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Synthesis And Applications Of Cyclopalladated Complexes Containing An (sp3)c-pd Bond

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SYNTHESIS AND APPLICATIONS OF CYCLOPALLADATED COMPLEXES CONTAINING AN (sp^3)C–Pd BOND

By

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This dissertation, submitted by Gerard Chepnda Dickmu in partial fulfillment of the requirements for the degree of Doctor of Philosophy from the University of North Dakota, has been read by the Faculty Advisory Committee under whom the work has been done, and is hereby approved.

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LIST OF ABBREVIATIONS

Ac	Acetyl
Acac	Acetylacetone
Ar	Aryl
Bn	Benzyl
Boc	*tert*-Butyloxycarbonyl
^{t}Bu	*tert*-Butyl
COD	Cyclooctadiene
CPC	Cyclopalladated complex
Cy	Cyclohexyl
DABCO	Diazabicyclooctane
dba	Dibenzylideneacetone
DBU	Diazabicycloundecene
DCC	1,3-Dicyclohexylcarbodiimide
DCM	Dichloromethane
de	Diastereomeric excess
DIPEA	Diisopropylethylamine
DMA	Dimethylacetamide
DME	1,2-Dimethoxyethane
dr	Diastereomeric ratio

ee	Enantiomeric excess
Et	Ethyl
EPR	Electron paramagnetic resonance
GC	Gas chromatography
HMPA	Hexamethylphosphine
HPLC	High performance liquid chromatography
$KPPh_2$	Potassium diphenylphosphide
Me	Methyl
Mes	2,4,6-Trimethylbenzyl
Naph	Naphthyl
NMP	*N*-methyl-2-pyrrolidone
NMR	Nuclear magnetic resonance
Ph	Phenyl
PHOX	Phosphino-oxazoline
Pr	Propyl
^{i}Pr	Isopropyl
TBS	*tert*-Butyldimethylsilyl
TEA	Triethylamine
Tf	Trifluoromethanesulfonyl
TfO	Trifluoromethanesulfonate
TLC	Thin-layer chromatography
THF	Tetrahydrofuran
TMEDA	*N,N,N′,N′*-Tetramethylethylenediamine

TMS	Tetramethylsilane
TOF	Turnover frequency
Tol	Tolyl
Xyl	3,5-Dimethylphenyl

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ABSTRACT

Cyclopalladated complexes (CPCs) possess a number of important properties and have been used in various application studies. However, preparation and uses of optically active CPCs with an (sp^3)C–Pd bond have not been thoroughly investigated.

In this dissertation, the synthesis and applications of new enantiopure CPCs derived from naturally occurring and optically active D-camphor and L-fenchone are described. The preparation of these CPCs, which contain an (sp^3)C–Pd bond, was accomplished by cyclopalladation of D-camphor *O*-methyloxime, L-fenchone *O*-methyloxime, L-fenchone oxime and camphor *N,N*-dimethylhydrazone using Pd(II) salts such as $Pd(OAc)_2$ and $Pd(MeCN)_2Cl_2$.

Phosphination reactions of CPCs derived from D-camphor *O*-methyloxime and L-fenchone *O*-methyloxime, as well as other *CN*-, *CS*- and *CP*-dimeric CPCs having an (sp^3)C–Pd bond, were investigated using $KPPh_2$. These alternative CPCs were obtained from 8-methylquinoline, tri-(*O*-tolyl)phosphine, 2,6-dimethylthioanisole and trimesitylphosphine. In each case, when the CPC reacted with 4.5 equiv. of $KPPh_2$, the corresponding *NP*-, *SP*- and *PP*-ligands were isolated in 13–51% yield. Reactions using only 1 equiv. of $KPPh_2$ gave μ-chloro-μ-diphenylphosphido-CPCs as main products in 26–56% yield.

Proposed structures of new compounds obtained in the reactions were confirmed by spectroscopic methods and in some cases by X-ray crystallography. Purity and

elemental composition of the synthesized complexes and organic compounds were confirmed by either satisfactory elemental analysis or high resolution mass spectra data.

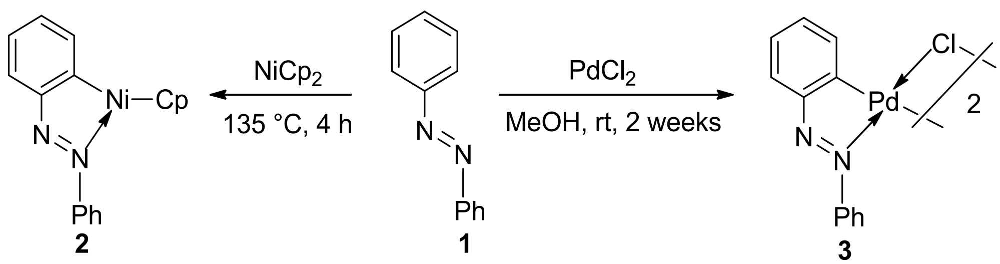
CHAPTER I

INTRODUCTION

I.1. Cyclopalladated Complexes Containing an (sp^3)C–Pd Bond

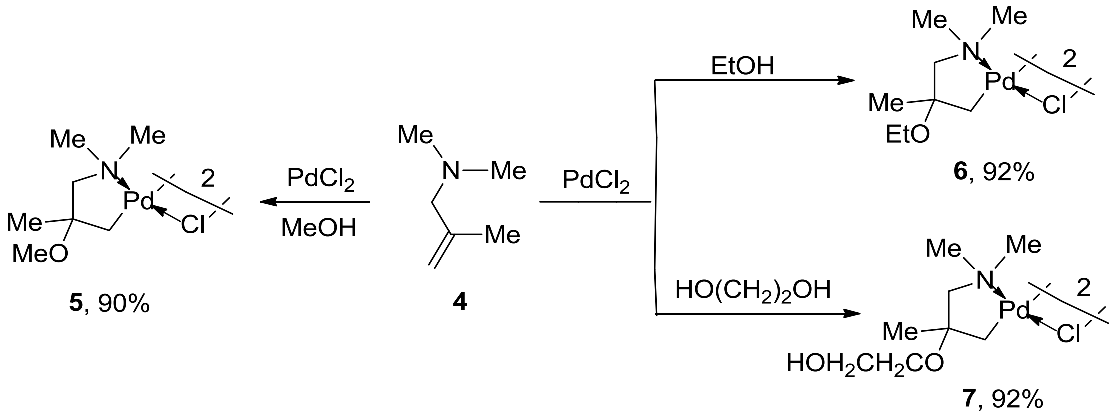
Cyclopalladated complexes (CPCs) are organometallic compounds with a sigma C–Pd bond, intramolecularly stabilized by a dative bond between Pd and a heteroatom to form three-, four-, five-, six- or seven-membered palladacycles. The heteroatoms commonly involved in CPC formation include N and P and more rarely S, Se, As and O.

