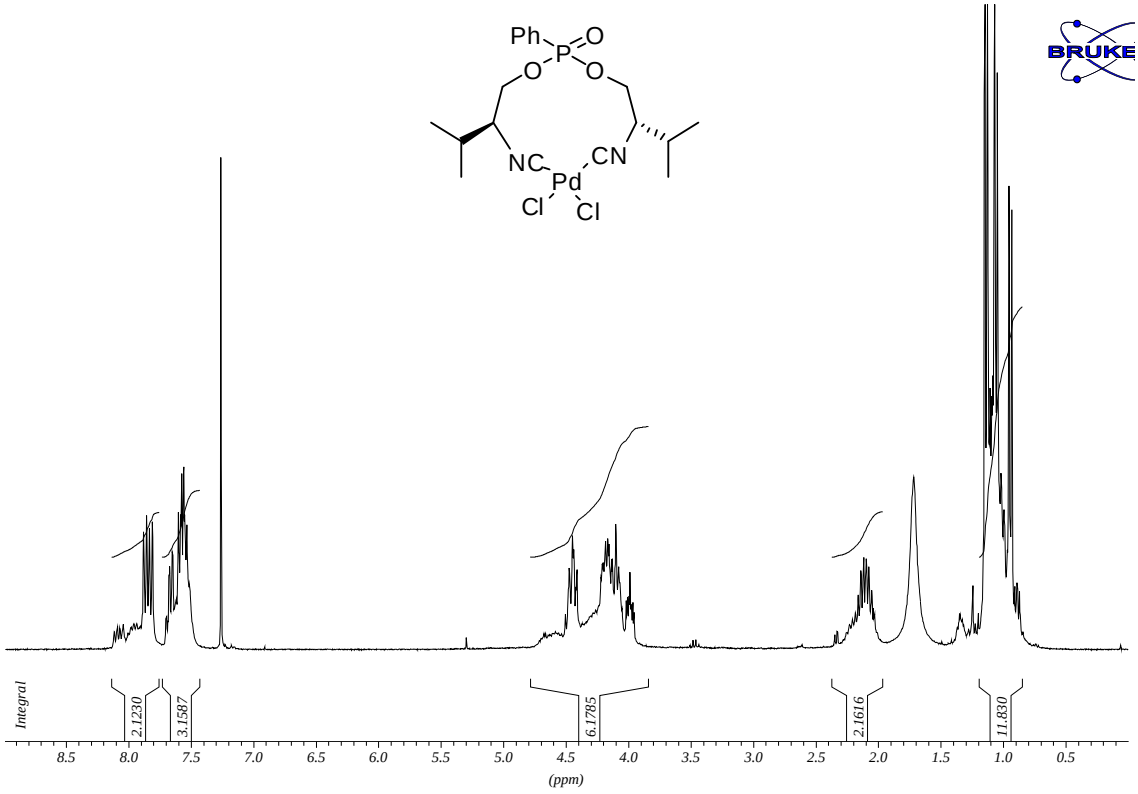


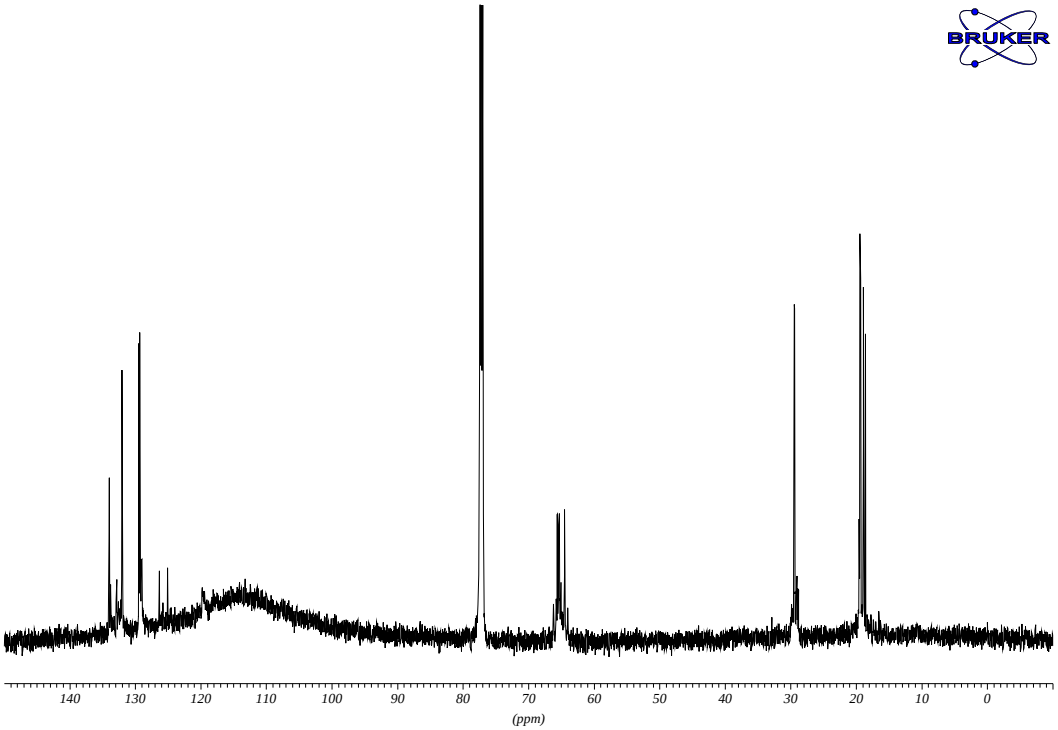
^{13}C DEPT-135 and ^{31}P NMR



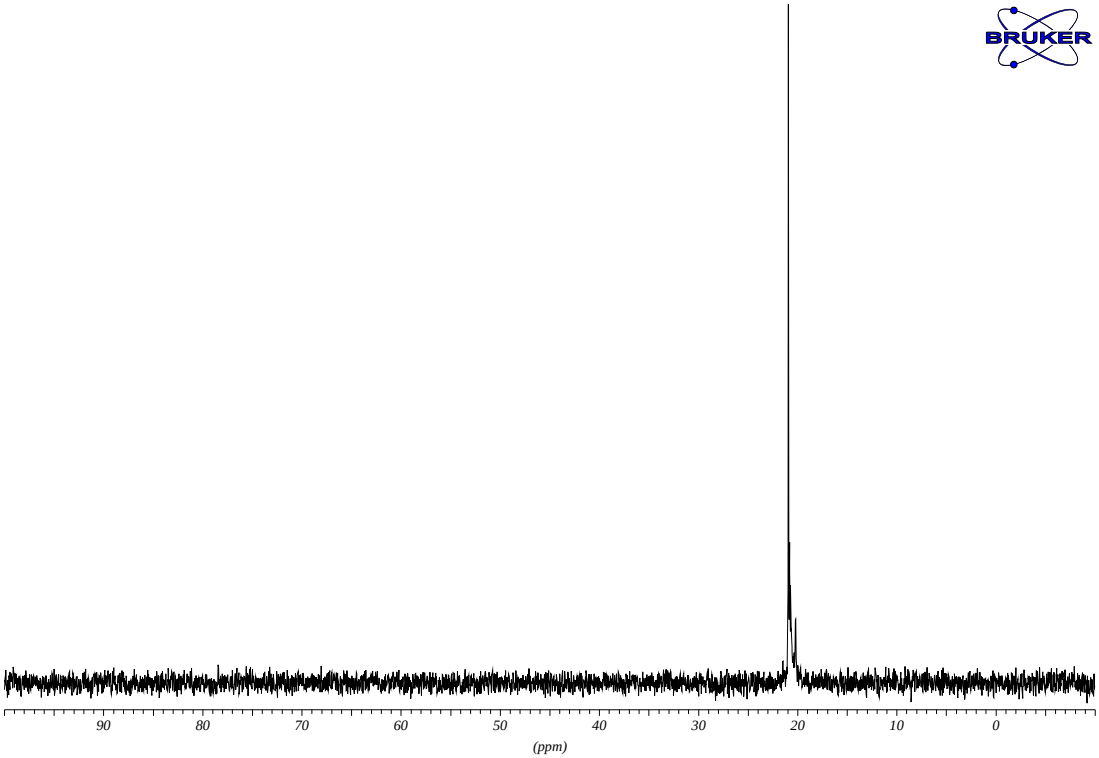


[$PdCl_2$(^{i}PrBINC)] (105c)

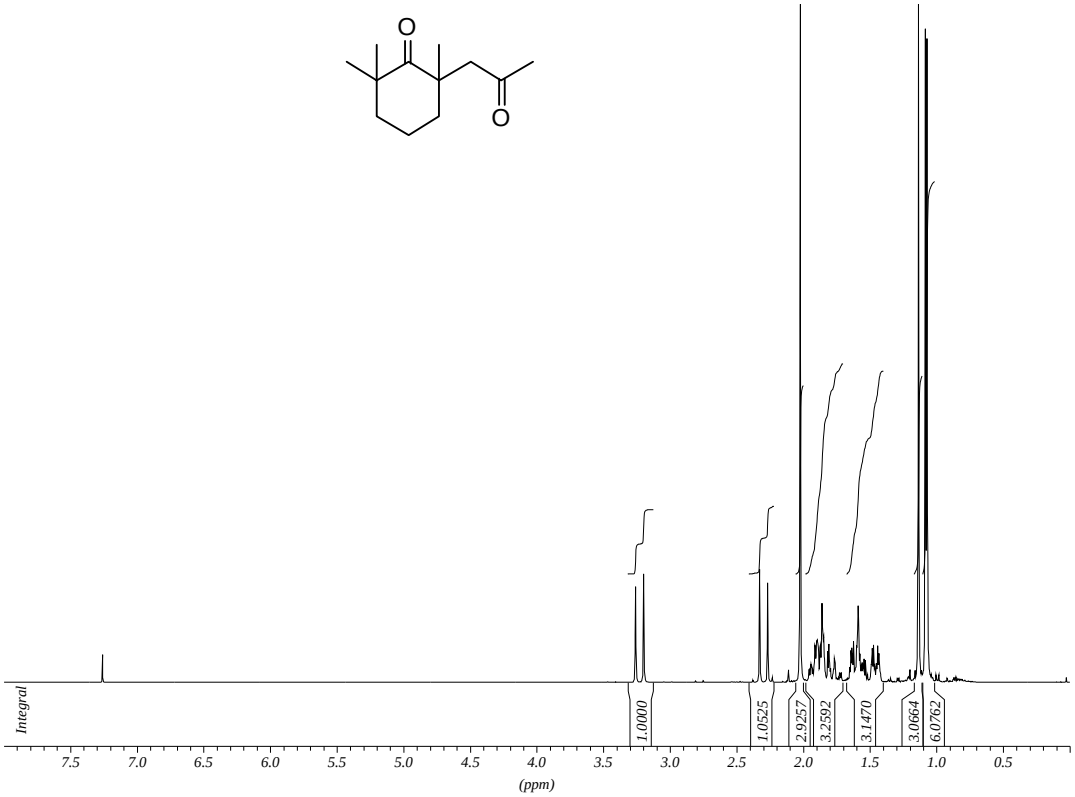


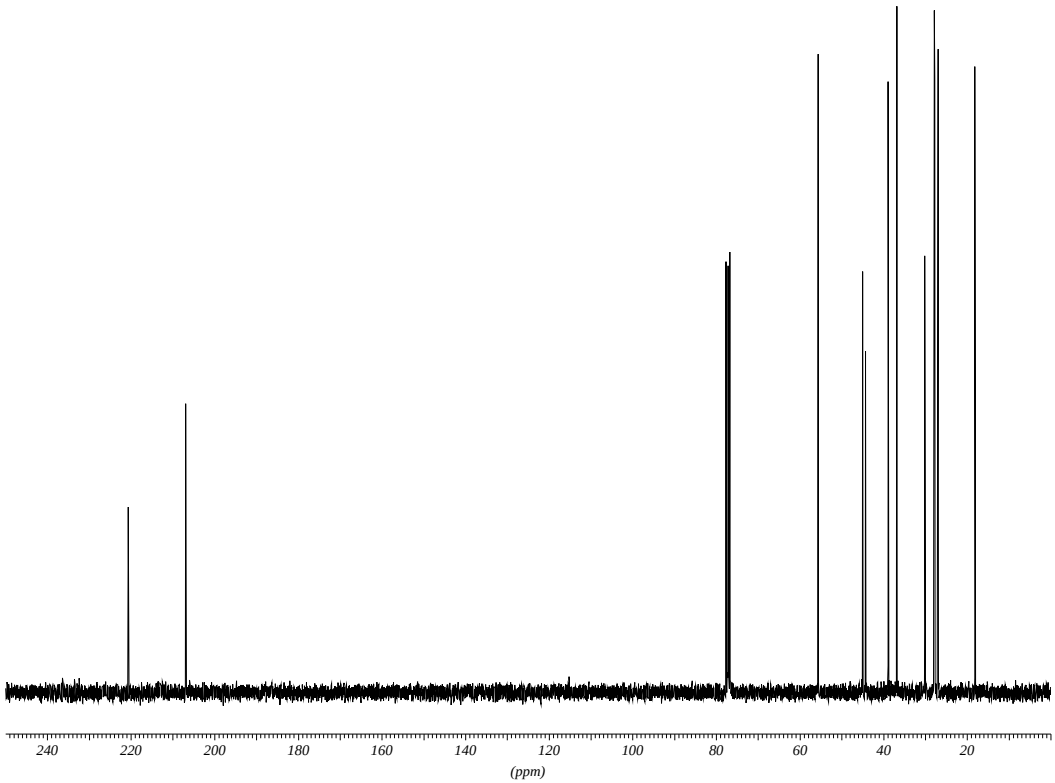


^{31}P NMR

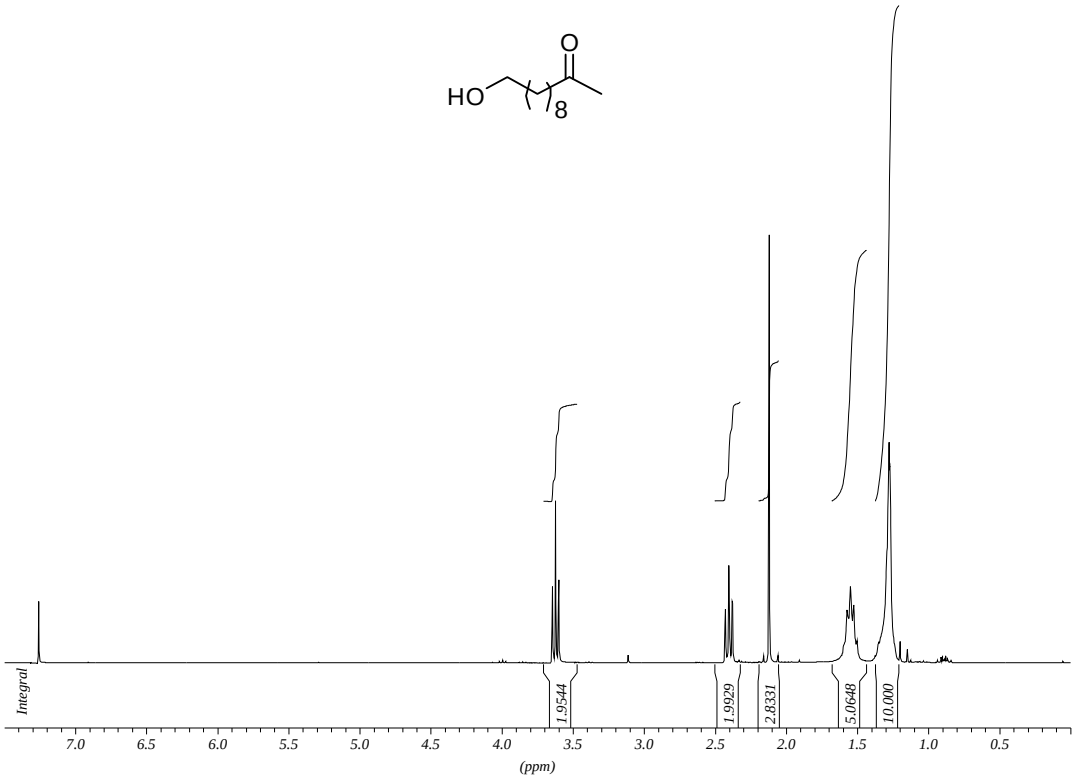


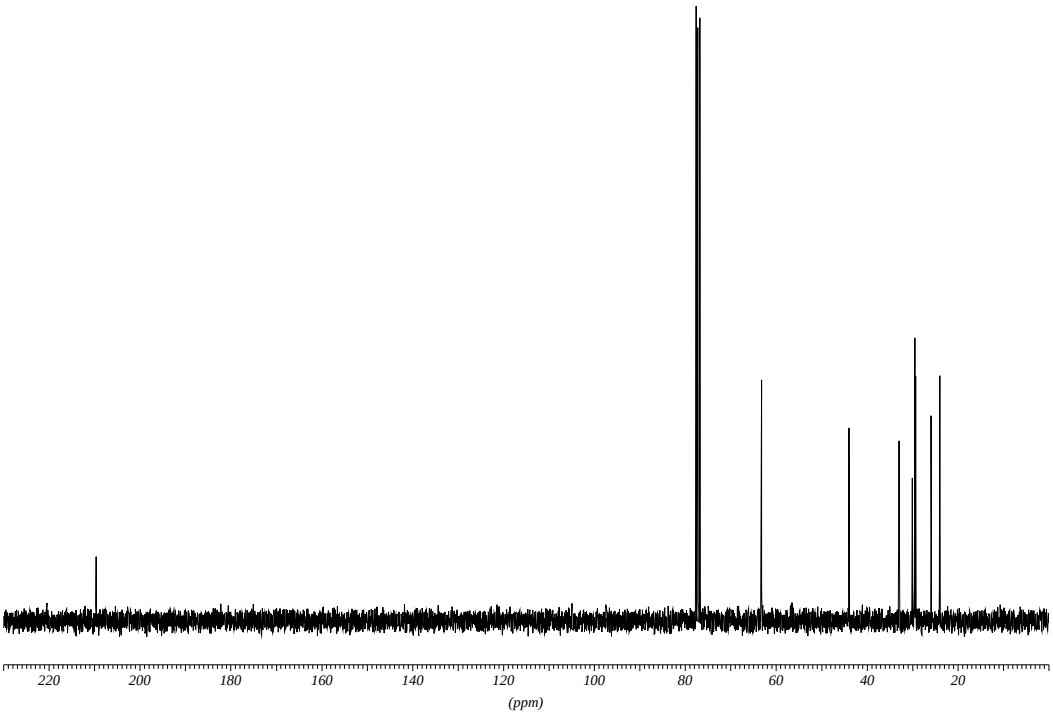
2, 2,6-trimethyl-6-(2-oxopropyl)-cyclohexanone