Cyclopalladated compounds have been known since the beginning of 1960s. In 1963, Kleiman and Dubeck investigated the reaction of dicyclopentadienylnickel ($NiCp_2$) and azobenzene (**1**) under both solvent and solvent-free conditions to furnish a new complex **2** (Scheme 1).[1]



Scheme 1. Synthesis of compound **2** and CPC **3** from azobenzene.

In 1965, Cope and Siekman reported an analogous reaction with $PdCl_2$ in an alcoholic solution to generate the first known palladacycle (**3**) (Scheme 1).[2] Soon after this study, five-membered palladacycles were obtained when *N,N*-dimethylbenzylamines were reacted with $PdCl_2$ under similar conditions.[2] These first palladacycles contained an aromatic (sp^2)C–Pd bond.[2] Cope et al. later investigated the reaction between Pd(II) reagents and allylic amines.[3] They found that *N,N*-dimethyl-2-methylallylamine (**4**) reacted with Li_2PdCl_4 or $PdCl_2$ in an alcohol to give the corresponding CPCs **6** and **7** (Scheme 2).[3] These are the first examples of the palladacycles with an (sp^3)C–Pd bond.[3]



Scheme 2. Synthesis of CPCs from *N,N*-dimethyl-2-methylallylamine.

Cyclometallation reactions have been observed with many transition metals, including Ru, Rh, Os, Pt, Ir, Fe, Ni, Co, Mn and others.[2, 4-8] Organopalladium compounds are especially valuable for several reasons. The C–Pd bond is known to react with numerous reagents to reliably yield functionalized products.[9-13] This versatility is in part due to the tolerance of palladium reagents to many functional groups and also due to the selective reactivity of cyclopalladated intermediates at the C–Pd bond.[14-16] Thus, cyclopalladation is an excellent route to many different bond linkages, including carbon-carbon, carbon-oxygen, carbon-nitrogen, carbon-sulfur, carbon-phosphorus and carbon-halogen bonds. Furthermore, the compatibility of palladium reagents such as $Pd(OAc)_2$ with a variety of directing groups enables the use of a wider variety of substances compared to other transition metal reagents. Finally, most reactions involving palladacycles are not sensitive to moisture and air, making the synthesis of complex organic molecules more facile.

Aliphatic palladacycles (here and later, all CPCs and palladacycles with an (sp^3)C–Pd will be called aliphatic) have a characteristic σ-bond between palladium and an sp^3–hybridized carbon of the ligand.[17-19] The (sp^3)C–H bond is generally inert due to the absence of either empty low-energy orbitals or filled high-energy orbitals, which can overlap with metal orbitals.[20, 21] Thus, reports of CPCs with an (sp^3)C–Pd bond are far outnumbered by those of palladacycles containing an (sp^2)C–Pd bond.

I.2. Classification of CPCs with an (sp^3)C–Pd Bond

CPCs containing an (sp^3)C–Pd bond are broadly divided into two types: benzylic (e.g., **8–10** in Chart 1) and aliphatic (e.g., **5–7** in Scheme 2). Benzylic CPCs are those in which the metal is bonded to a benzylic carbon, while palladium in aliphatic CPCs is bonded to an sp^3-hybridized carbon. The organic moiety of both benzylic and aliphatic CPCs can be either an anionic four-electron (*CY*) or six-electron (*YCY*) donor (Figure 1).[4, 22] CPCs of the latter type are examples of pincer complexes.

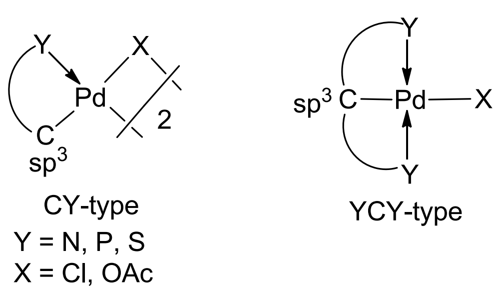


Figure 1. *CY*- and *YCY*-palladacycles.

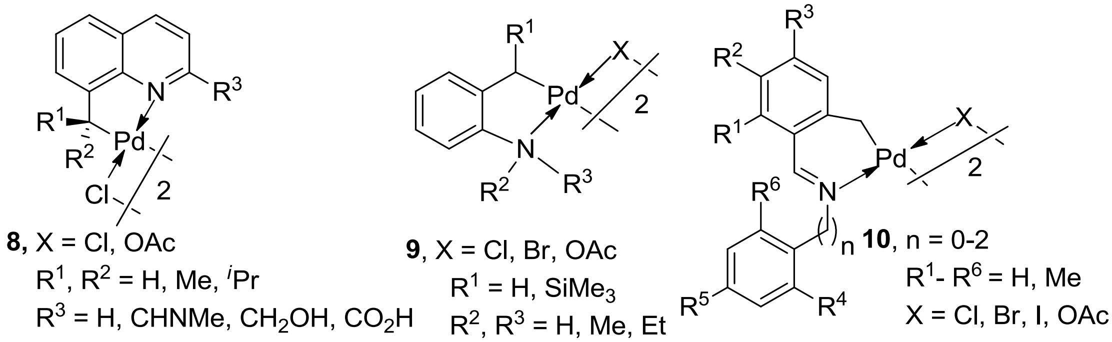


Chart 1. Examples of benzylic *CN*-palladacycles.

While all *YCY*-type complexes are mononuclear, the *CY*-analogs can be mono-, di-, and trinuclear.[4, 22] Di- and trinuclear complexes can exist as cis and trans geometric isomers with halogen, acetate or other bridging moieties (Figure 2).[4, 22] Acetato-bridged trinuclear aliphatic CPCs derived from 1-*tert*-butylpyrazole,[23] *N,N*-dimethylneopentylamine[24] and 2-*tert*-butyl-4,4-dimethyl-2-oxazoline[25] have been reported by the research groups of Alonso, Hiraki, and Balavoine, respectively. Preparation of the acetato-bridged trinuclear benzylic CPC derived from 2-(dimethylamino)toluene has been discussed by Pfeffer.[26, 27] Although acetate and chloride are the most common bridging ligands in CPCs with (sp^2)C–Pd bonds, *N,O*-imidate ligands like succinimidate, phthalimidate and maleimidate[28, 29] as well as carboxylato groups like oxalato, *n*-alkylcarboxylato, *n*-oxaalkylcarboxylato, *p*-alkoxyphenylacetato and *p*-alkoxybenzoato have also been reported.[30]

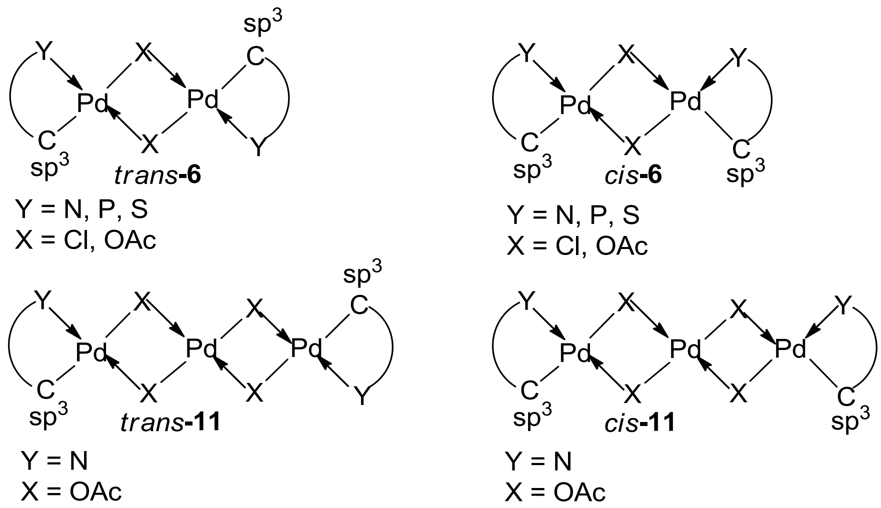


Figure 2. Trans and cis geometric isomers of CPCs.

CPCs can also be classified based on the donor heteroatom bonded to the metal, e.g., *CN*-, *CP*-, *CS*- and *CO*-type palladacycles. The donor atom Y is responsible in part for the ring size of CPCs since it delivers the palladium reagent to a particular C–H bond where palladation occurs. While *CY*-type benzylic CPCs contain mostly five- or six-membered palladacycles,[31-34] their aliphatic counterparts can also be three-[35, 36] or four-membered.[37-39]

I.2.1. *CN*-Palladacycles

Common directing groups for benzylic *CN*-CPCs include the pyridine, aniline and imine moieties. Hartwell et al. synthesized the first example of a benzylic *CN*-palladacycle (**10**) from 8-methylquinoline in 1970 via C–H bond activation using Li_2PdCl_4.[40] Thereafter, many research groups reported other examples, particularly those derived from 2-substituted 8-alkylquinolines,[41-47] *ortho*-alkyl-substituted *N,N*-dialkylanilines,[27, 48-50] and *N*-mesitylbenzylideneamines.[51-55] In 1978–1981, Deeming and Rothwell studied the cyclopalladation of 8-alkylquinolines with various substituents (Me, Br, CHO, CH=NMe, CH_2OH and CO_2H) at the 2 position.[42, 43, 47] They determined that the 2-substituted derivatives of 8-alkylquinolines were readily palladated using $Pd(OAc)_2$ when the substituent was either CH=NMe, CH_2OH or CO_2H, while every attempt to metalate the analogs with Me, Br, or CHO groups did not work.[42, 43, 47] During the same time, Pfeffer et al., while studying reactions of *ortho*-alkyl-substituted *N,N*-dialkylanilines with $LiPdCl_4$, observed demethylation at the NMe_2 group to give *N*-alkylanilines.[26, 27, 56] Reactions of *ortho*-alkyl-substituted *N,N*-dialkylanilines with $Pd(PhCN)_2Cl_2$ and $Pd(OCCF_3)_2$ provided coordination complexes.[26, 27, 56] They were able to palladate only *ortho*-methyl-substituted *N,N*-dialkylanilines using $Pd(OAc)_2$ to get trinuclear CPCs which were converted to the dinuclear chloro-bridged analogs upon treatment with LiCl.[26, 27, 56] The dinuclear μ-Cl-CPC was subsequently reacted with AgOAc to regenerate the acetate-complexes.[26, 27, 56] The research groups of Gómez, Sales, Liu, Fernández and Munno have investigated the cyclopalladation of *N*-mesitylbenzylideneamines using $Pd(OAc)_2$.[52-55, 57] Palladation preferentially took place at the aromatic carbon to give five-membered endo-palladacycles.[52-55] The six-membered analogs generated via palladation at a benzylic carbon required higher temperatures.[52-55]