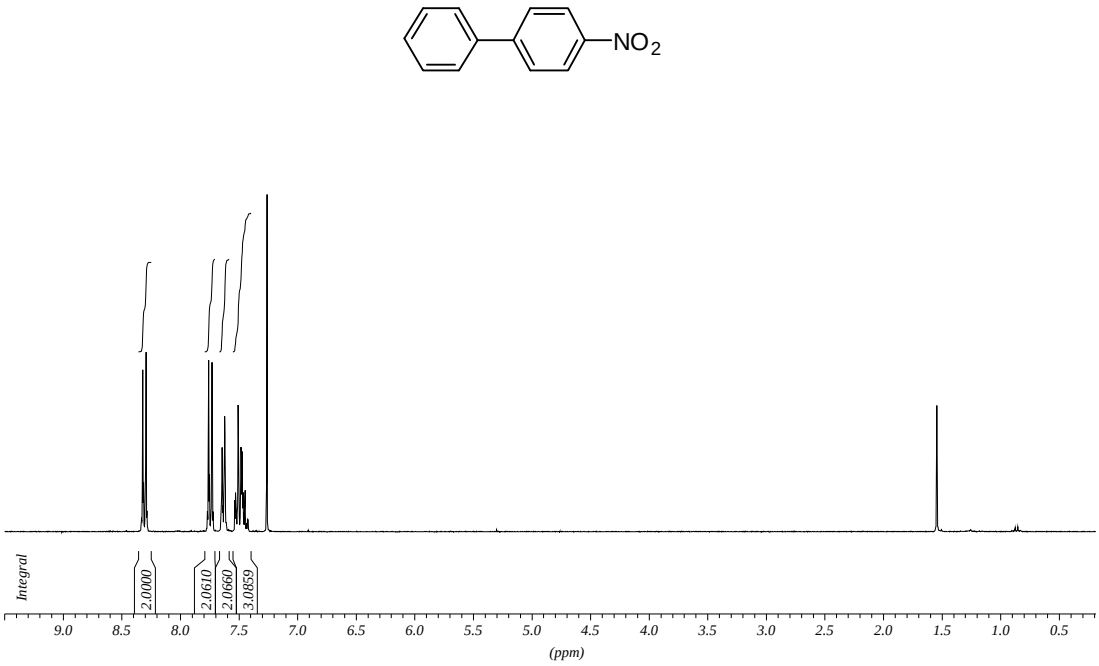


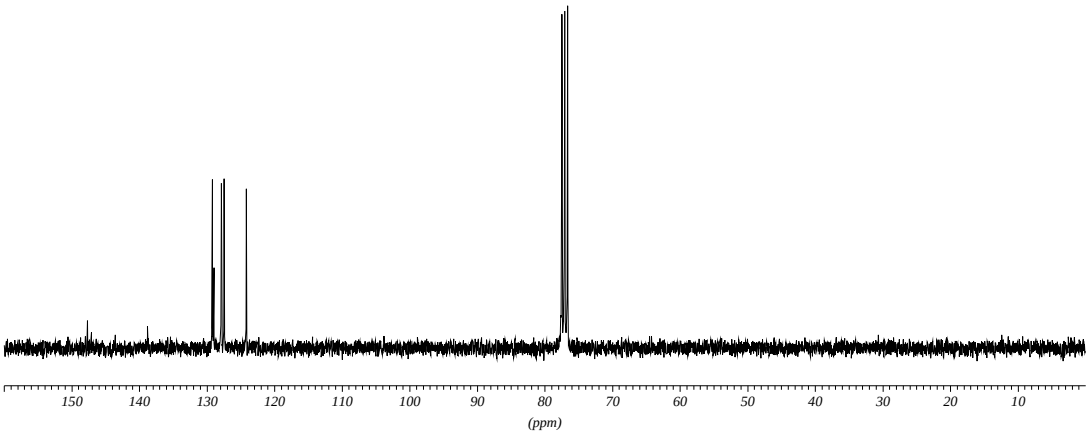
10-hydroxy-2-undecanone



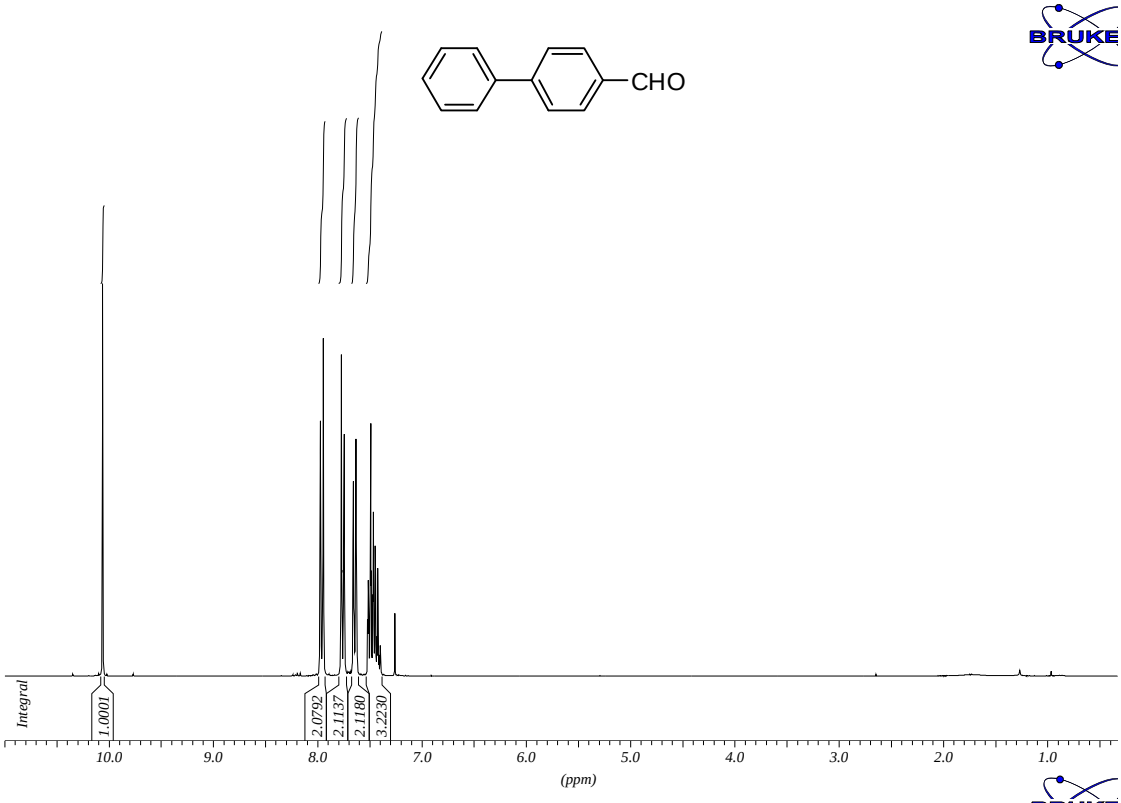


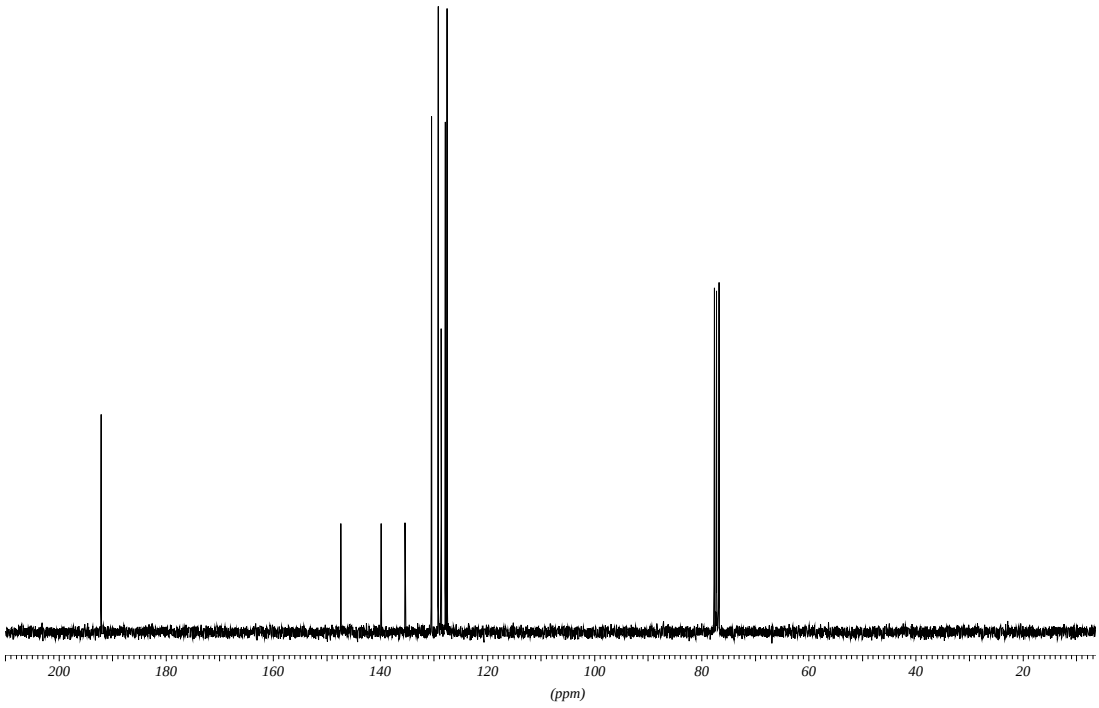
4-nitrobiphenyl



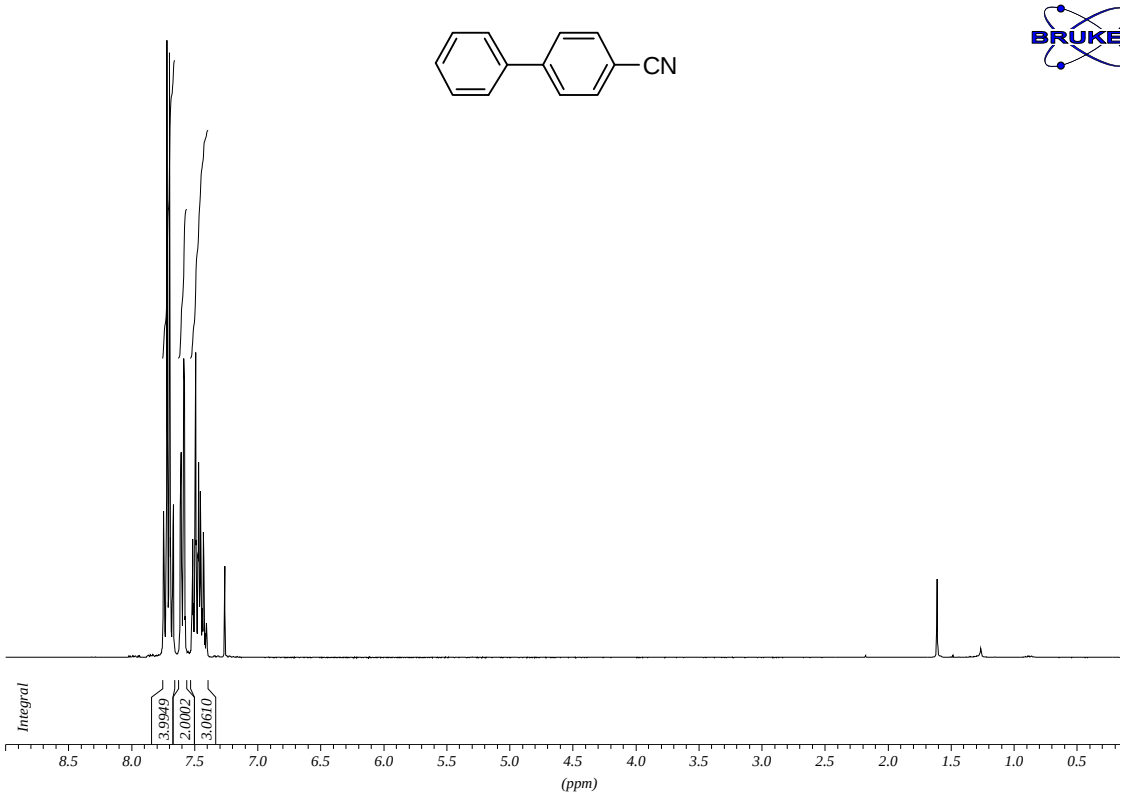


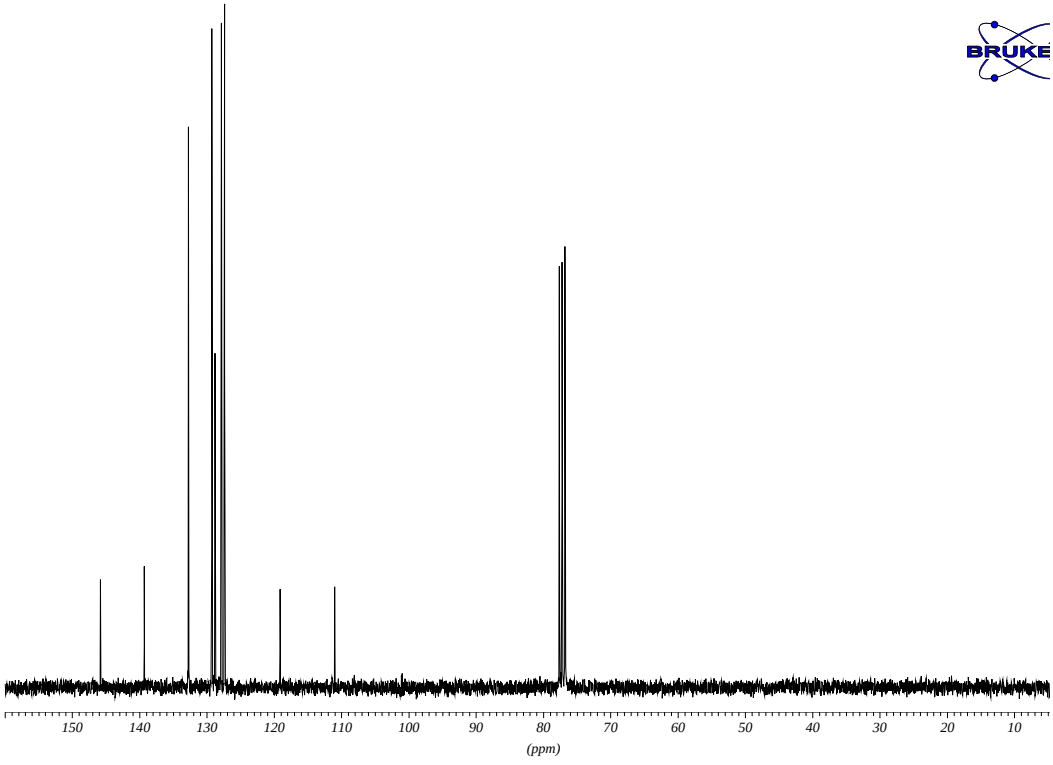
Biphenyl-4-carbaldehyde



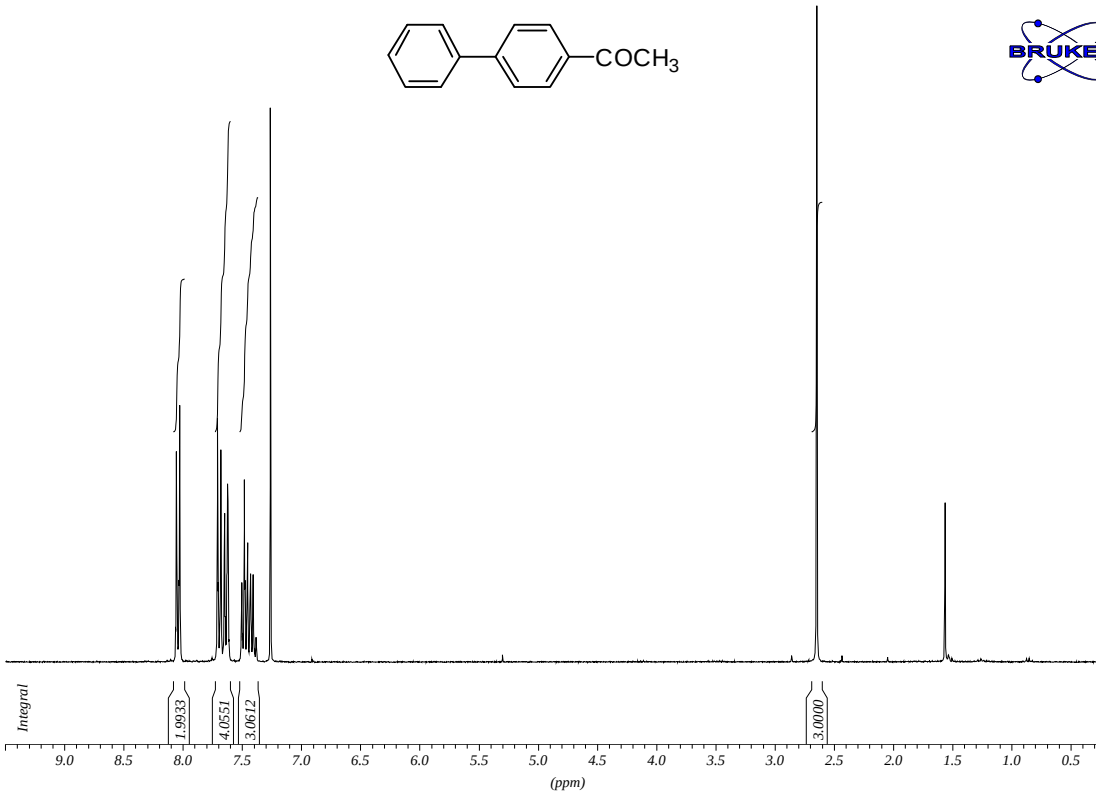


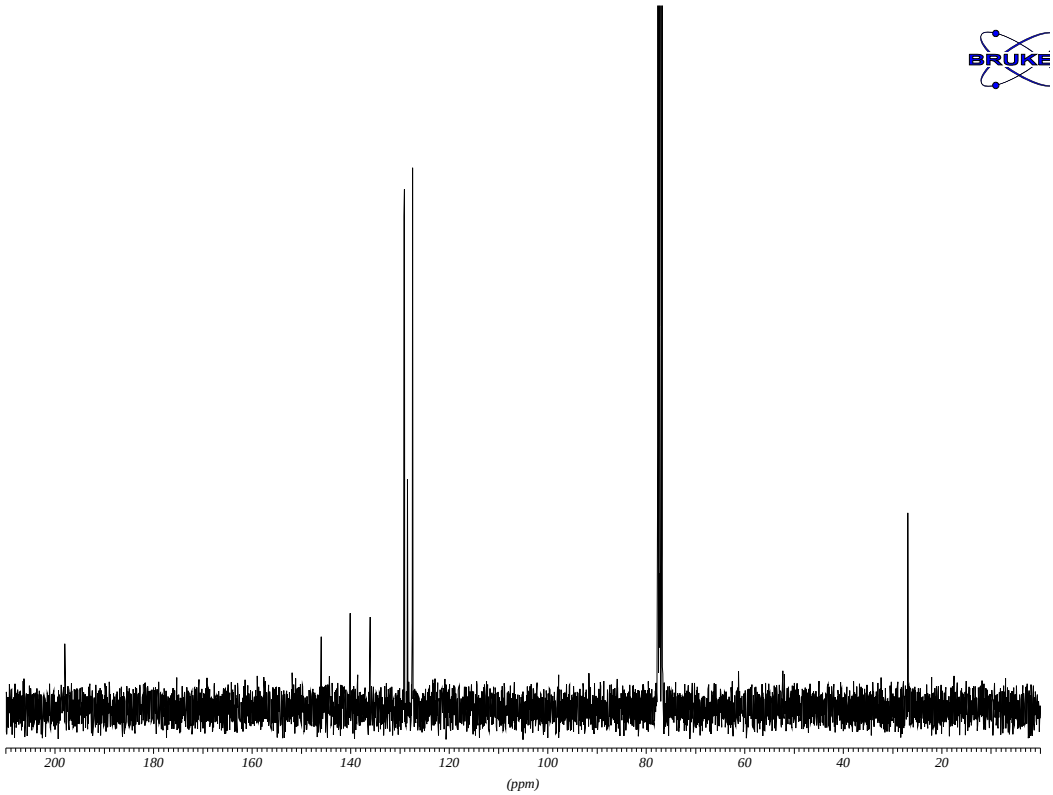
Biphenyl-4-carbonitrile



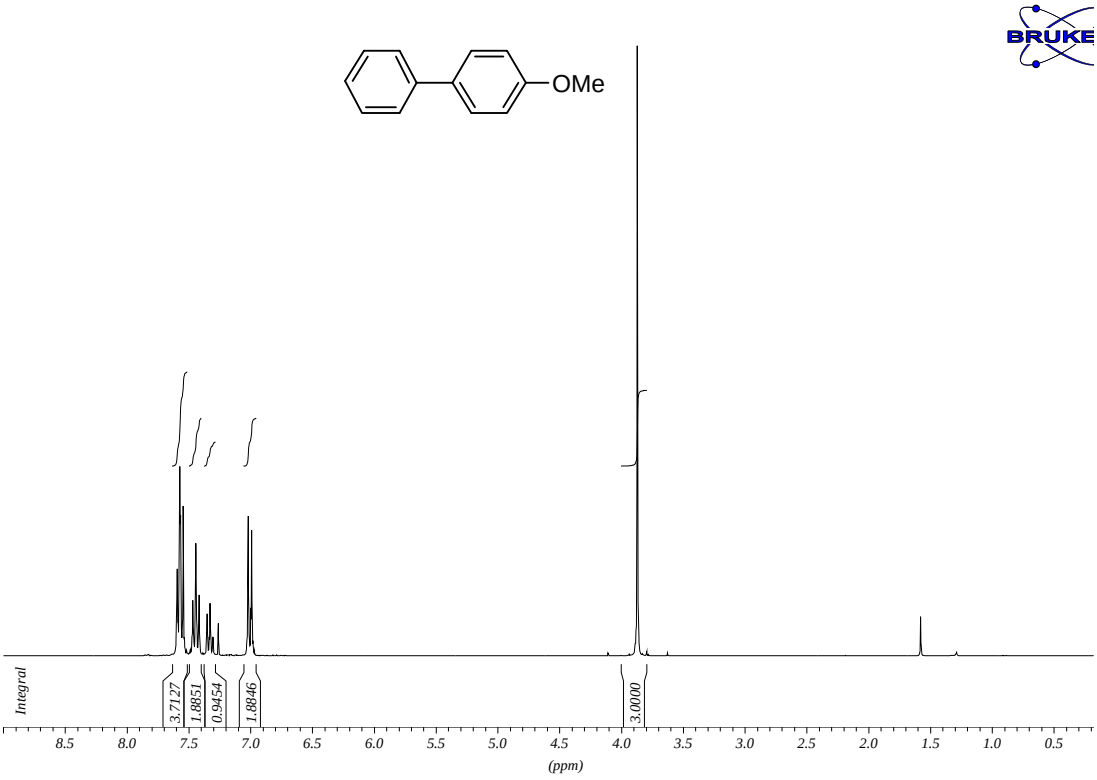


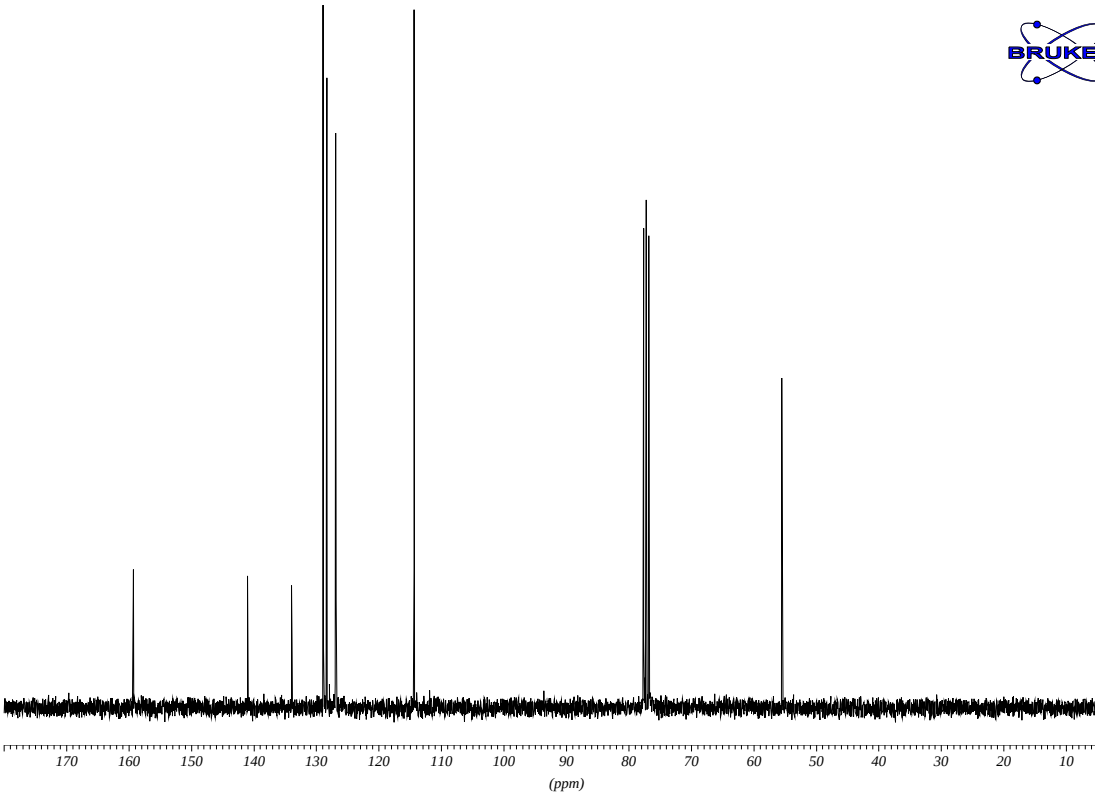
1-(biphenyl-4-yl)ethanone



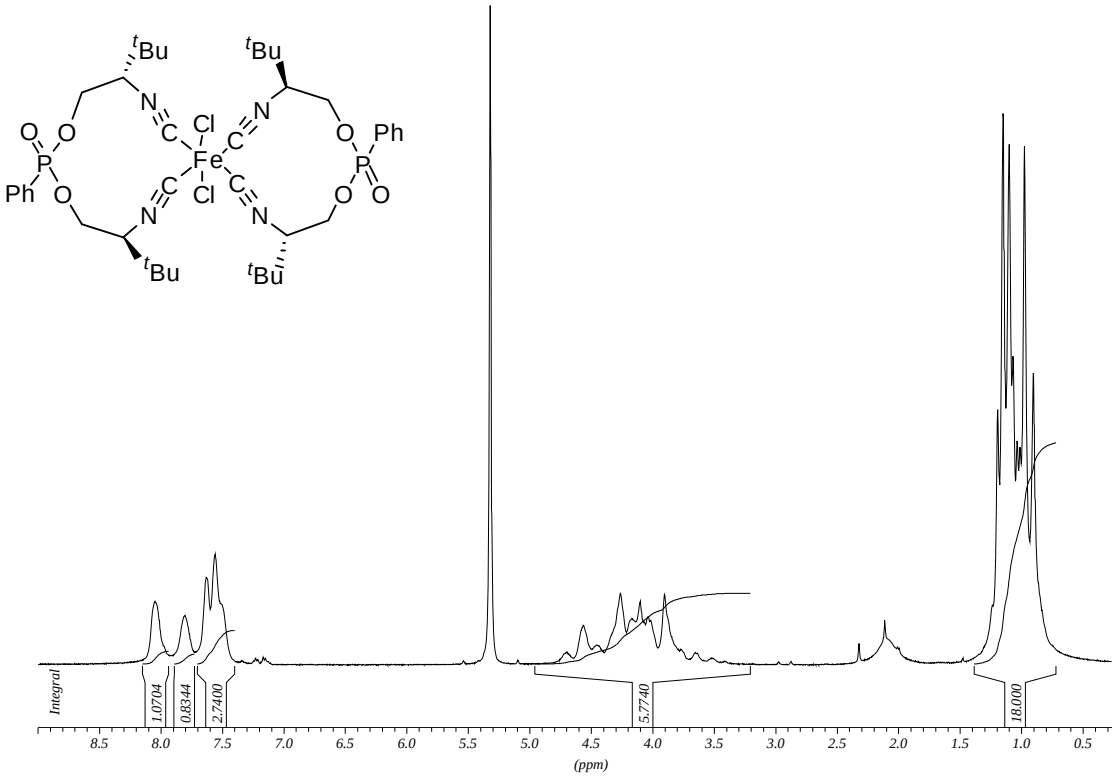


4-methoxybiphenyl

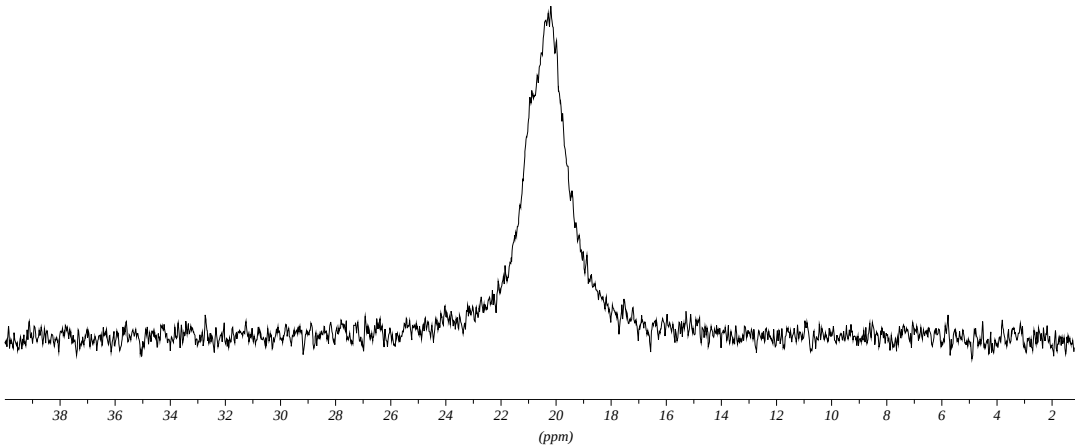