Aliphatic *CN*-palladacycles have been reported with a variety of nitrogen-containing directing groups: oxime (including their *O*-substituted derivatives), hydrazone, ketazine, oxazoline, pyridine, amine, benzothiazole, pyrazole, urethane and acetanilide. Aliphatic five- and six-membered oxime palladacycles **12** include those with ordinary oxime (NOH), *O*-methyl oxime (NOMe) or *O*-acetyl oxime (NOAc) directing groups.[17, 58-65] In 1978, Shaw et al., synthesized the first example of a CPC[58] containing an NOH directing group while those containing the NOAc directing group were introduced simultaneously in 1985 by the groups of Nishilyama,[60] and Baldwin.[59, 61] CPCs with a hydrazone directing group (**13a**) are usually five-membered and were first introduced by Shaw and his collaborators in 1978.[58] Such CPCs have an *sp*^{3} nitrogen coordinated to the Pd center. In 1983, Galli and Gasparrini reported a case of a hydrazone CPC (**13b**) in which the *sp*^{2} nitrogen was coordinated to the Pd center.[66] This could be attributed to the stability of five-membered palladacycles compared to the six-membered rings that are formed if coordination occurs at the *sp*^{3} nitrogen.[66] In 1994 and 1995, Echavarren et al. worked on the synthesis of the PPh_3 adducts of type **13** CPCs upon reaction of the preligand (*N,N*-dimethylhydrazone) with $Pd(PPh_3)_2Cl_2$ and NaOAc in MeCN.[67, 68] Shaw et al. synthesized five-membered ring CPCs of type **14** containing ketazine as the directing group.[63] Clinet et al. worked on the five-membered ring CPCs derived from oxazoline (type **15**).[25] Our group also reported such CPCs.[18, 69] In 1983 through 1992, Hiraki and his collaborators studied five- and six-membered ring CPCs (**16**) containing the pyridine moiety as the directing group.[70-72] Recently, Rourke et al. reported five-membered ring CPCs **16** containing the pyridine moiety as the directing group.[73, 74] Aliphatic *CN*-palladacycles (**17**) containing the amino directing group were introduced in 1967 by Cope et al.[3] and since then many of such CPCs have been reported.[19, 24, 75-85] In 1986, Hiraki et al. reported five-membered CPCs (**18**) with the benzothiazole moiety as the directing group,[86] while in 1992, Alonso et al. synthesized five-membered CPCs (**19**) with the pyrazole moiety as the directing group.[23] In 1994, Henderson et al. reported four-membered palladacycles **20** and **21** derived from urethane and acetanilide ligands.[87-89]

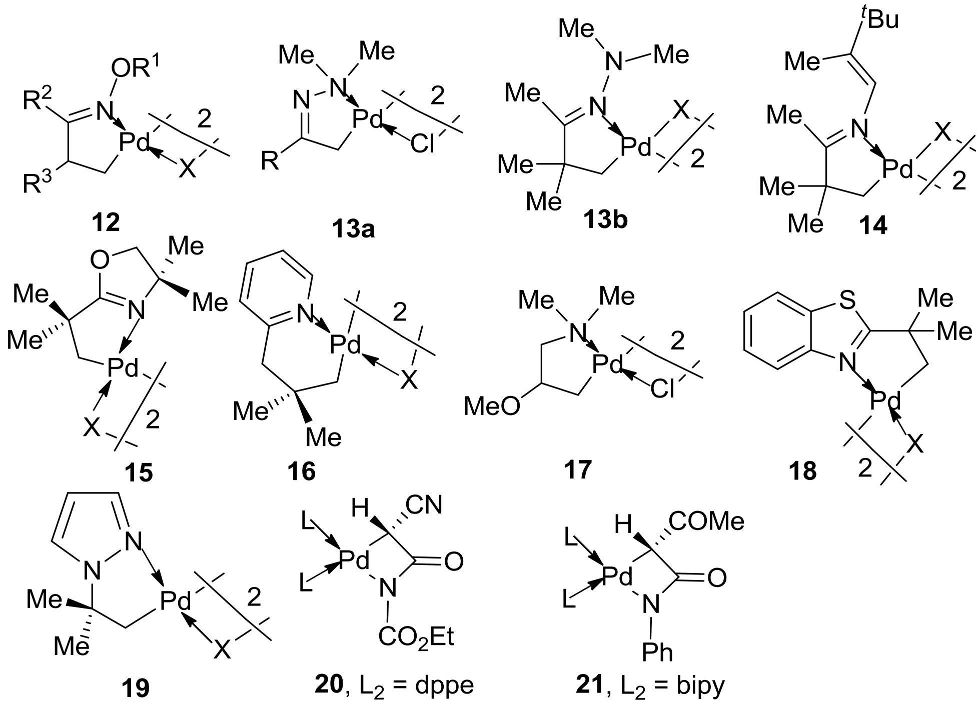


Chart 2. Aliphatic *CN*-palladacycles with different directing groups.

I.2.2. *CP*-Palladacycles

Benzylic *CP*-CPCs are usually five-membered and synthesized from aryl- or benzylphosphines. Benzylic CPCs **22** were first reported in 1972 by Shaw et al.[90] and since then many groups have either worked on their synthesis or their application as catalysts in cross-coupling reactions.[31, 32, 91-105] Recently, Hou et al. prepared rare six-membered benzylic CPCs **23**.[101] Joshaghani et al. also recently synthesized a benzylic biphenyl-based phosphine CPC **25**.[93] A unique three-membered benzylic palladacycles **24** was obtained from bidentate derivatives of a phosphaalkene.[106]

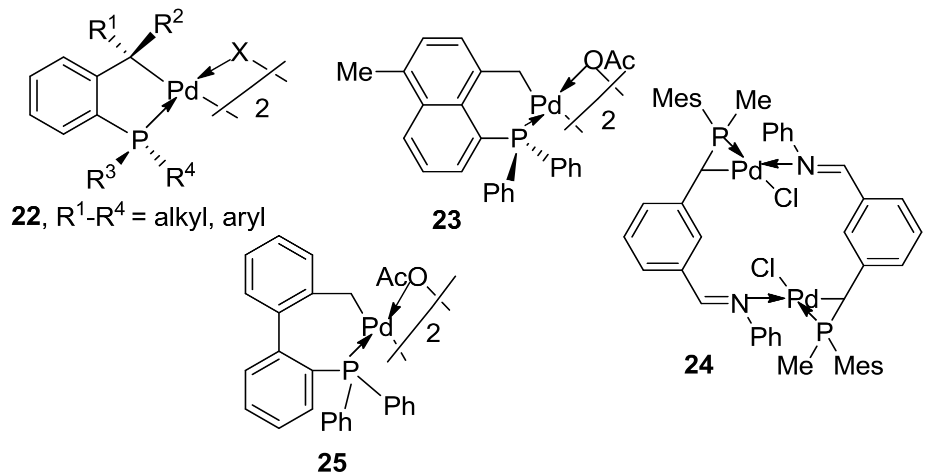


Chart 3. Benzylic *CP*-palladacycles.

The majority of aliphatic *CP*-CPCs prepared from alkylphosphines are five-membered. Examples include palladacycles (type **26**) obtained by the palladation of ^{t}Bu$_2$^{i}PrP and ^{i}Pr$_3$P.[107-109] Four-membered P-containing palladacycles are also known. In 1977, Goel et al. synthesized the four-membered ring CPC **27** from ^{t}Bu$_3$P.[37-39] Later, Werner and Kraus developed a method to form similar palladacycles from ^{t}Bu$_3$P and ^{t}Bu$_2$PhP by the reaction of their coordination complexes with AgOAc.[110] Interestingly, Milstein isolated the dinuclear five-membered aliphatic *CP*-palladacycle **28** with a mono-bridging diphosphine.[108]

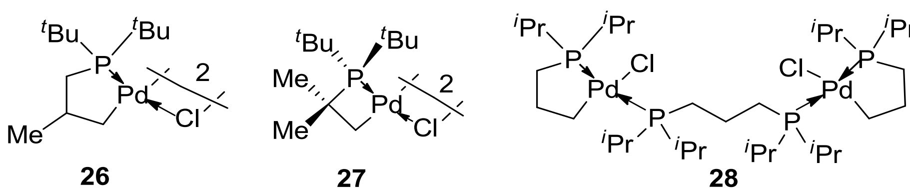


Chart 4. Examples of *CP*-palladacycles.

I.2.3. *CS*-Palladacycles

Like phosphorus, sulfur is a relatively soft donor atom and well suited for the soft Lewis acid Pd(II). Both benzylic and aliphatic palladacycles containing a sulfur directing group have been reported.

In 1989, Pfeffer et al. reported benzylic five-membered *CS*-CPCs (**29**) synthesized from 2,6-dimethylthioanisole.[111, 112] More recently, Vicente et al. discussed the synthesis of benzylic five-membered *CS*-CPCs from aryldithioacetals.[113, 114]

Aliphatic *CS*-palladacycles can be derived from a sulfide, thioamide, or thiourea. The first sulfide-derived palladacycle **30** was published by Okawara et al. in 1976.[35]. That complex had a rare three-membered ring.[35] The five-membered ring sulfide palladacycles of type **31** were reported by the groups of Holton and Pfeffer.[75, 82, 111, 112] An unusual method was described by Albéniz et at. for four- to six-membered palladacycles of type **30** by insertion reactions at the Pd-aryl bond.[115] Leaver et al. made available the five-membered thioamide-derived aliphatic *CS*-CPC **32**.[116] Groups of Dunina and Pfeffer reported related five-membered thioamide-derived CPCs **33**.[111, 117, 118]

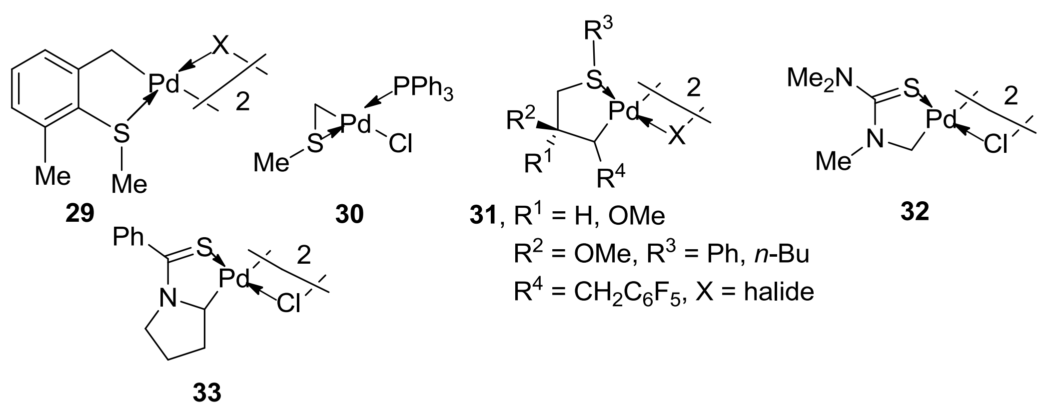


Chart 5. Examples of *CS*-palladacycles.

I.2.4. *CO*-Palladacycles

Despite the fact that oxygen-containing moieties are relatively hard ligands, *CO*-CPCs have also been reported. Palladacycles derived from aldehydes (**34**) were obtained by the groups of Elsevier, Vrieze, Sen and Osakada.[119-123] Singh et al. also reported the aliphatic *CO*-palladacycle **35** with a hydroxyl donor moiety.[118, 124] Recently, Lindsell et al. observed the oxidation addition of 2-hydroxymethylbenzyl chloride with $Pd(PPh_3)_4$ in toluene to afford the benzylic CPC **36**.[125]

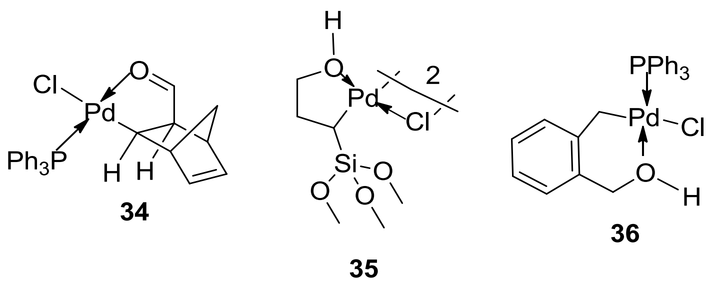
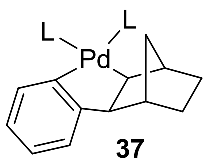


Chart 6. Example of *CO*-palladacycles.