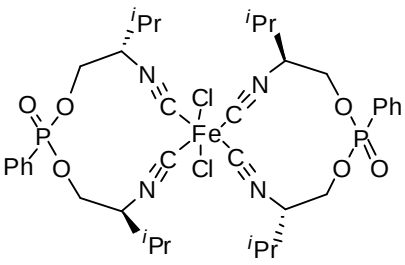
Complex 118b: ^{1}H NMR

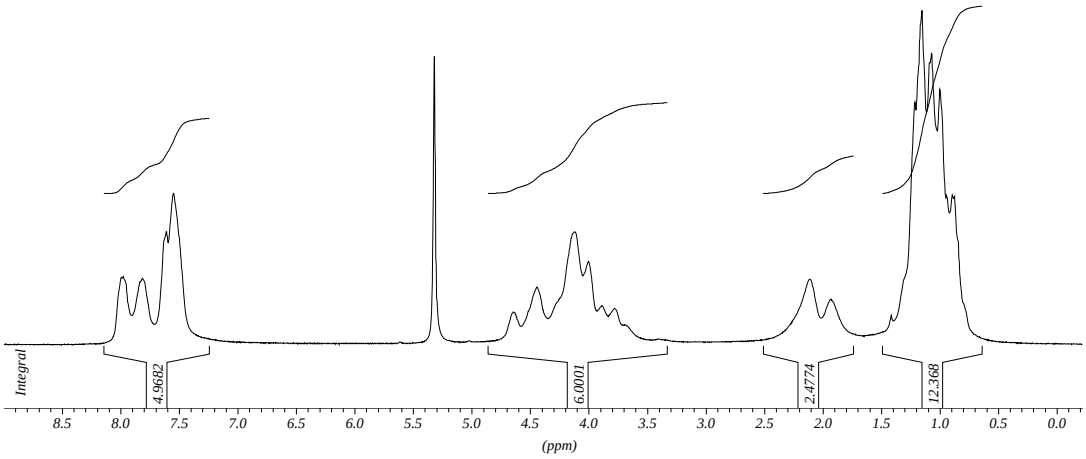


^{31}P NMR

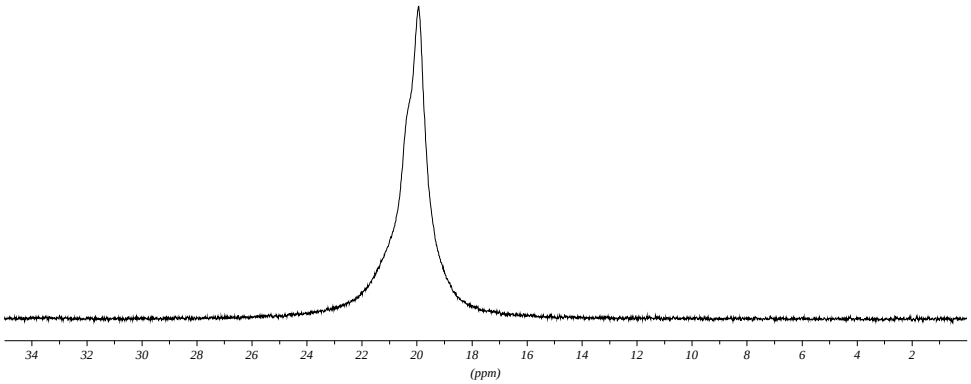


Complex 118c: ^{1}H NMR

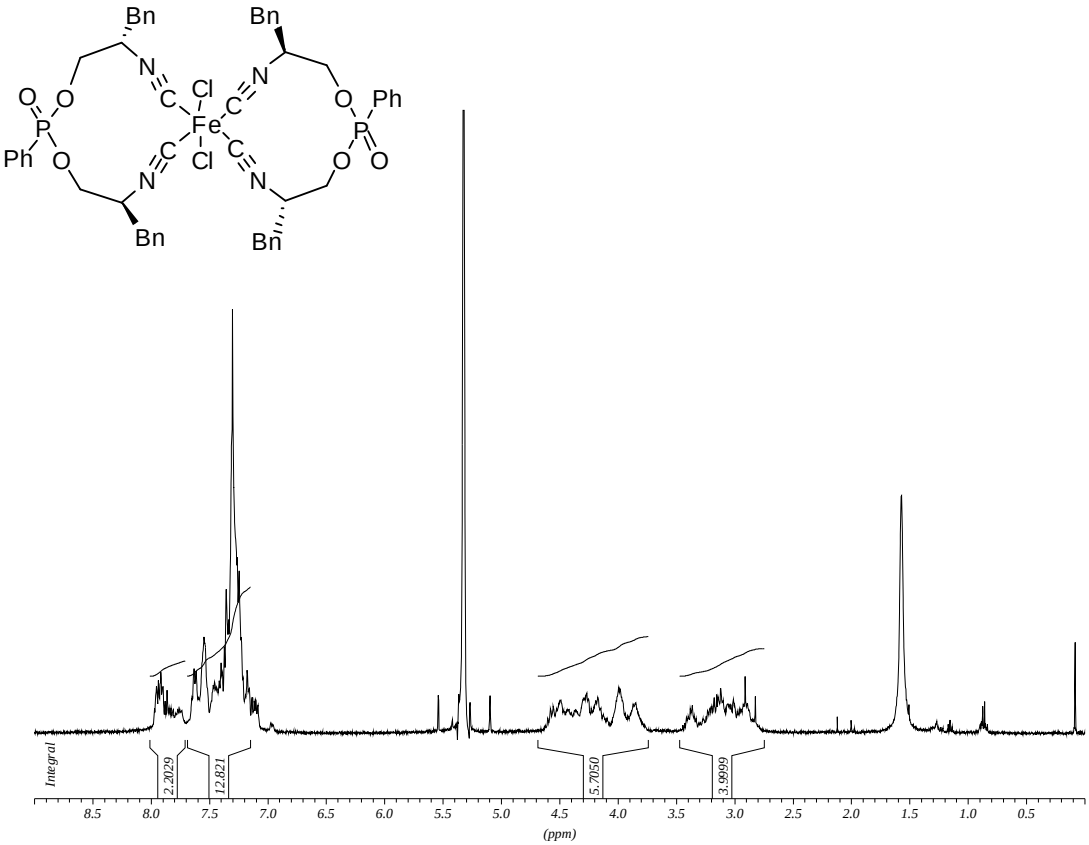




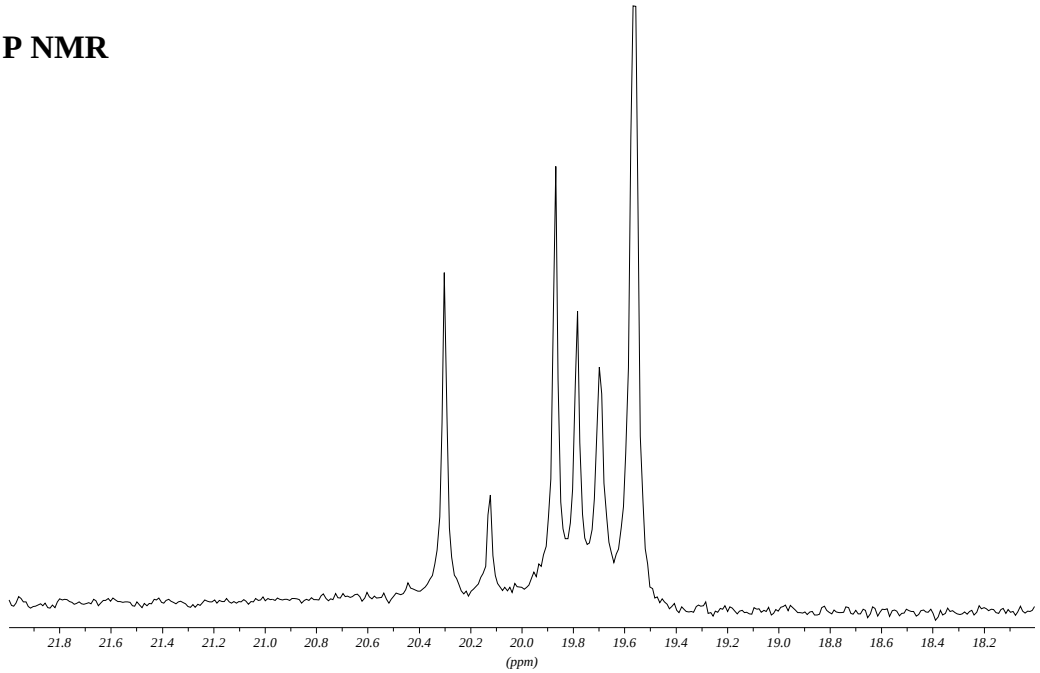
^{31} P NMR



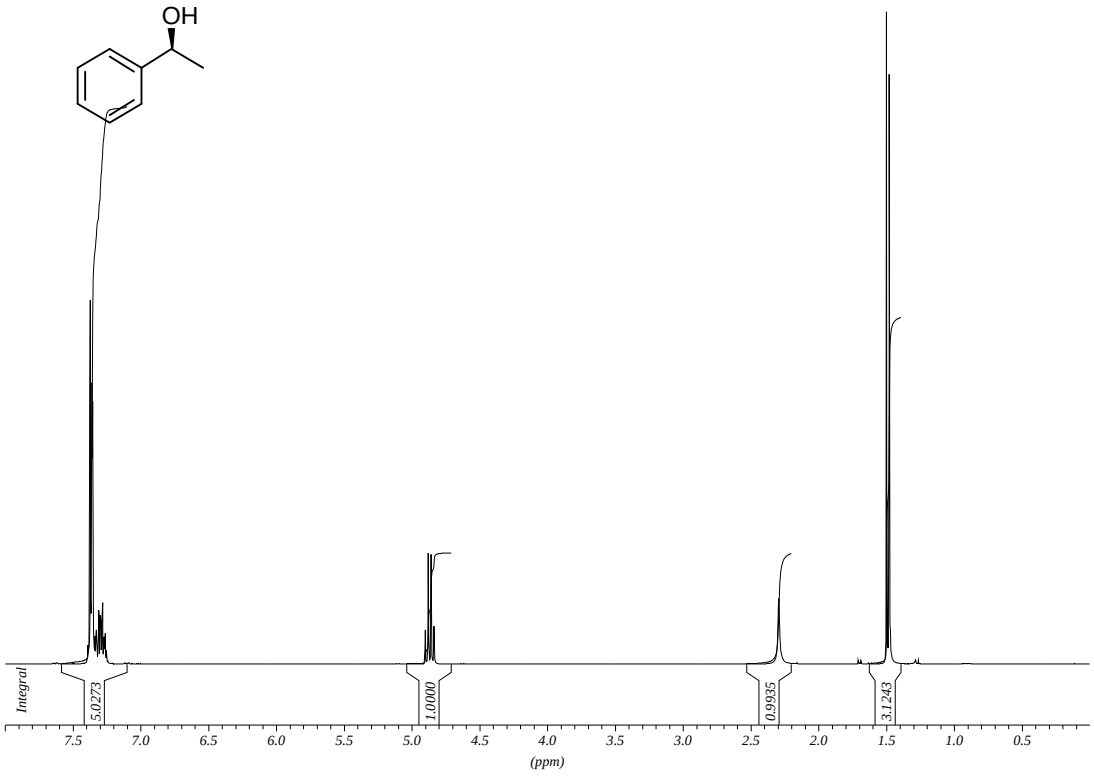
Complex 118a: ^{1}H NMR

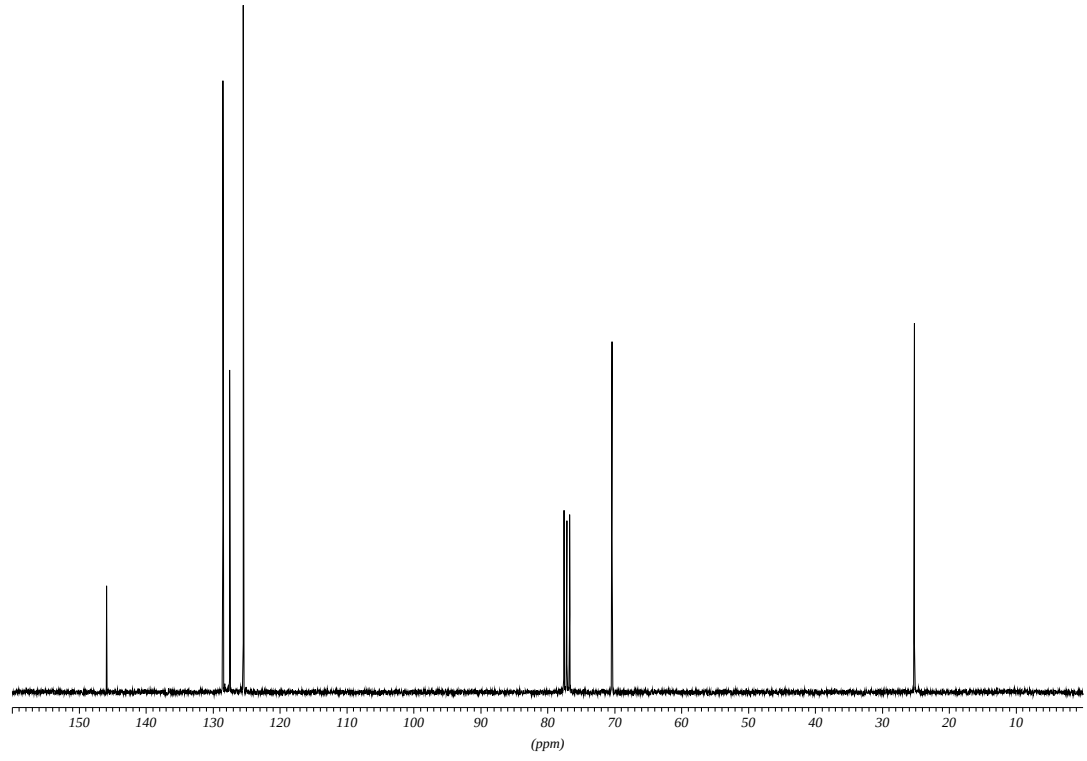


^{31} P NMR

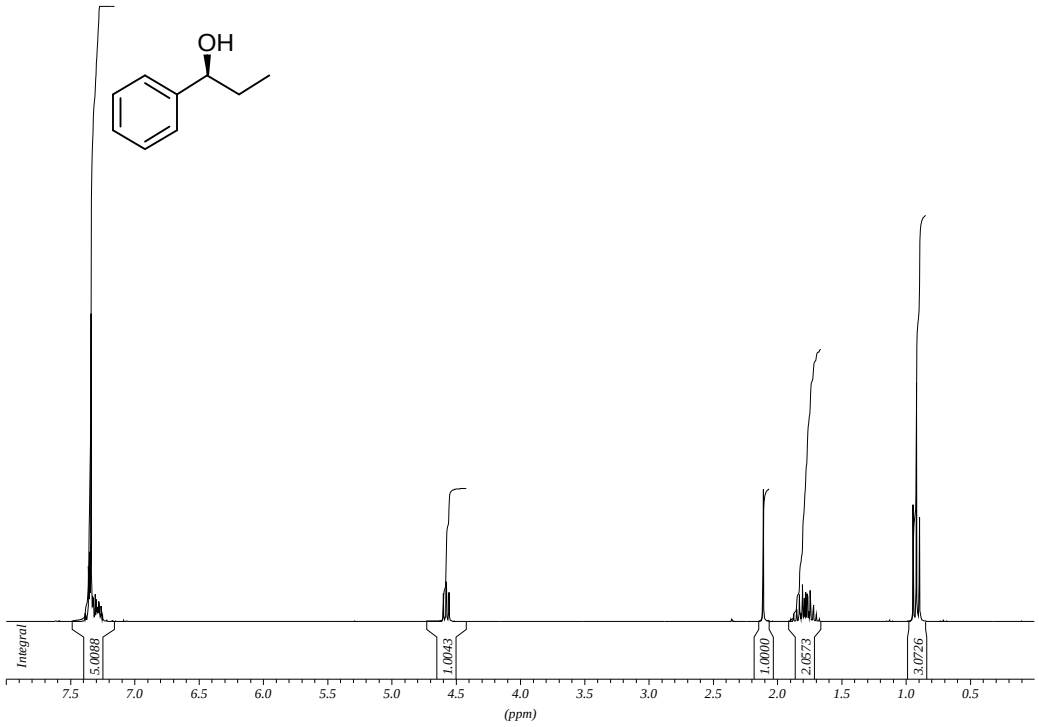


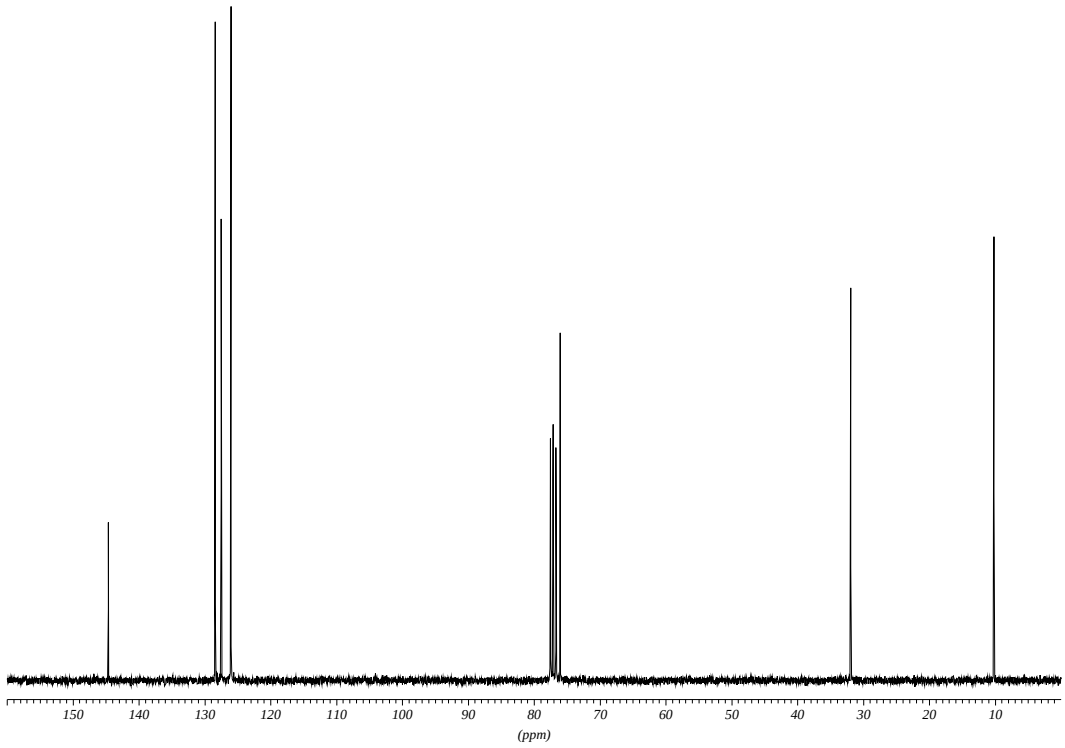
(*S*)-1-phenylethanol



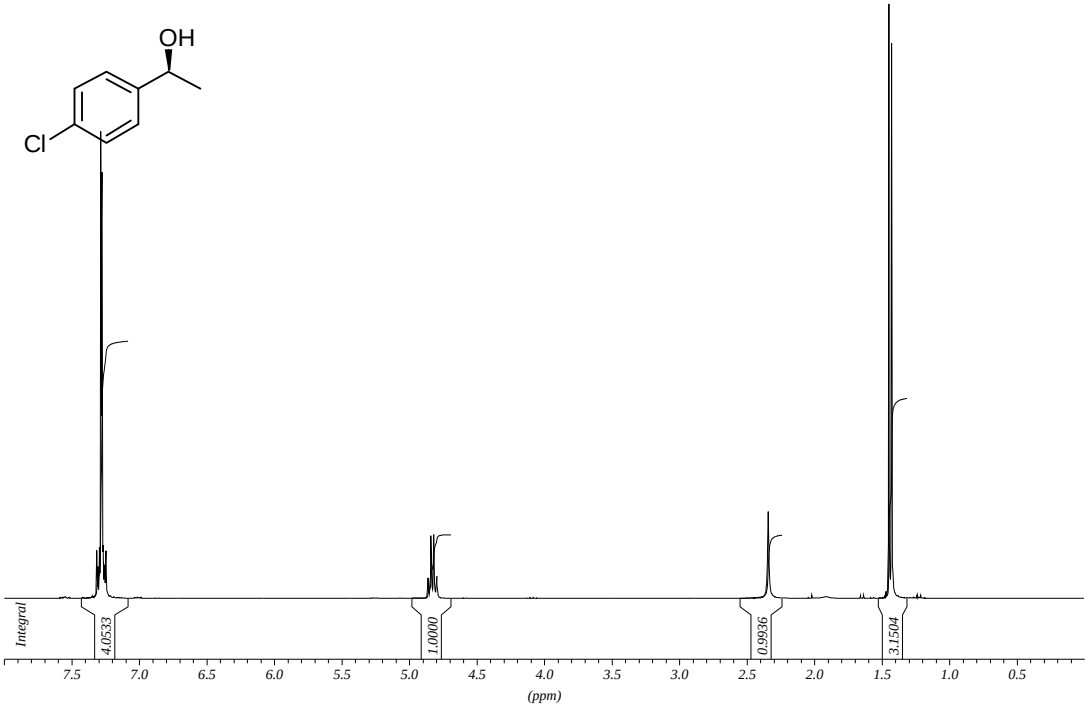


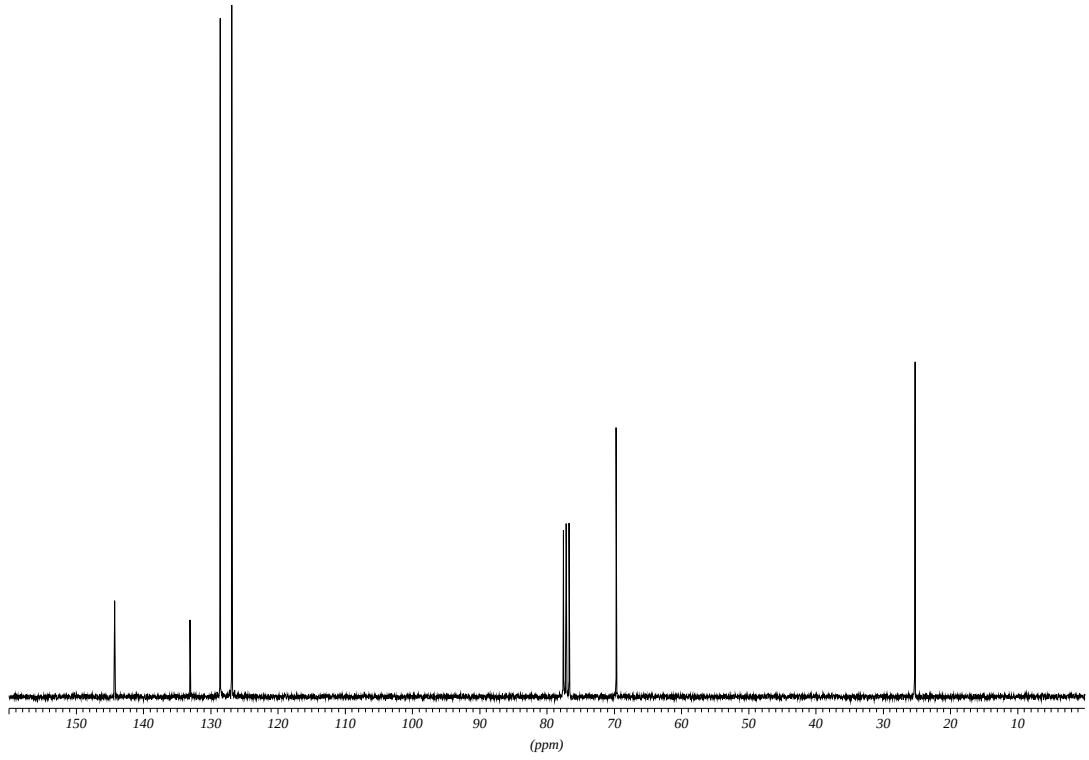
(*S*)-1-phenylpropan-1-ol



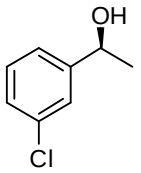