I.2.5. *CC*-Palladacycles

In 1999, Catellani et al. reported the *CC*-palladacycles **37**, in which one of the carbon atoms bonded to the palladium center was sp^3-hybridized while the other was sp^2-hybridized.[126-129] Earlier in 1998, Hashni et al. obtained complex **38** with both carbon atoms sp^3-hybridized.[130, 131]



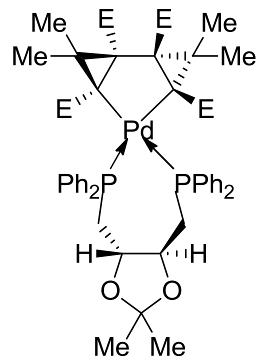


Chart 7. Examples of *CC*-palladacycles.

I.2.6. Pincer Palladacycles

Pincer palladacycles contain ligands with three or sometimes four chelating atoms. They can be subdivided based on the number (tridentate or tetradentate) and type of chelating atoms, e.g., tridentate *CNO*,[132, 133] *NCN*,[134] *NCO*,[135] *NNC*,[136-138] *CNN*,[139, 140] *CNC*,[138, 141] *CNS*[142] and *PCP*[143-148] and tetradentate *CNNC*[138, 149] and *CNNO*.[150]

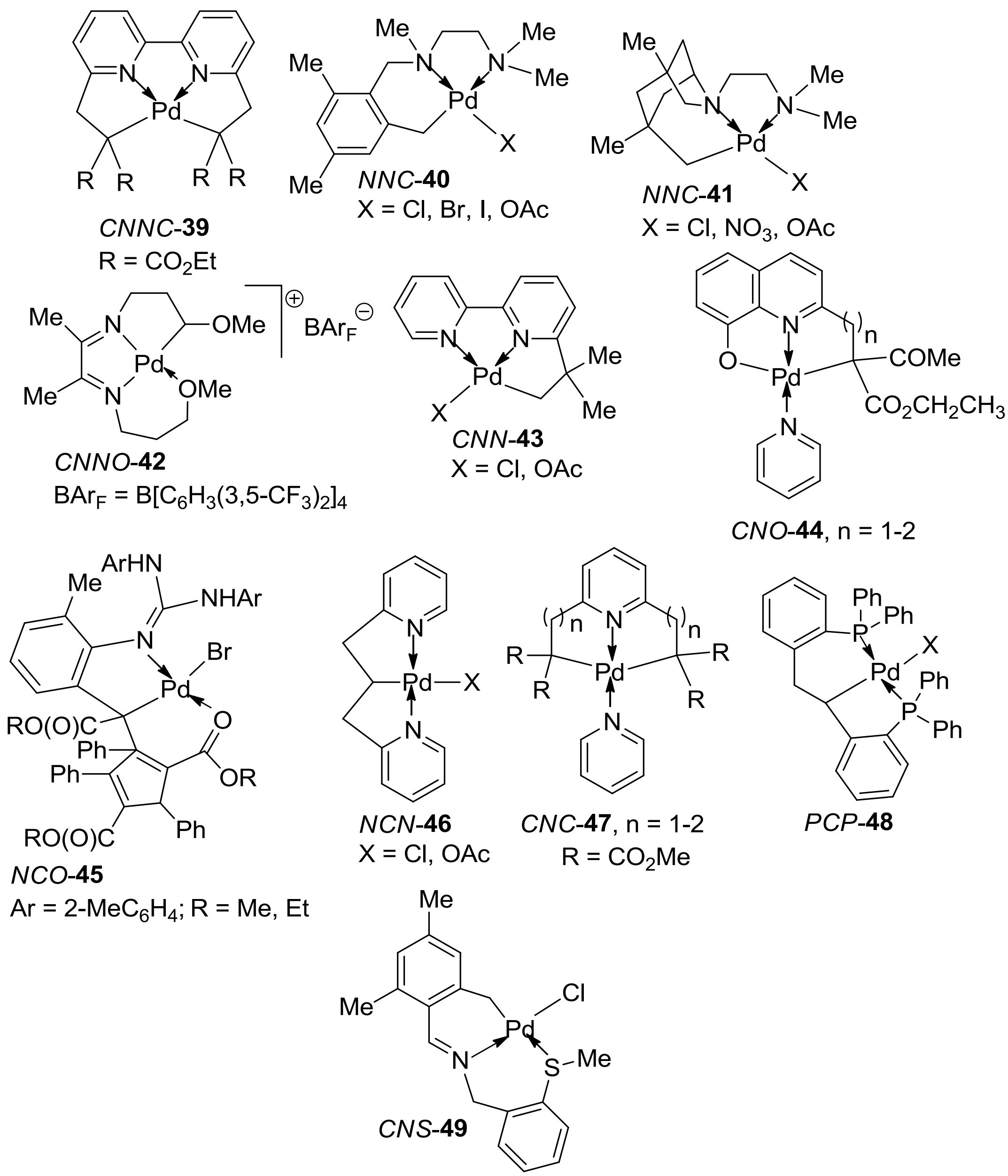
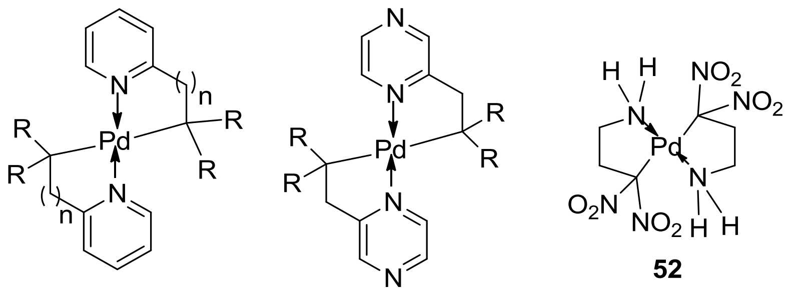


Chart 8. Examples of pincer palladacycles.