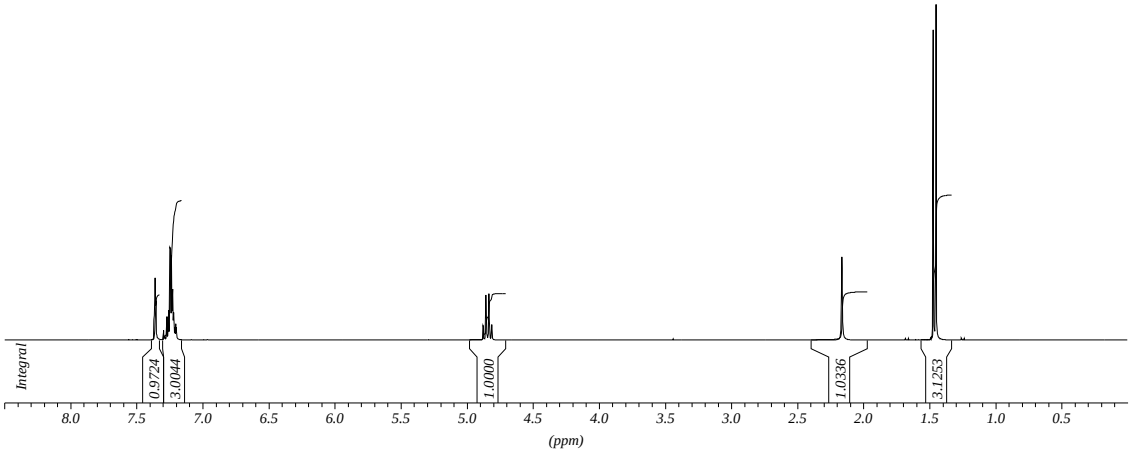
(*S*)-1-(4-chlorophenyl)ethanol

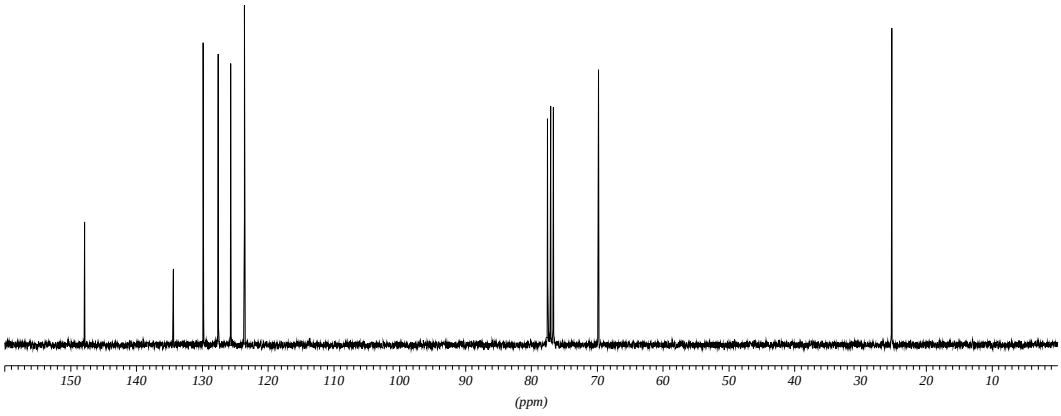




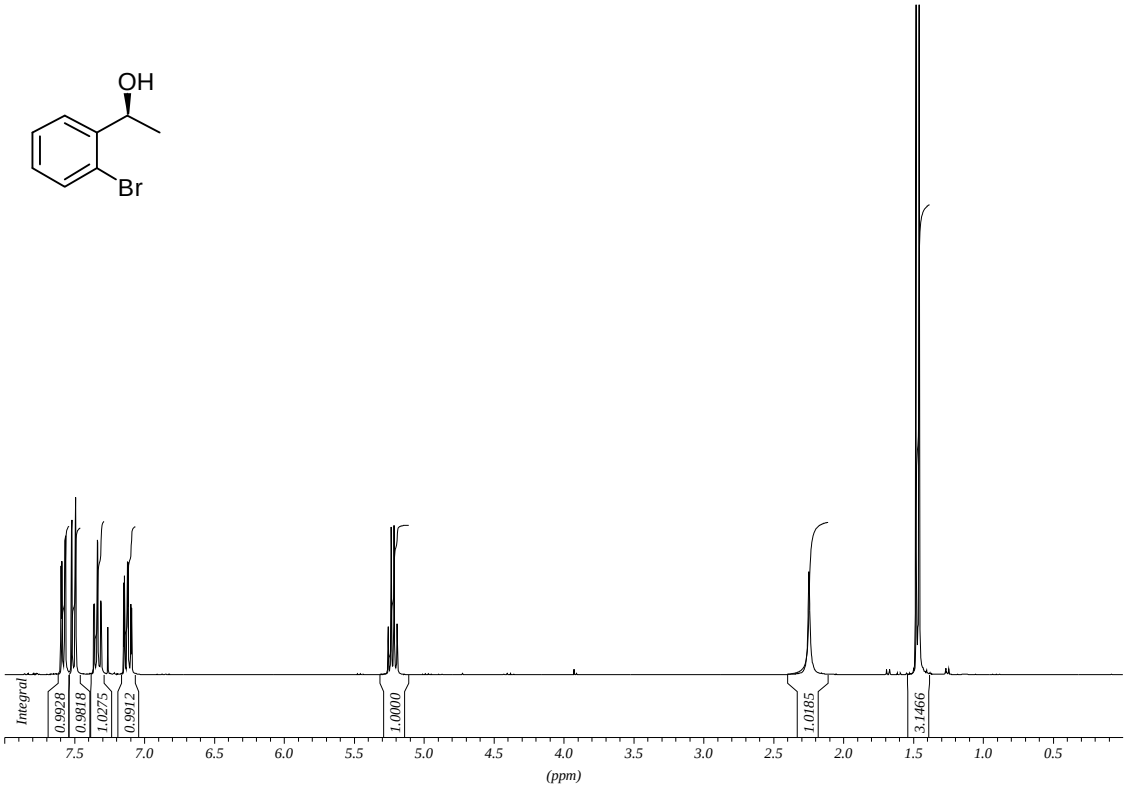
(*S*)-1-(3-chlorophenyl)ethanol

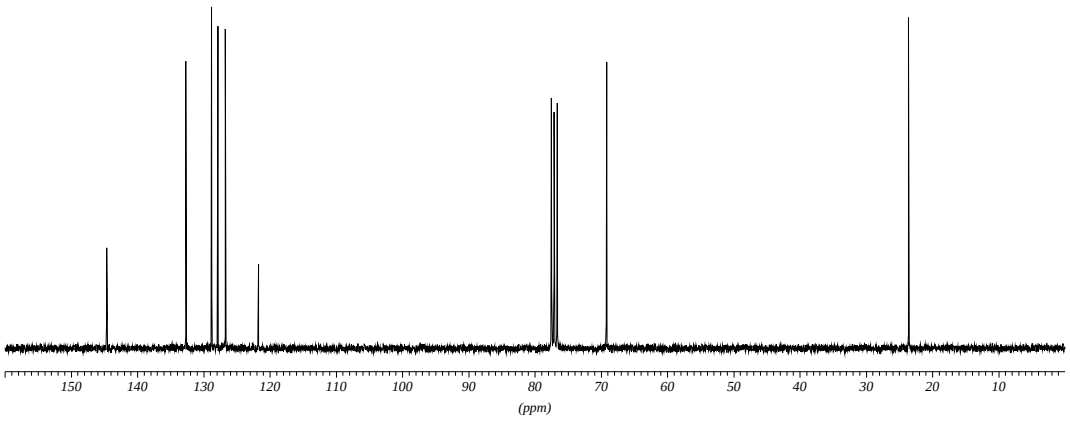




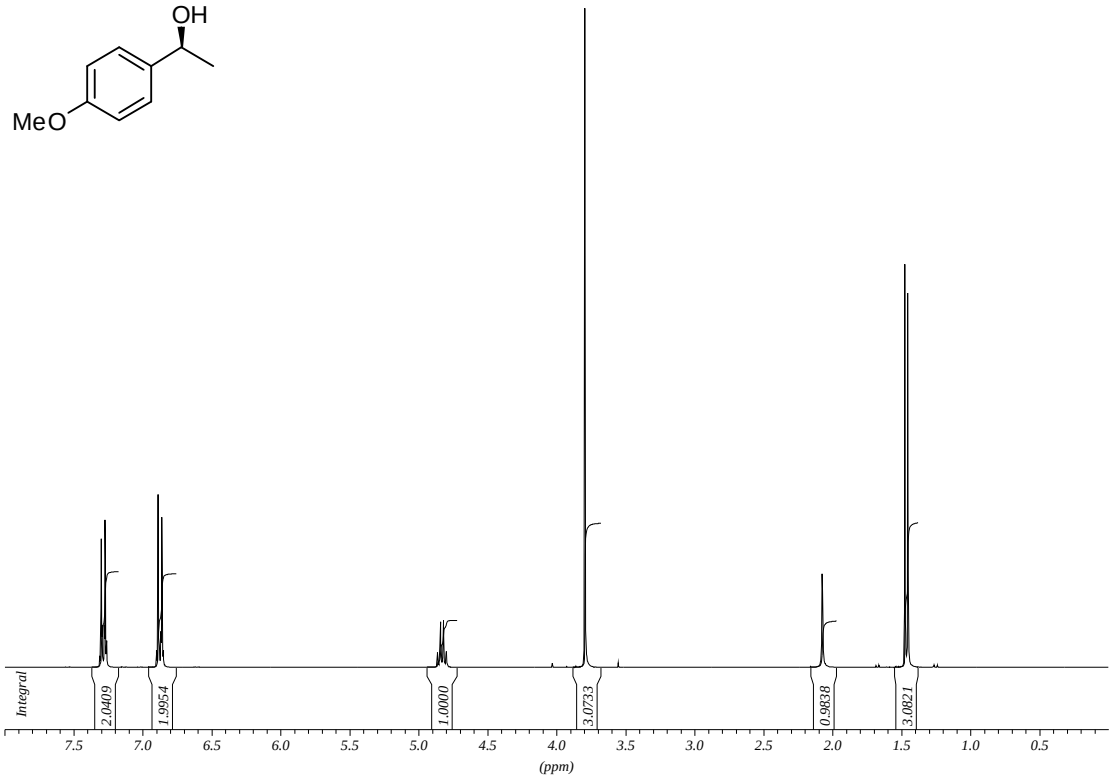


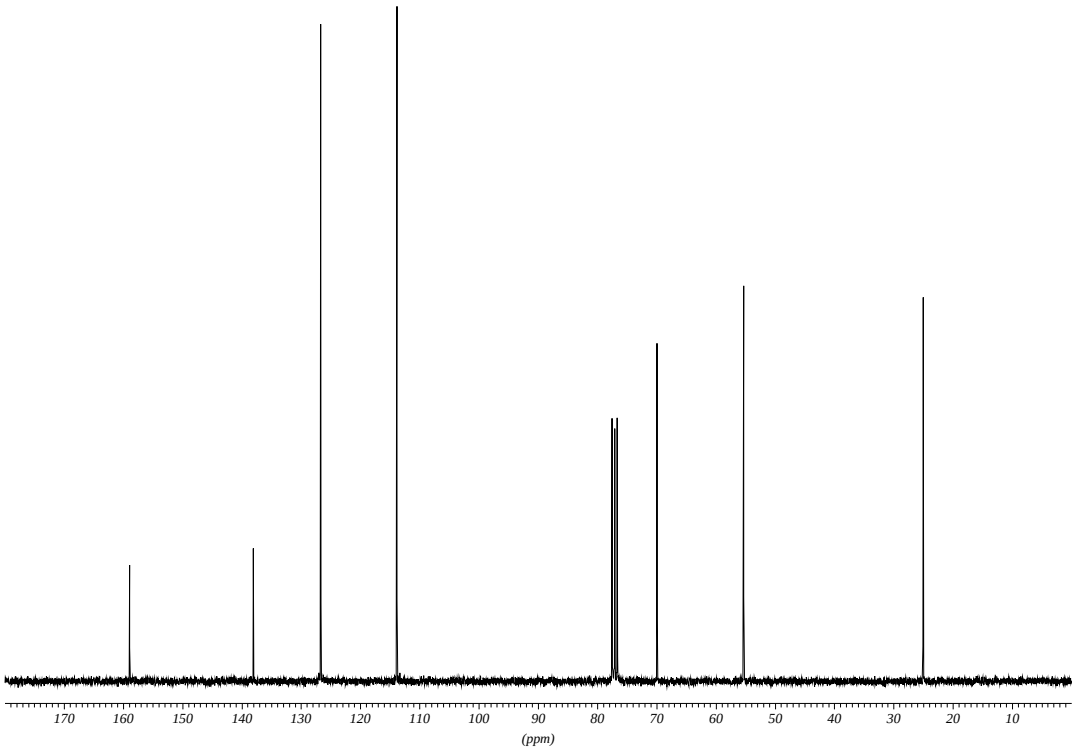
(*S*)-1-(2-bromophenyl)ethanol



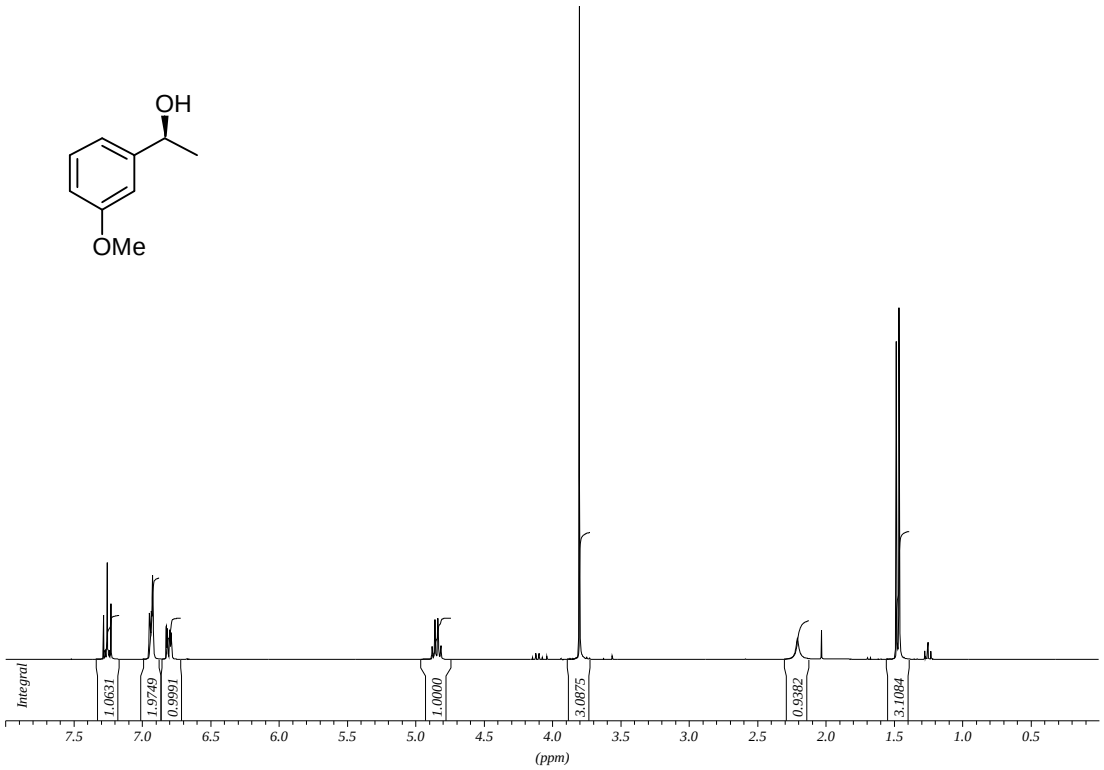


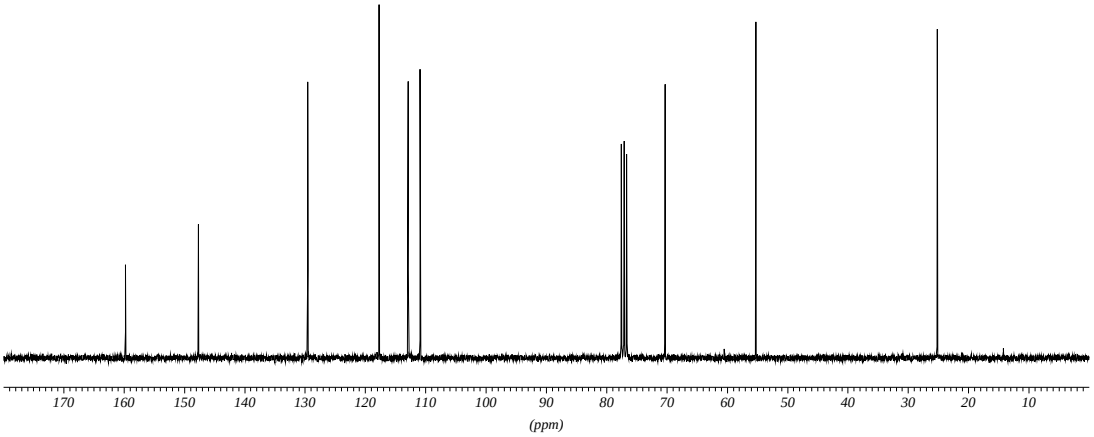
(*S*)-1-(4-methoxyphenyl)ethanol



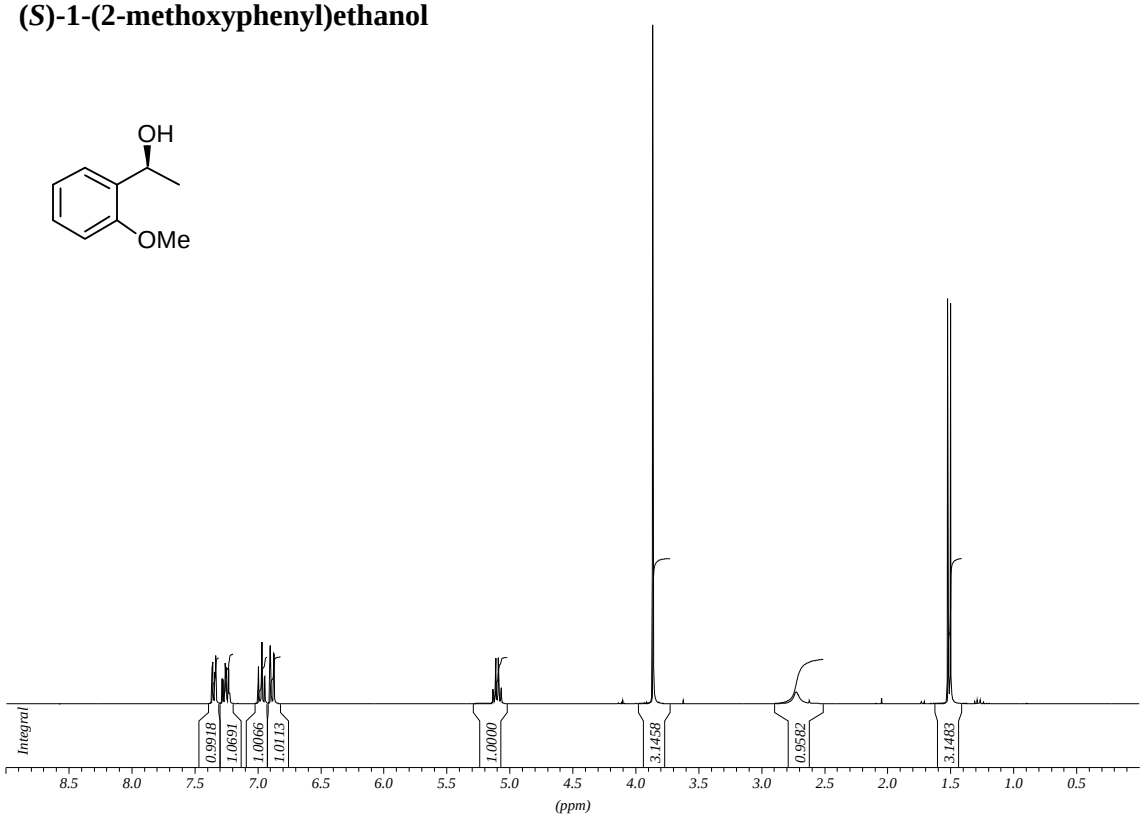


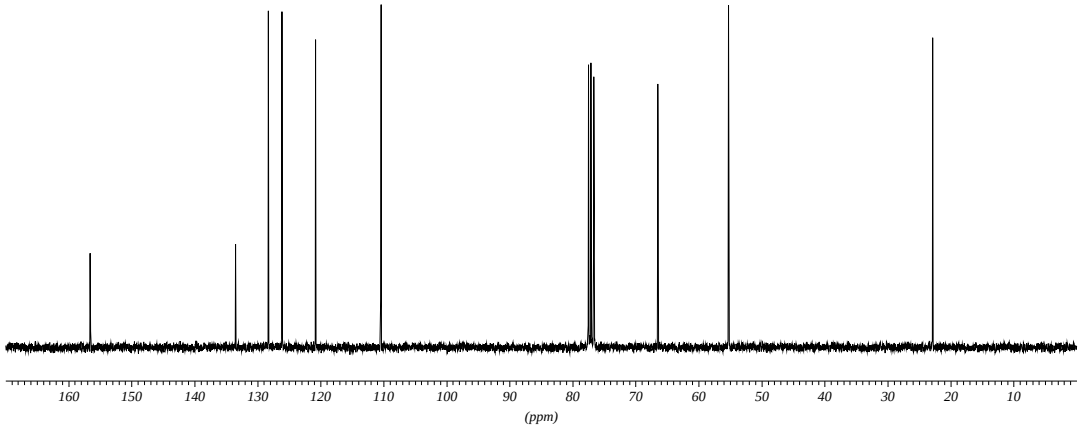
(*S*)-1-(3-methoxyphenyl)ethanol



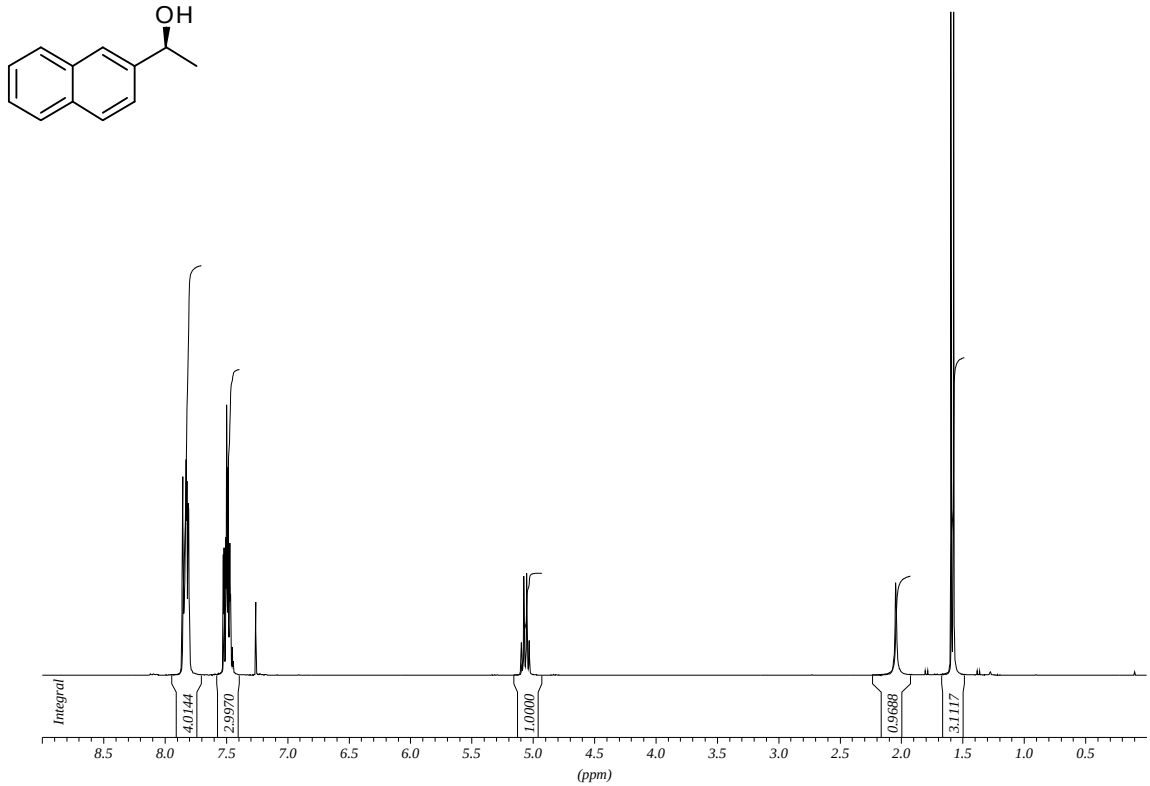


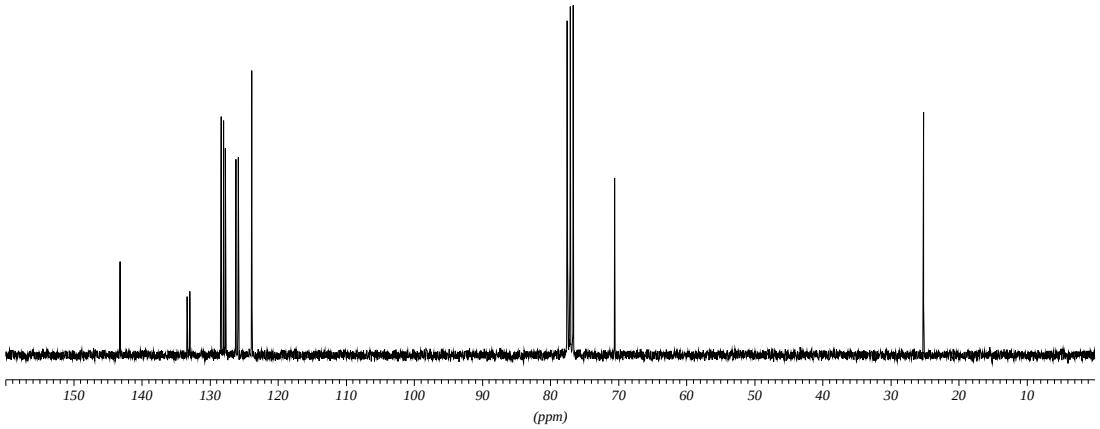
(*S*)-1-(2-methoxyphenyl)ethanol



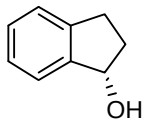


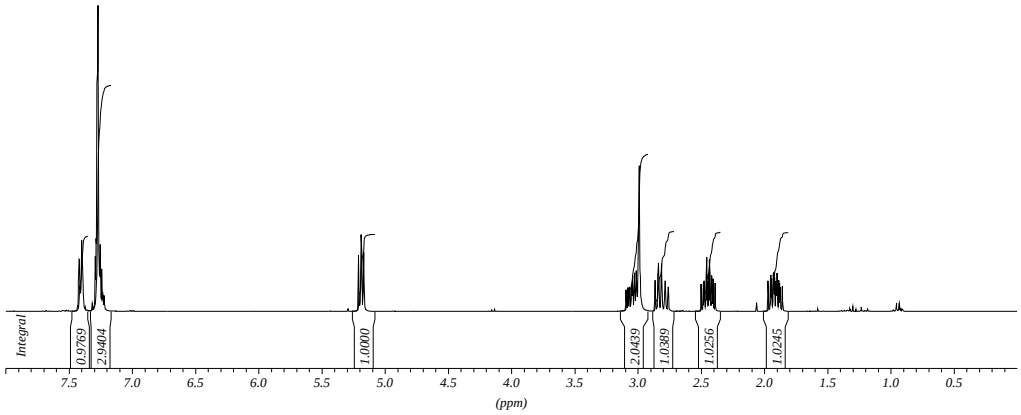
(*S*)-1-(naphthalen-2-yl)ethanol

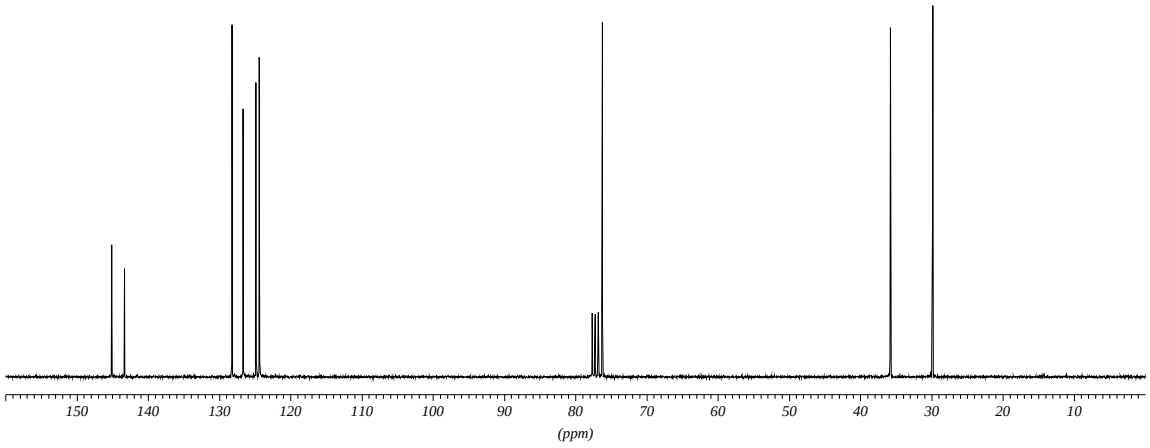




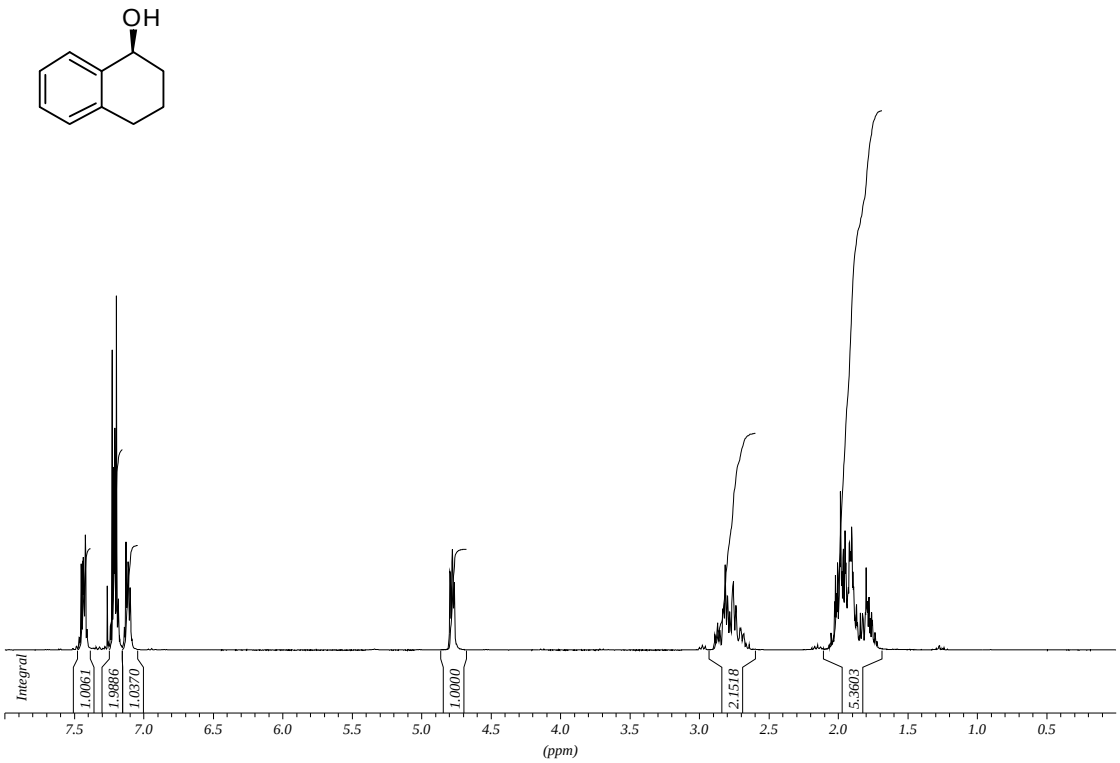
(*S*)-2,3-dihydro-1H-inden-1-ol

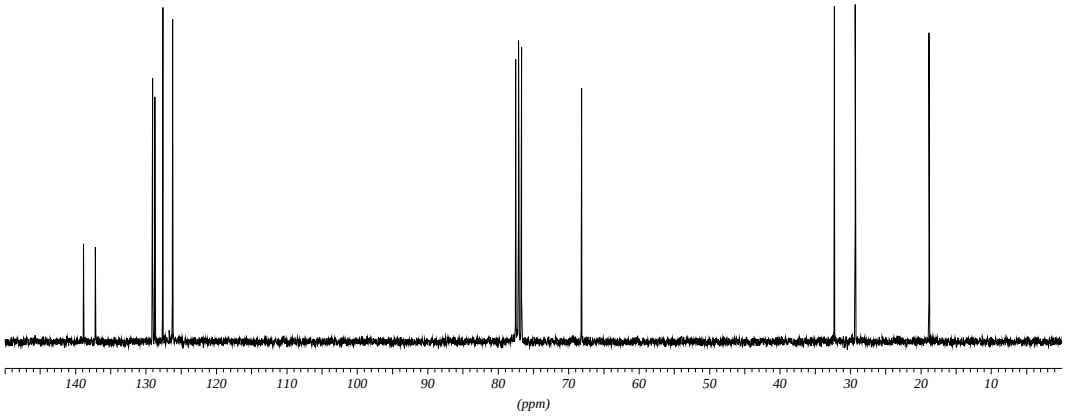




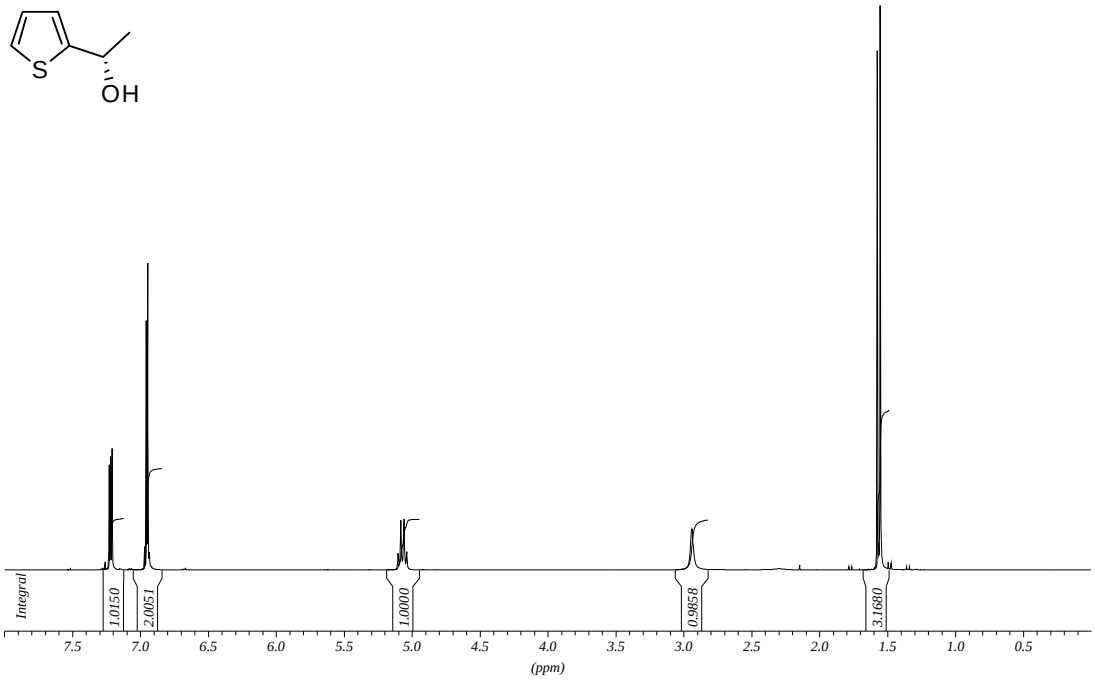


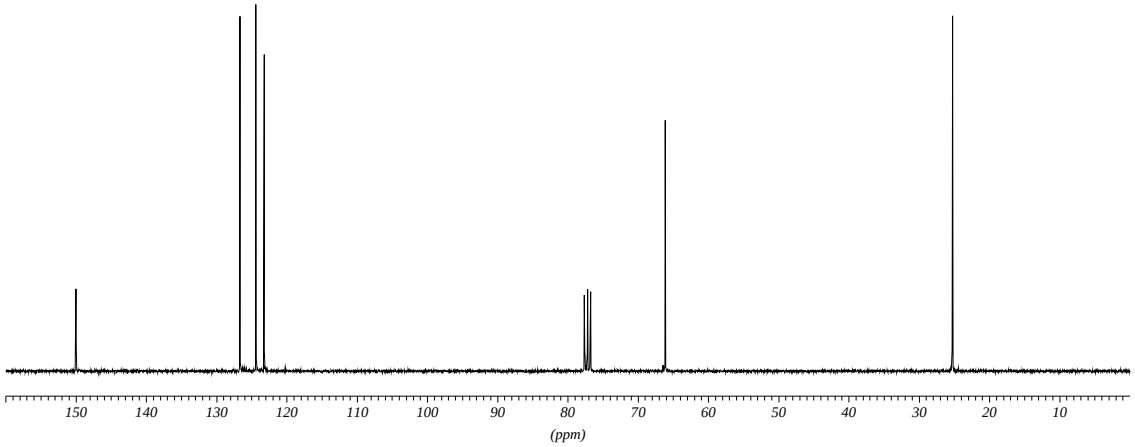
(*S*)-1,2,3,4-tetrahydronaphthalen-1-ol



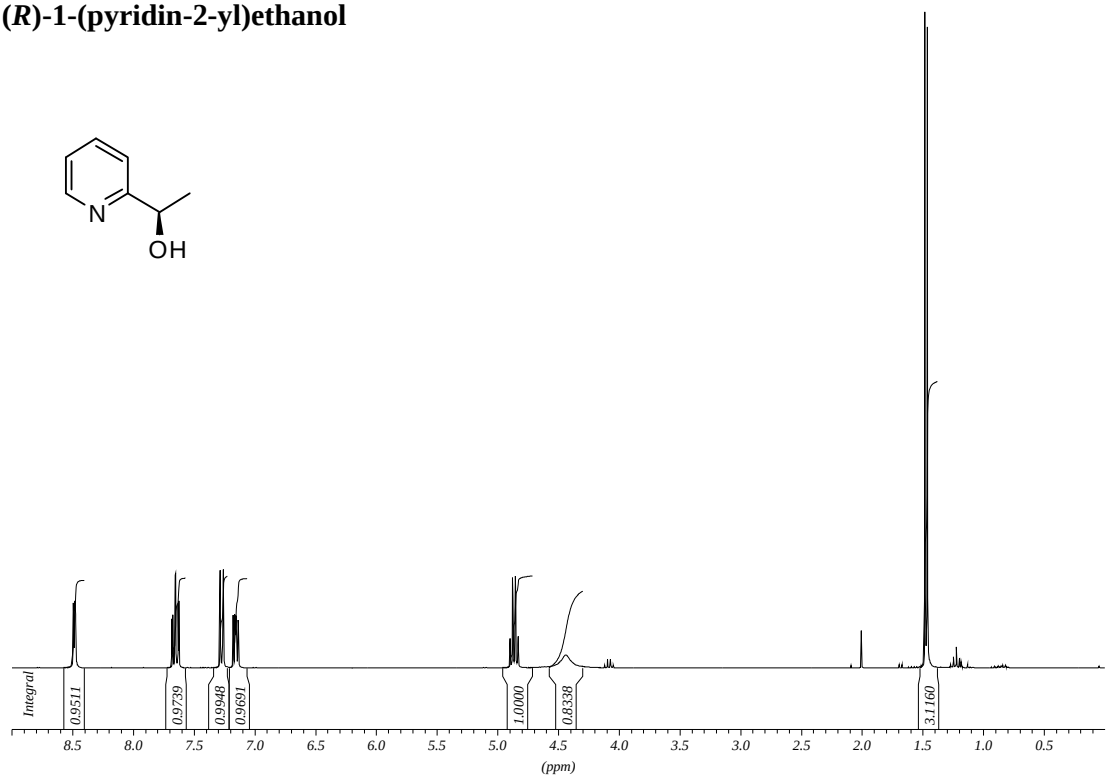


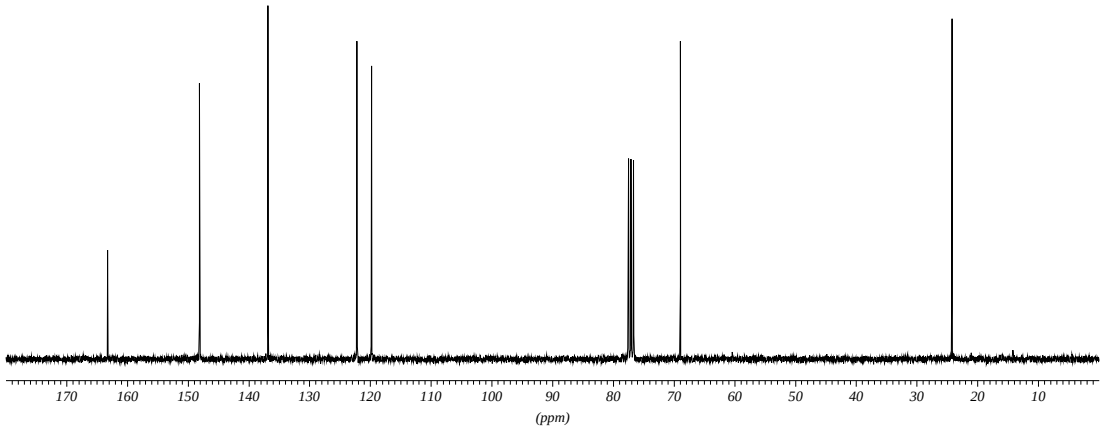
(*S*)-1-(2-Thienyl)ethanol



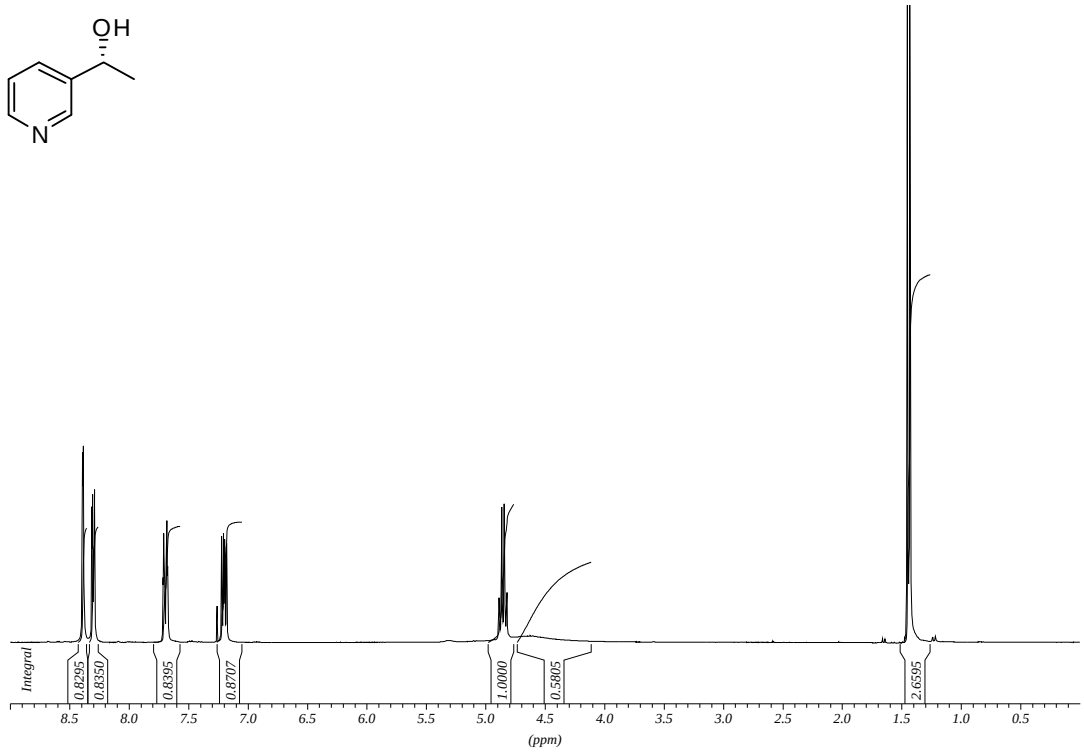


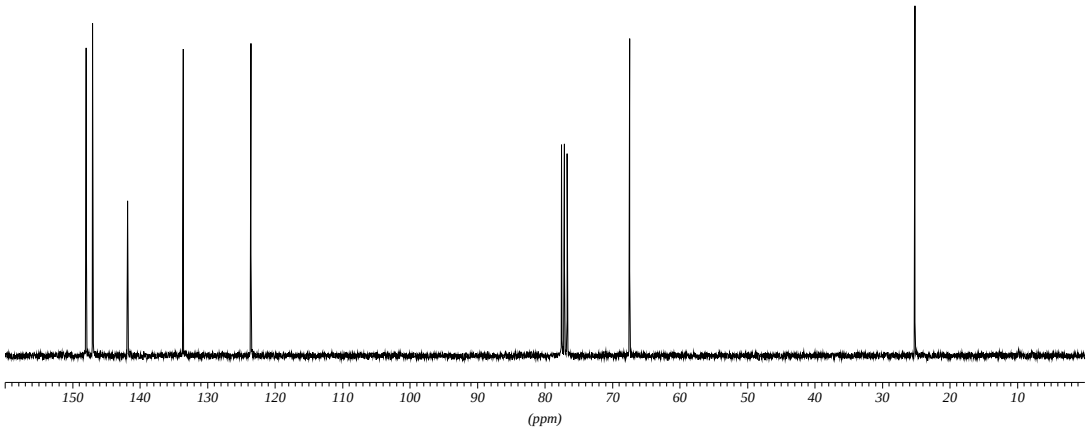