I.2.7. Spiro Palladacycles

These are bis-chelated mononuclear palladacycles formed by two bidentate ligands bound to a single Pd center. They have a characteristic C2 axis perpendicular to the plane of the molecule and passing through the Pd center. The chelation at the Pd center must be trans; cis[48] chelations give mononuclear CPCs which are not spiro. There are only three types of the ligands which were used to prepare such complexes. The research group of Newkome has synthesized five- and six-membered spiro palladacycles **50** and **51** from pyridine and pyrazine derivatives, respectively (Chart 9).[138, 151] Fedorov et al. reported the spiro CPC **52** from the reaction of 3,3-dinitropropylamine with $PdCl_2$.[152]



50, n = 1-2
R = CO_2Me

51, R = CO_2Me

52

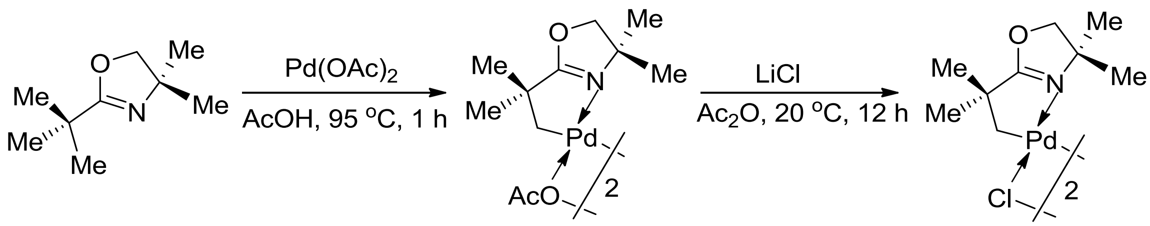
Chart 9. Examples of spiro palladacycles.

I.3. Synthesis of Palladacycles Containing an (*sp*^{3})C–Pd Bond

The methods available for the synthesis of palladacycles include C–H activation with a Pd(II) reagent, oxidative addition, transmetalation and nucleophilic addition.

I.3.1. Pd(II)-Promoted C–H Bond Activation

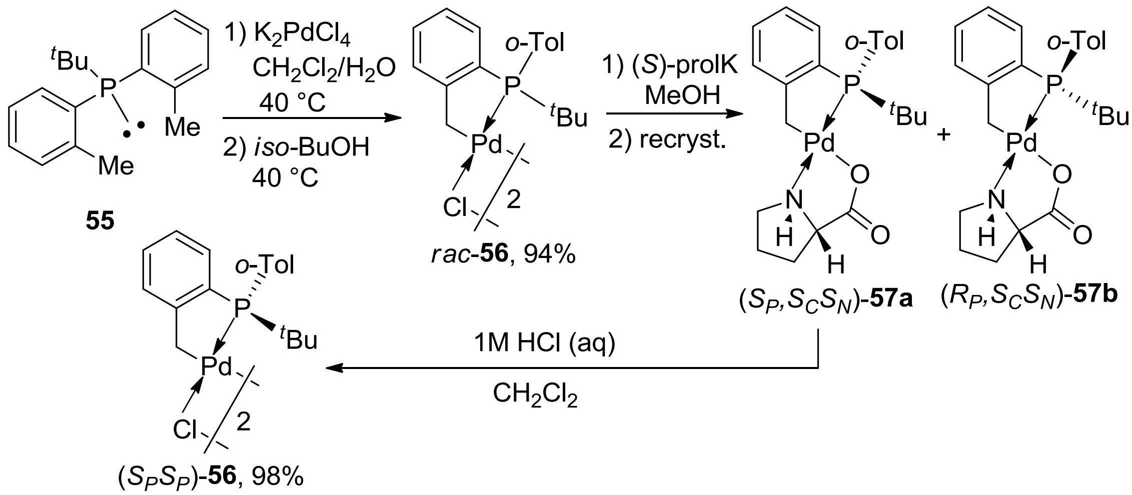
Direct cyclopalladation using Pd(II) salts such as $Pd(OAc)_2$, M_2PdCl_4 (M = Na, Li, K) and $Pd(MeCN)_2Cl_2$ is the most common method for synthesizing palladacycles in general and those containing an (*sp*^{3})C–Pd bond in particular. Ligands that have been palladated using this method include amines,[24, 56, 76, 77, 136, 152] imines,[51-55, 132, 150] pyridines,[42, 43, 47, 70-72, 133, 134, 138-141, 151] pyrazines,[151] hydrazones,[58, 63, 66-68] oximes,[58, 59, 61, 63] pyrazoles,[23, 149] ketazines,[63] oxazolines,[18, 25, 69] phosphines,[31, 32, 37, 90, 91, 97, 100, 101, 105, 107, 109, 110, 143-148, 153] sulfides,[111] thioureas,[111, 116, 117] thioamides,[116] acetanilides,[89] and thiazoles.[86] $Pd(OAc)_2$ in acetic acid, benzene or toluene is the most common way to achieve palladation at an (*sp*^{3})C–H bond.[17-19, 23, 25, 31, 32, 42, 51, 54, 70, 72, 86, 111, 132, 134, 153, 154] For example, in 1990, Clinet et al. reported, the synthesis of CPC **15** through the activation of an (*sp*^{3})C–H bond on the *tert*-butyl group of 2-*tert*-butyl-4,4-dimethyl-2-oxazoline using $Pd(OAc)_2$ in AcOH followed by chloride substitution (Scheme 3).[25]



53 **54** **15**, 92%

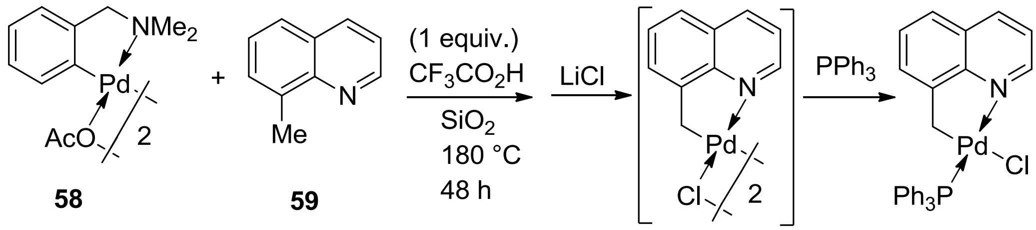
Scheme 3. Synthesis of aliphatic CPC **15** from 2-*tert*-butyl-4,4-dimethyl-2-oxazoline **53**.