(*R*)-1-(pyridin-2-yl)ethanol



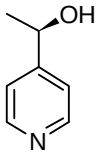


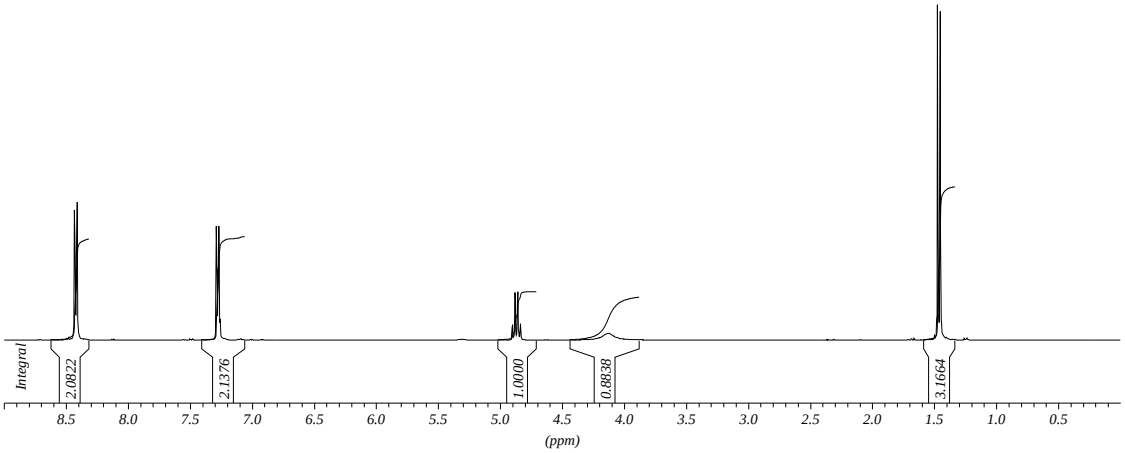
(*R*)-1-(pyridin-3-yl)ethanol

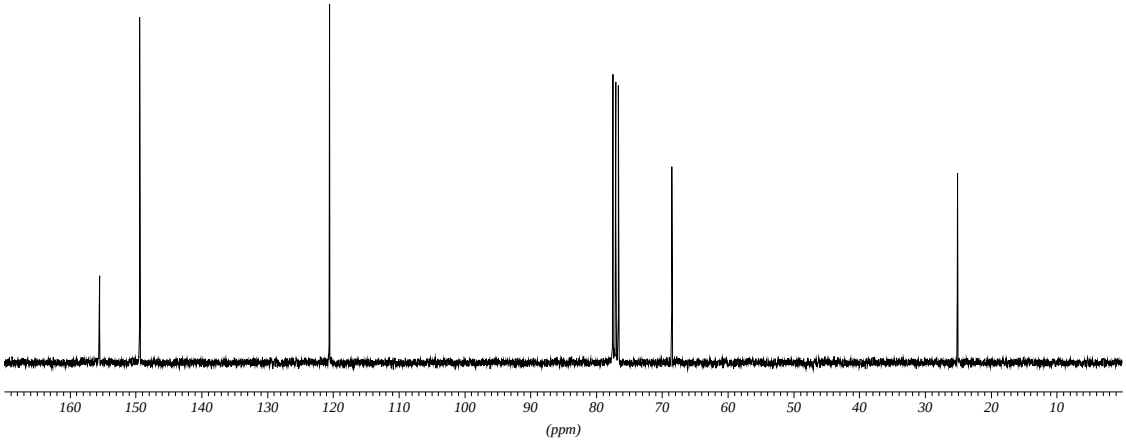




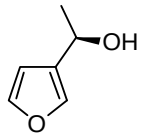
(*R*)-1-(pyridin-4-yl)ethanol

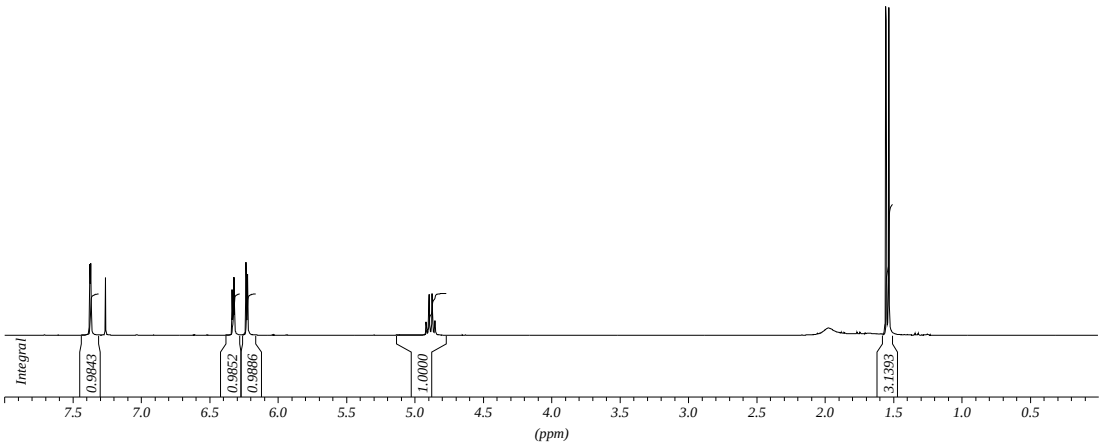


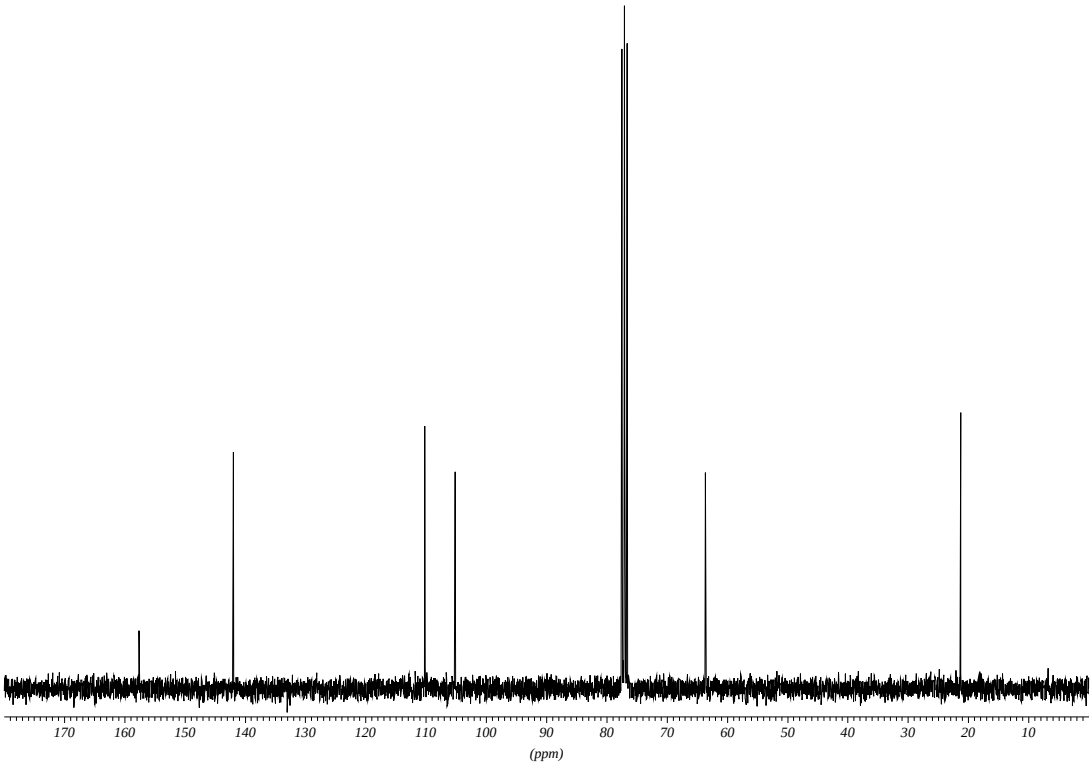




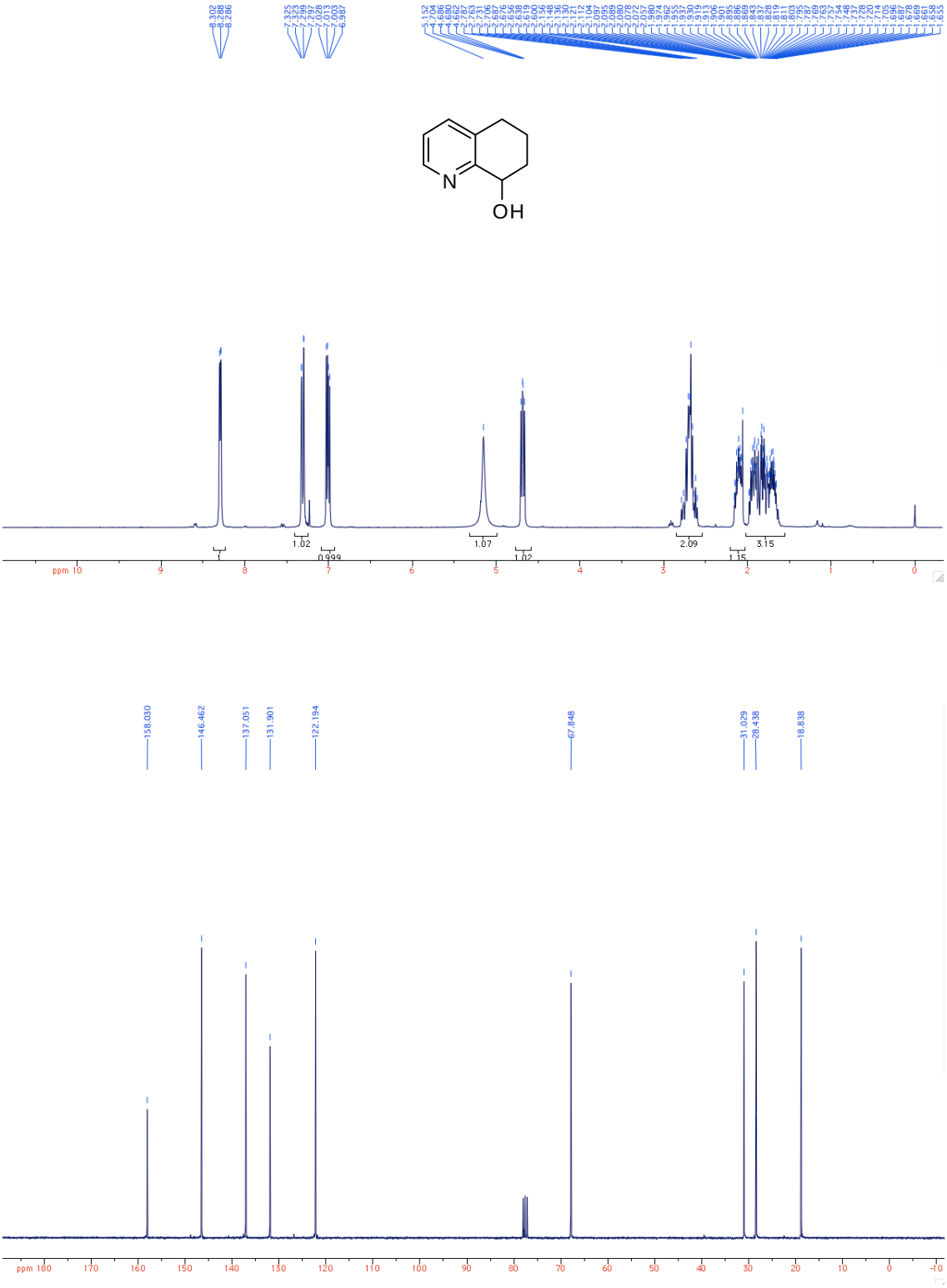
(*R*)-1-(furan-3-yl)ethanol



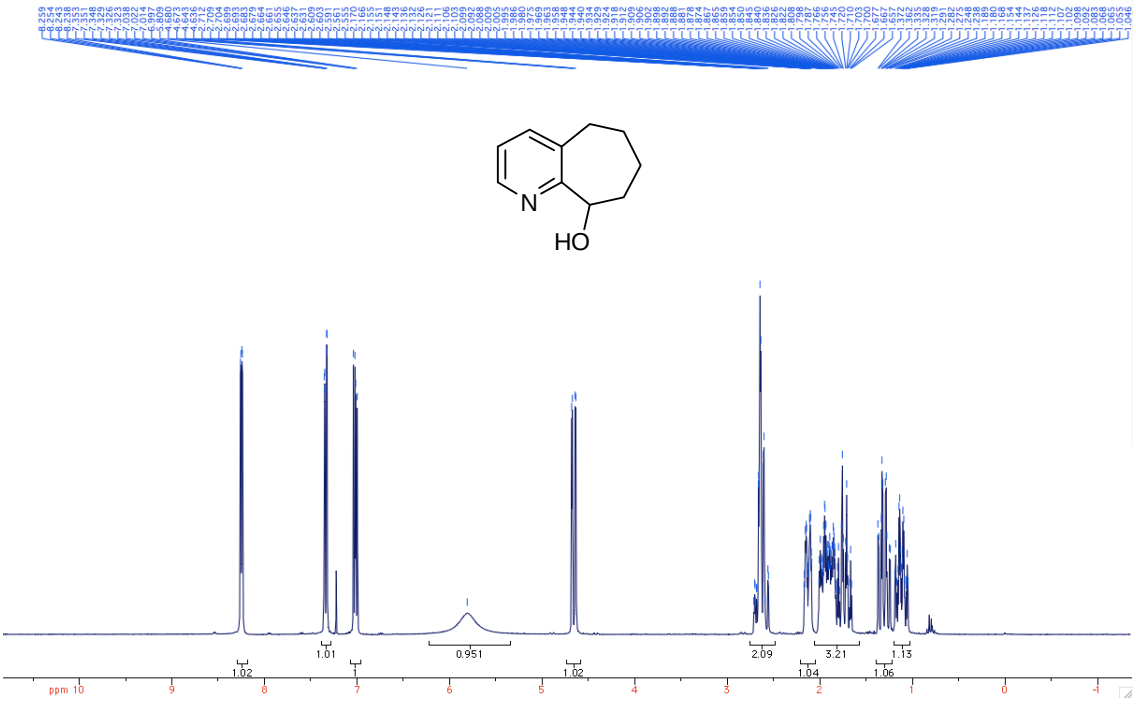


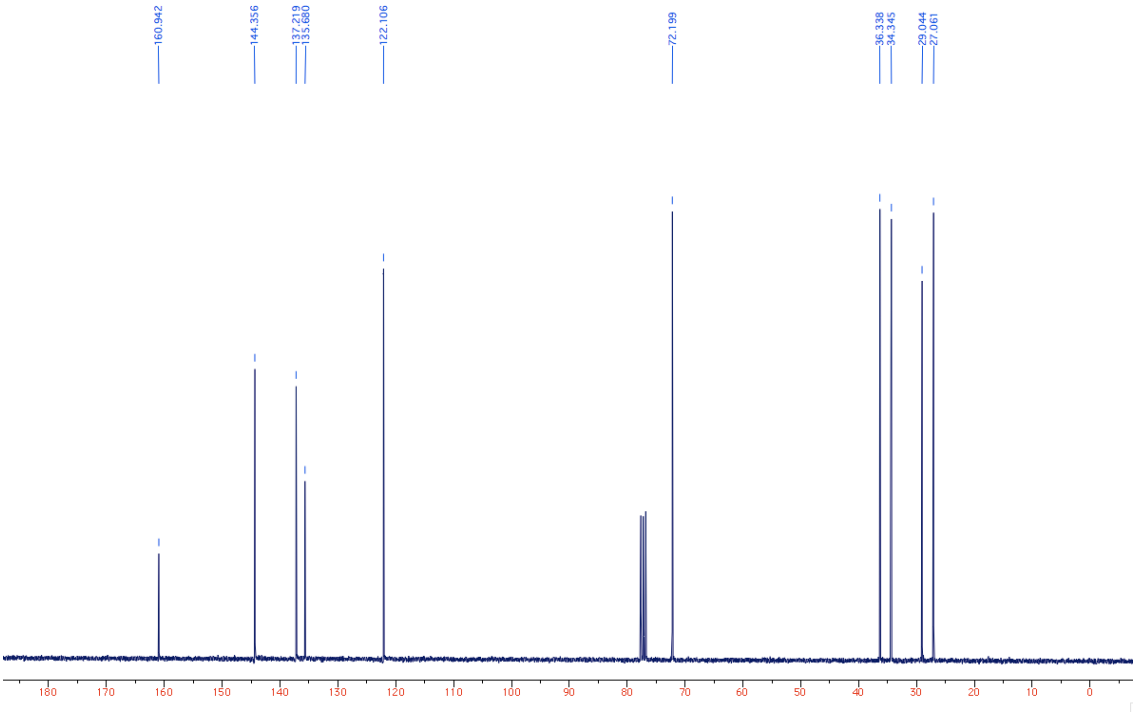


8-hydroxy-5,6,7,8-tetrahydroquinoline

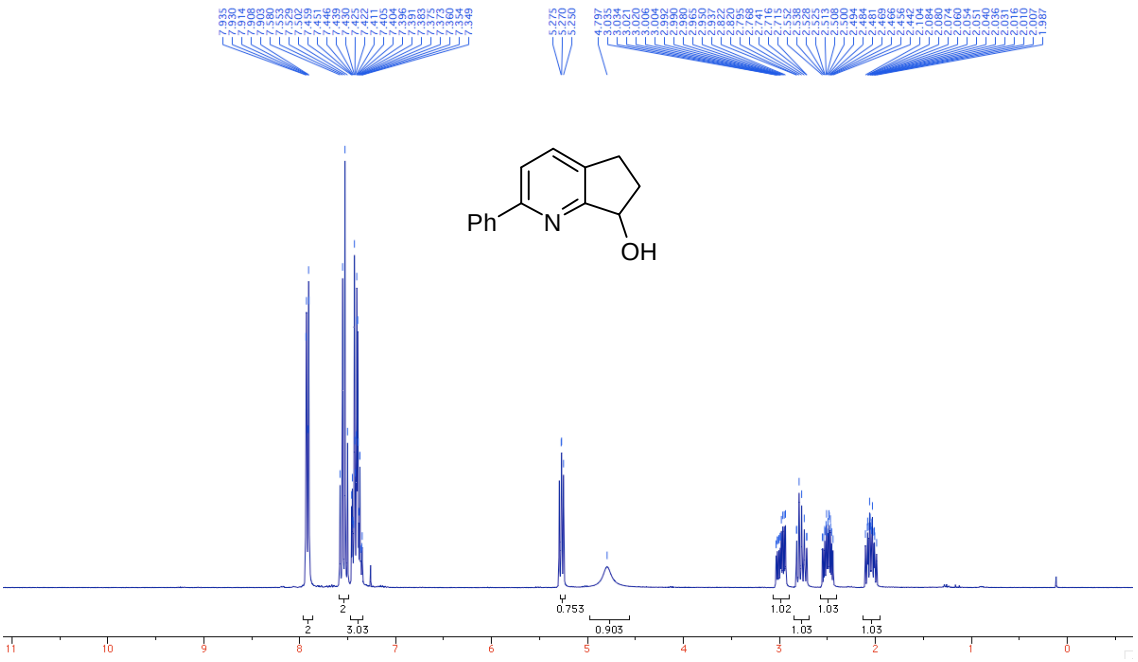


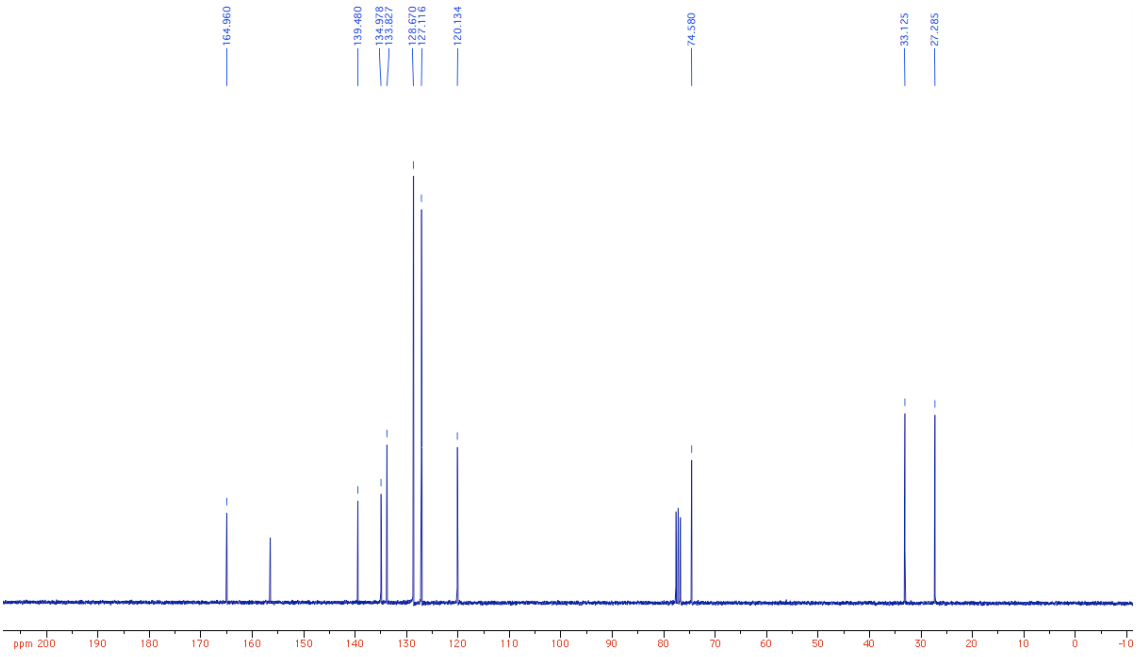
9-hydroxy-6,7,8,9-tetrahydro-5H-cycloheptapyridine



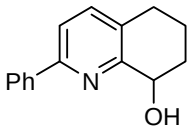


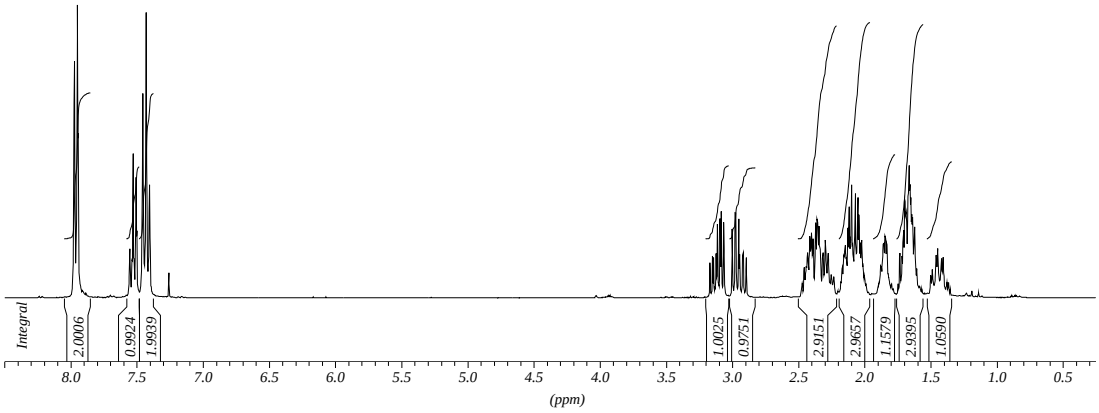
2-phenyl-7-hydroxy-6,7-dihydro-5H-cyclopentapyridine

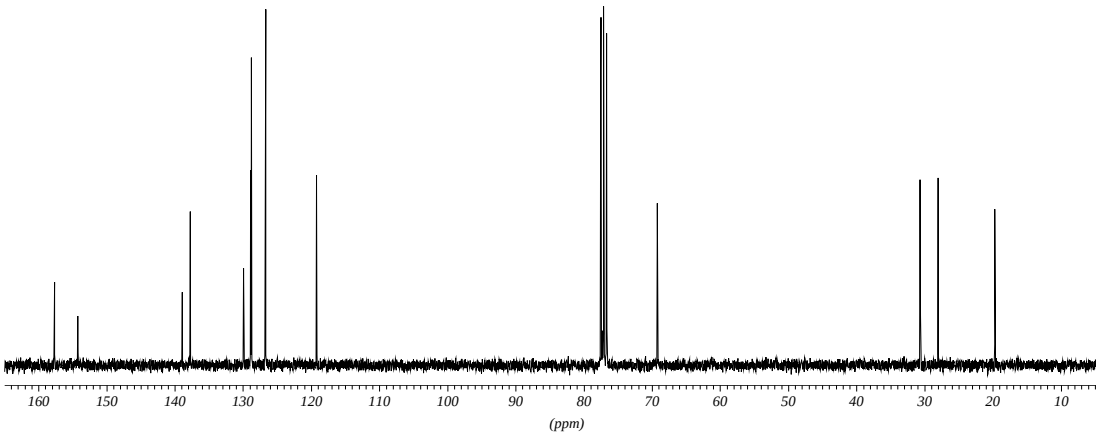




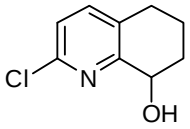
8-hydroxy-2-phenyl-5,6,7,8-tetrahydroquinoline

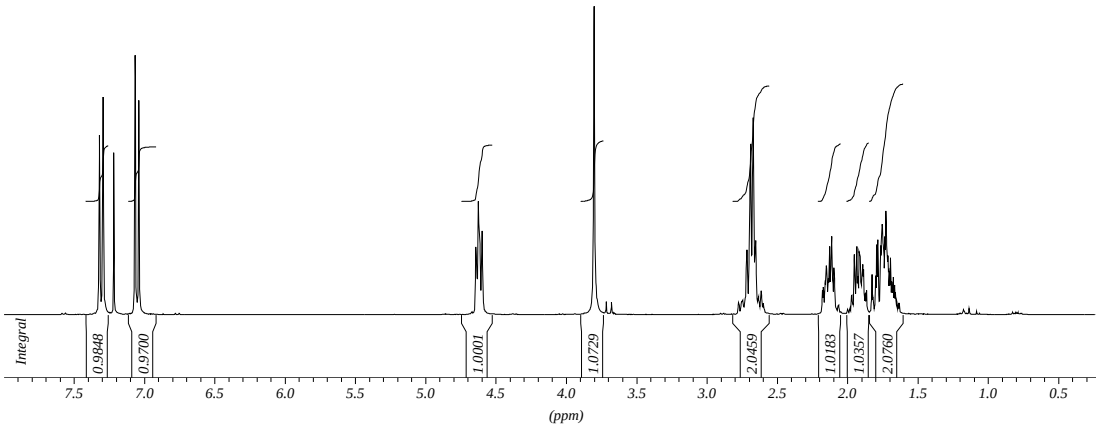


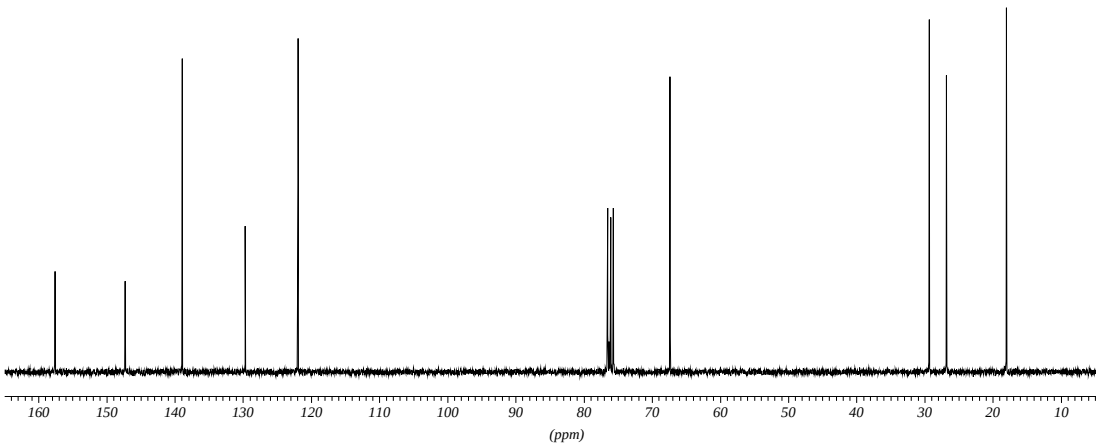




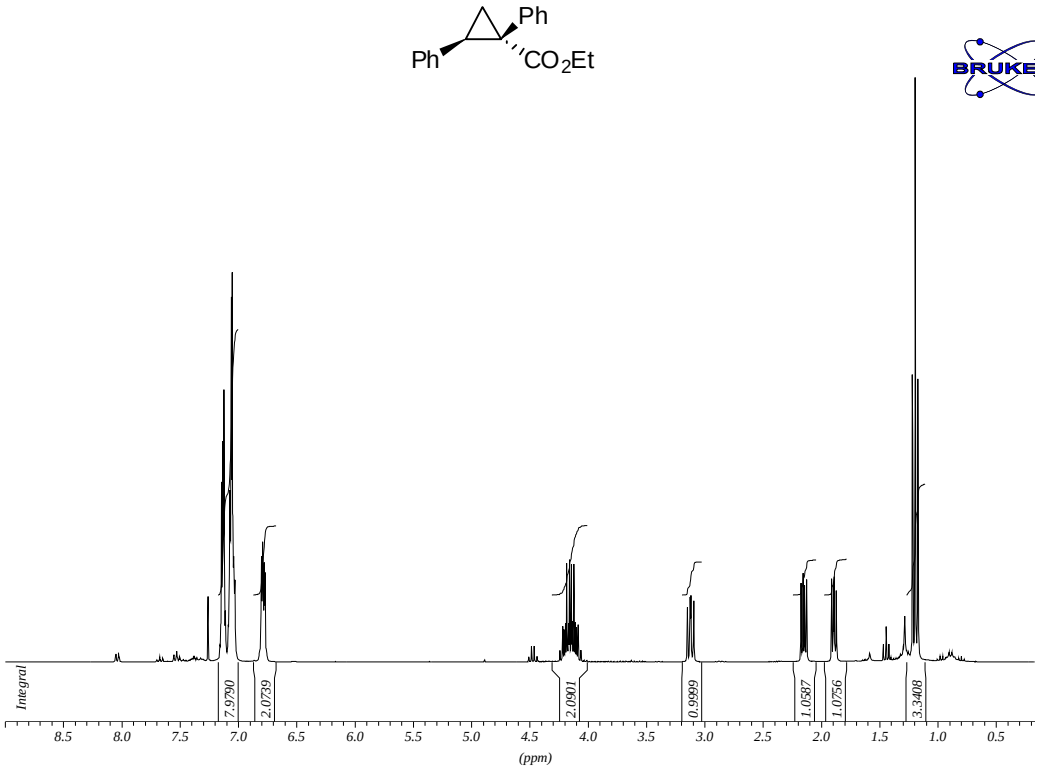
8-hydroxy-2-chloro-5,6,7,8-tetrahydro-2-quionoline

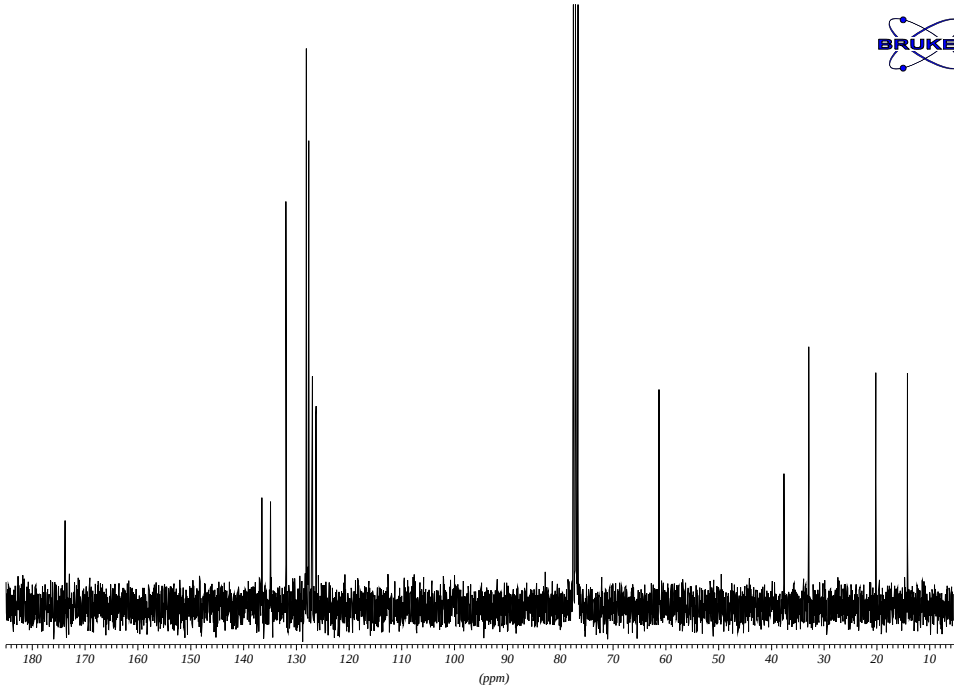




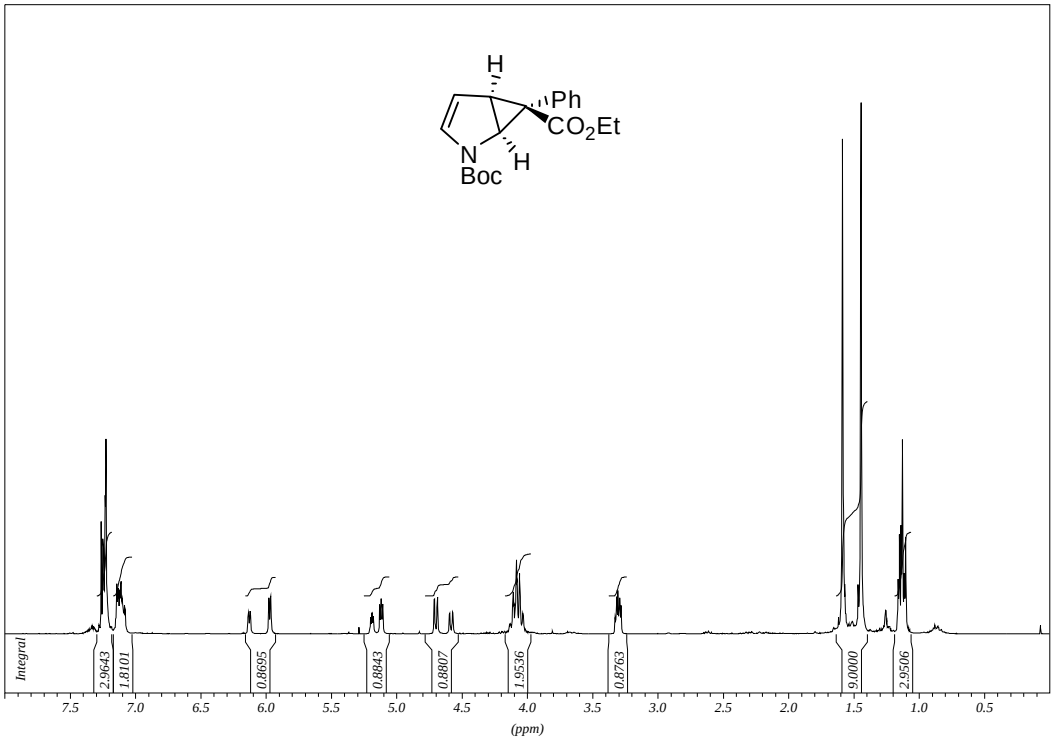


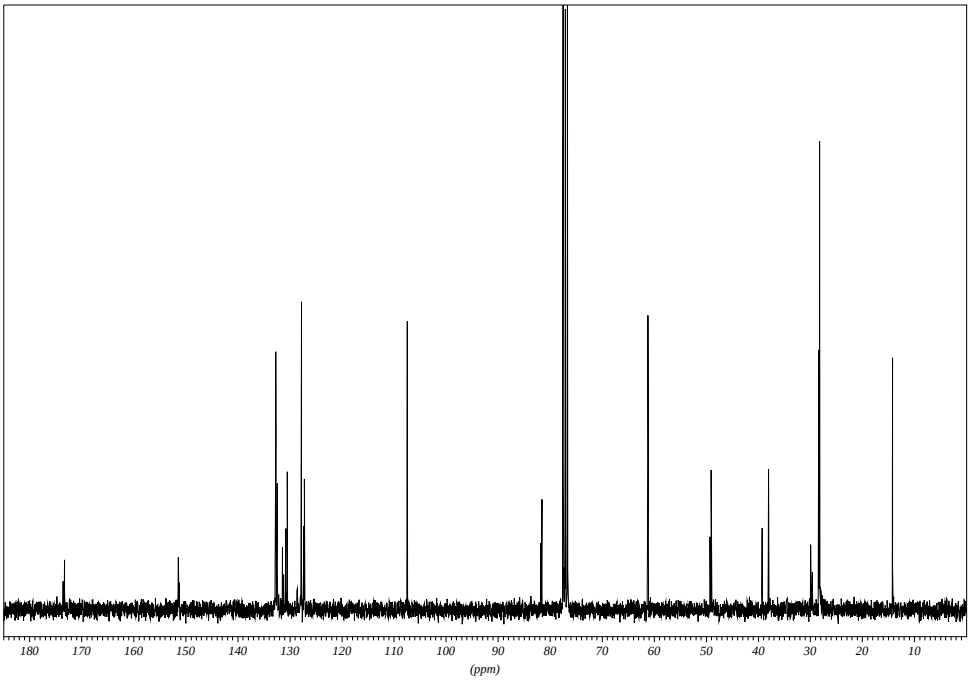
(1*S*, 2*R*)-ethyl-1,2-diphenylcyclopropanecarboxylate



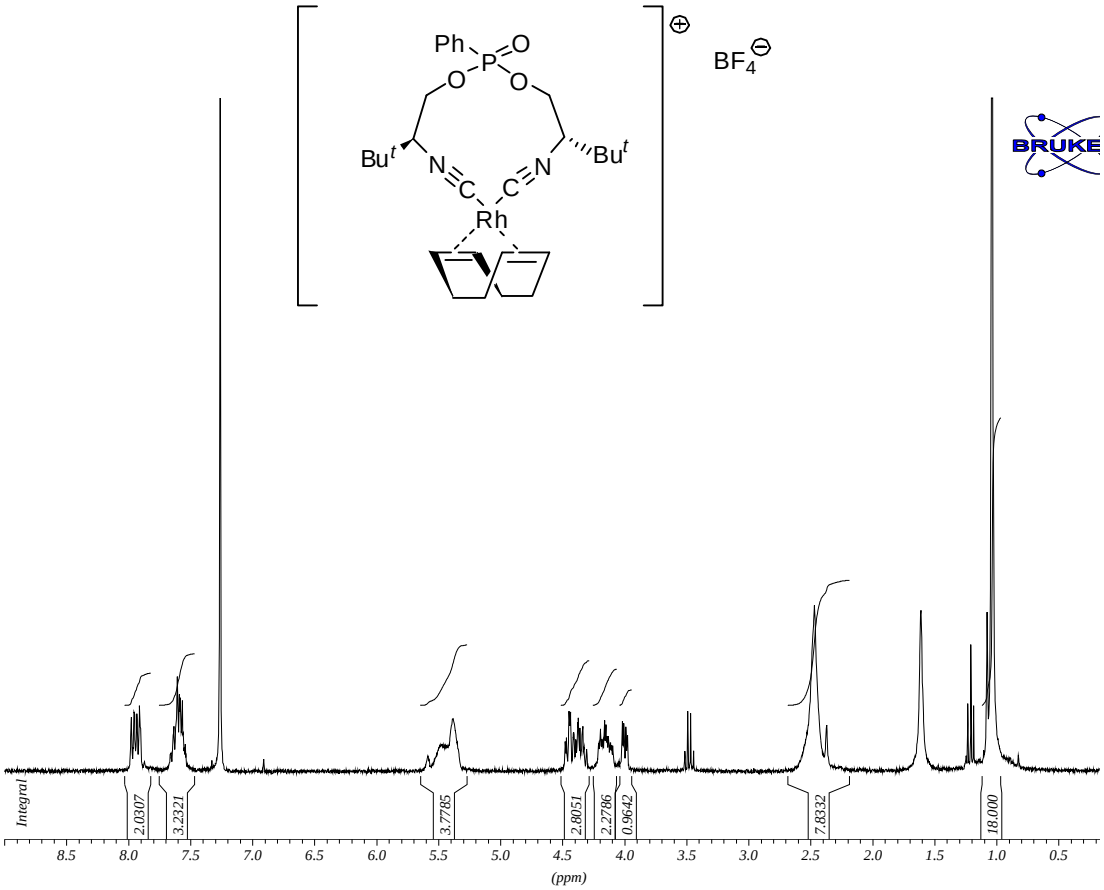


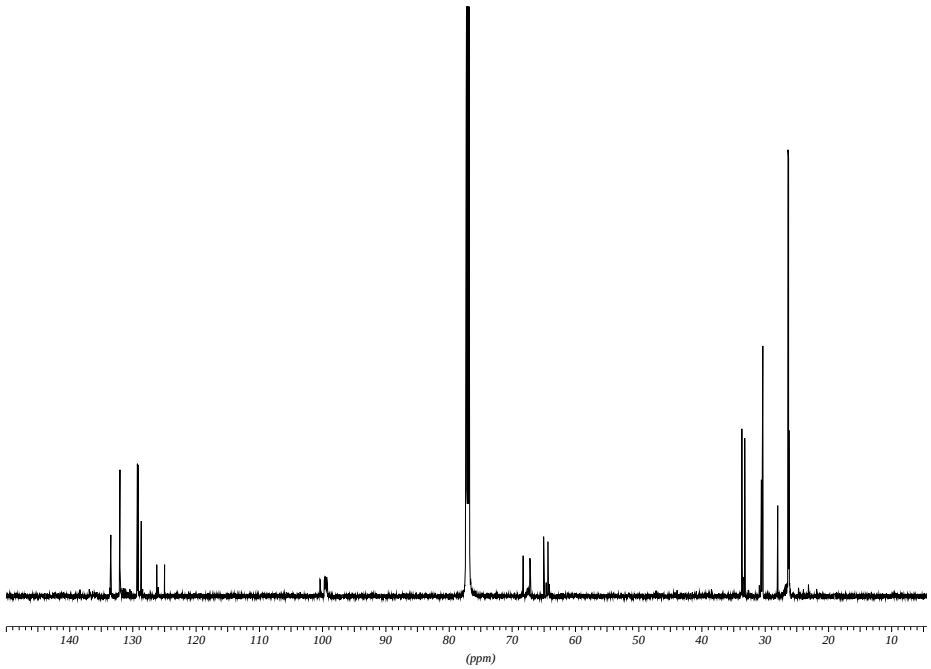
2-*tert*-butyl 6-ethyl 6-phenyl-2-azabicyclo[3.1.0]hex-3-ene-2,6-dicarboxylate



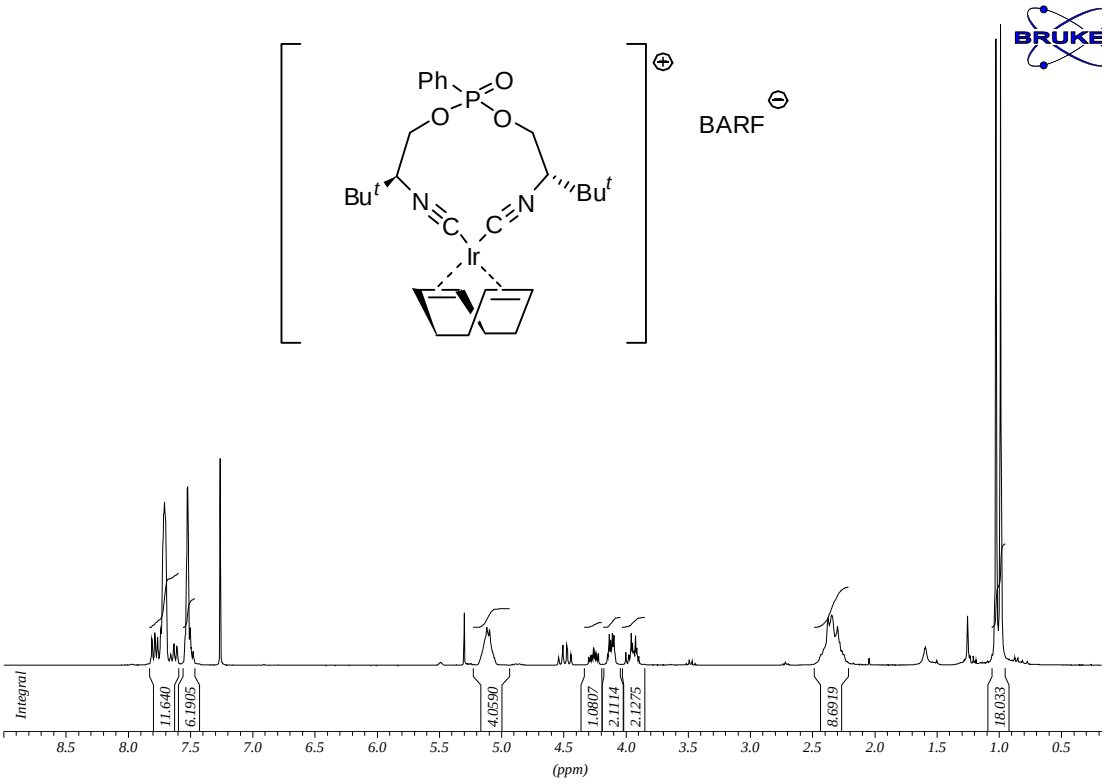


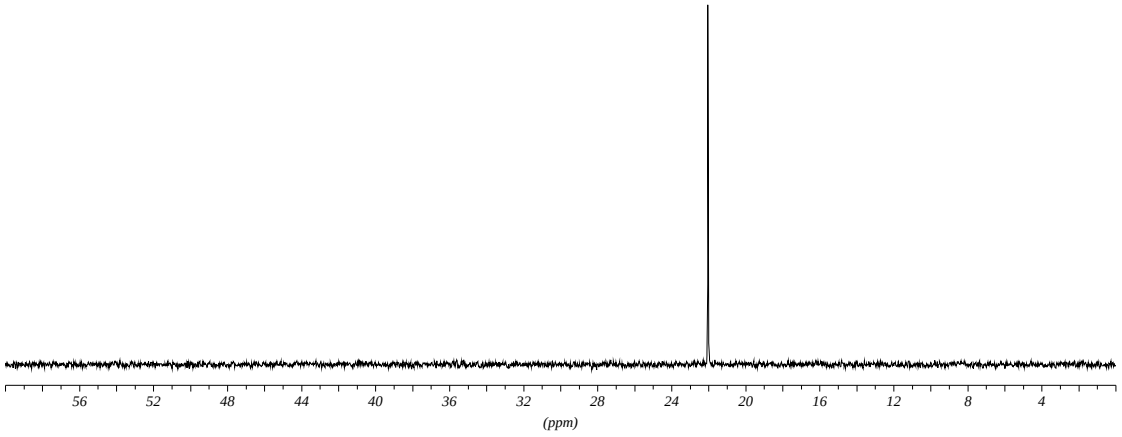
[Rh(COD)(^{t}Bu BINC)]BF_4 (120)



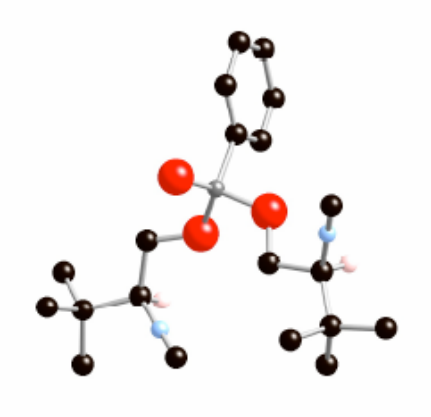


[Ir (COD) (^{t}Bu BINC)]BARF (121)





2. X-Ray Diffraction Structure



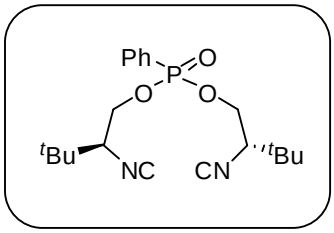


Table 1: Crystal data and structure refinement for **72b**

Crystal Data

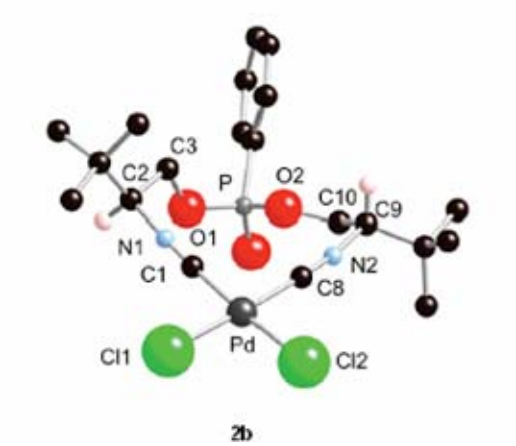
Empirical formula	$C_{20}H_{29}N_2O_3P$
Formula weight	376.42
Crystal size	0.330 x 0.320 x 0.250 mm
Crystal description	parallelepiped
Crystal colour	colourless
Crystal system	Orthorhombic
Space group	P 21 21 21
Unit cell dimensions	a = 6.02119(6) Å α = 90°
	b = 18.63424(18) Å β = 90°
	c = 19.10723(18) Å γ = 90°
Volume	2143.84(4) $Å^3$
Z, Calculated density	4, 1.166 Mg/m^3
Absorption coefficient	1.298 mm^{-1}
F(000)	808

Data Collection

Measurement device type	Oxford Diffraction Gemini Ultra
Measuremnet method	omega-scan
Temperature	123 K
Wavelength	1.54184 Å
Monochromator	graphite
Theta range for data collection	3.31 to 62.23°
Index ranges	-6<=h<=6, -18<=k<=21, -19<=l<=21
Reflections collected / unique	9780 / 3285 [R(int) = 0.0231]
Reflections greater I>2\s(I)	3077
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.74366

Refinement

Refinement method	Full-matrix least-squares on F^2
Hydrogen treatment	
Data / restraints / parameters	3285 / 0 / 241
Goodness-of-fit on F^2	1.097
Final R indices [I>2sigma(I)]	R1 = 0.0278, wR2 = 0.0750
R indices (all data)	R1 = 0.0296, wR2 = 0.0757
Absolute structure parameter	0.029(17)
Largest diff. peak and hole	0.171 and -0.171 e.Å^{-3}



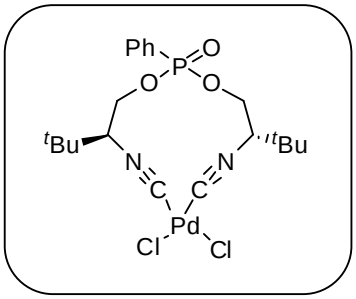


Table 2: Crystal data and structure refinement for **105b**.

Crystal Data

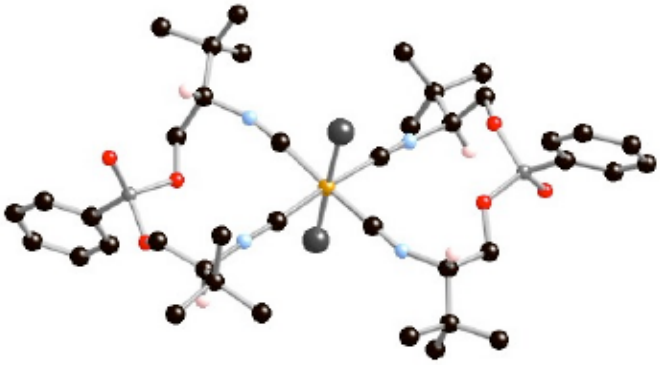
Empirical formula	$C_{20}H_{29}Cl_2N_2O_3PPd,C_6H_6$	
Formula weight	631.85	
Crystal size	0.160 x 0.050 x 0.050 mm	
Crystal description	platelike	
Crystal colour	colourless	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 10.0888(3) Å	α = 90°
	b = 13.1038(3) Å	β = 90°
	c = 23.1132(5) Å	γ = 90°
Volume	3055.60(13) $Å^3$	
Z, Calculated density	4, 1.373 Mg/m^3	
Absorption coefficient	7.223 mm^{-1}	
F(000)	1296	

Data Collection

Measurement device type	Oxford Diffraction Gemini Ultra
Measurement method	omega-scan
Temperature	123 K
Wavelength	1.54184 Å
Monochromator	graphite
Theta range for data collection	3.82 to 66.59°
Index ranges	-10<=h<=11, -15<=k<=15, -26<=l<=27
Reflections collected / unique	13503 / 4998 [R(int) = 0.0367]
Reflections greater I>2\s(I)	4711
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00000 and 0.58188

Refinement

Refinement method	Full-matrix least-squares on F^2
Hydrogen treatment	
Data / restraints / parameters	4998 / 0 / 316
Goodness-of-fit on F^2	1.046
Final R indices [I>2sigma(I)]	R1 = 0.0332, wR2 = 0.0799
R indices (all data)	R1 = 0.0355, wR2 = 0.0810
Absolute structure parameter	0.017(8)
Largest diff. peak and hole	1.061 and -0.284 e. $Å^{-3}$



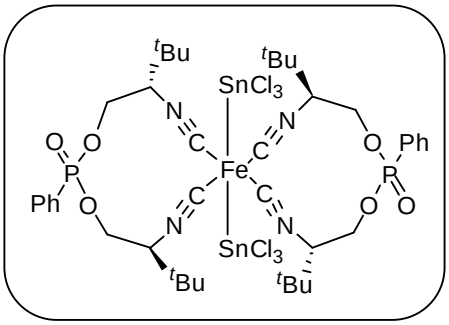


Table 3: X-ray structure of complex **119d** (Cl atoms on Sn were omitted for clarity).

Crystal Data

Empirical formula	$C_{40}H_{54}C_{l6}FeN_4O_6P_2Sn_2$	
Formula weight	1254.79	
Crystal size	0.18 x 0.14 x 0.08 mm	
Crystal description	prism	
Crystal colour	yellow	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 11.1616(18) Å	α = 90°
	b = 21.663(5) Å	β = 101.547(17)°
	c = 11.9040(16) Å	γ = 90°
Volume	2820.1(9) $Å^3$	
Z, Calculated density	2, 1.478 Mg/m^3	
Absorption coefficient	1.515 mm^{-1}	
F(000)	1256	

Data Collection

Measurement device type	STOE-IPDS diffractometer
Measuremnet method	rotation
Temperature	297(1) K
Wavelength	0.71073 Å
Monochromator	graphite
Theta range for data collection	1.86 to 25.30°
Index ranges	-13<=h<=13, -25<=k<=26, -13<=l<=13
Reflections collected / unique	33590 / 9649 [R(int) = 0.1039]
Reflections greater I>2\s(I)	4594
Absorption correction	Analytical
Max. and min. transmission	0.8093 and 0.6981

Refinement

Refinement method	Full-matrix least-squares on F^2
Hydrogen treatment	
Data / restraints / parameters	9649 / 1 / 550
Goodness-of-fit on F^2	0.836
Final R indices [I>2sigma(I)]	R1 = 0.0559, wR2 = 0.1119
R indices (all data)	R1 = 0.1206, wR2 = 0.1302
Absolute structure parameter	0.02(4)
Largest diff. peak and hole	0.767 and -0.608 e. $Å^{-3}$

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- CSIR-UGC/NET: Qualified for junior research fellowship, December 2005.
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- Synthesis and Applications of Chiral bis(isonitrile) Ligands-(Poster Presentation) - IASOC 2008, Ischia, Italy.
- Efficient aerobic Wacker oxidation of styrenes using novel palladium bis(isonitrile) catalysts -(Poster Presentation)-2nd German Indian Symposium (2009), Liepzig, Germany.
- Application of Iron (II) –bis(isonitrile) catalysts in the Asymmetric Transfer Hydrogenation of Ketones- (Poster Presentation) -5th Heidelberg Forum of Molecular Catalysis (2009), Heidelberg, Germany.

PUBLICATIONS

- **Anu Naik**, Liu Meina, Manfred Zabel, and Oliver Reiser*, Efficient aerobic Wacker oxidation of styrenes using novel palladium bis(isonitrile) catalysts, *Chem. Eur. J*. **2010**, *16*, 1624.
- **Anu Naik**, Tapan Maji, Oliver Reiser*, Iron (II)-Bis(isonitrile) Complexes: Novel Catalysts in Asymmetric Transfer Hydrogeantions of Aromatic and Heteroaromatic Ketones. (Submitted).

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