Alkali salts of tetrachloropalladate, though weaker palladating agents than palladium acetate, have also been used for palladations at (*sp*^{3})C–H bonds.[40, 42, 43, 59, 62, 64, 149, 153] In 1972, Cheney and Shaw succeeded in cyclopalladating di-*tert*-butyl-*O*-tolylphosphine **55** using Na_2PdCl_4. The product was the racemic P*-chiral phosphapalladacycle **56** with an (*sp*^{3})C–Pd bond,[153] which turned out to possess a very high catalytic activity in C–C coupling reactions.[92, 94-96, 155-158] Dunina et al. reported the resolution of P*-chiral phosphapalladacycle *rac*-**56** using potassium (*S*)-prolinate (Scheme 4).[100]



Scheme 4. Synthesis of the optically active *P**-chiral benzylic *CP*-CPC (*SpSp*)-**56**.

Synthesis of aliphatic CPCs through C–H activation can also be achieved by transcyclopalladation.[34, 159, 160] Transcyclopalladation is a ligand-exchange reaction between a nonmetallated preligand and a palladacycle to form a new CPC.[159] This reaction often requires the presence of either AcOH or CF_3CO_2H as a reaction promoter.[159, 160] In 1984, Ryabov et al. reported the synthesis of CPC **8**, which has a benzylic (sp^3)C–Pd bond, in 64% yield in the reaction of palladacycle **58** with 8-methylquinoline (**59**) at 50 °C for 24 h in AcOH–$CHCl_3$.[159] Later, the same researchers increased the yield of complex **8** to 94% upon using the acetate-bridged CPC **58**.[161] The same reaction was also performed on SiO_2 without a solvent. In order to remove the product from SiO_2, the dimeric complex **8** was converted to the more soluble triphenylphosphine adduct **60** upon treatment with PPh_3 (Scheme 5).[34] The yield of **60** was 46%.



58 59 8 **60**, 46%

Scheme 5. Trancyclopalladation of 8-methylquinoline with CPC **58** on SiO_2.

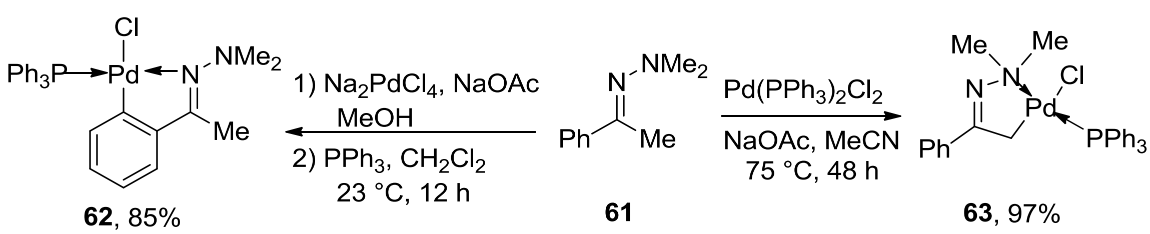
Ryabov in one of his reviews on mechanism of C–H bond activation stated that cyclopalladation through C–H bond activation follows an electrophilic mechanism when an aromatic ligand is involved.[6] The other suggested mechanistic routes include oxidative addition and σ-bond metathesis.[8] It is now obvious that there is no single mechanism for C–H bond activation that is applicable to all types of substrates and Pd(II) reactants.[136] Furthermore, the mechanisms of C–H bond activations for aromatic and aliphatic substrates should be different. Cyclopalladation at (sp^3)C–H bonds is usually believed to proceed through the transition state which exhibits agostic (three-center two-electron) interactions between the C–H bond and the metal atom.[162] Agostic interactions have been observed for metallations at (sp^3)C–H bonds using transition metal reagents.[73, 163-165] In 2009, Rouke and his group reported the X-ray structure of an agostic complex while working on the metallation of 2-*tert*-butyl-6-(4-fluorophenyl)pyridine using K_2PtCl_4.[73] Later, they were able to obtain an X-ray structure for the agostic complex when $Pd(OAc)_2$ was used as the metallating agent.[74]

Challenges in the Synthesis of Aliphatic Palladacycles Through C–H Bond Activation

Besides the inertness of (sp^3)C–H bonds, synthesis of aliphatic palladacycles through C–H bond activation has two other fundamental challenges: (1) how to selectively palladate an (sp^3)C–H bond in the presence of a competing aromatic (sp^2)C–H bond and

(2) how to achieve palladation of 2° and 3° carbons instead of primary, particularly those in the *tert*-butyl moiety.

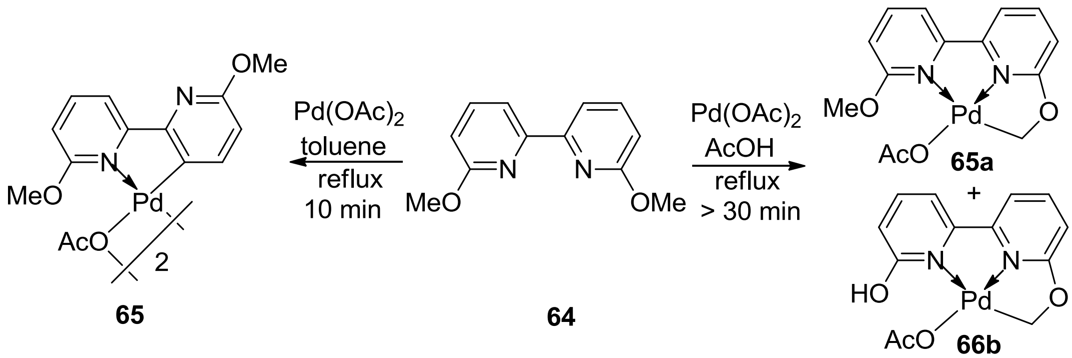
In general, aromatic C–H bond activation is favored over aliphatic C–H bond activation.[54] Nonetheless, several research groups have reported palladation at a (sp^3)C–H bond in the presence of a competing aromatic C–H bond achieved using the appropriate palladation agent and conditions.[67, 68, 76, 139, 140, 166] In 1994, Echavarren and Cardenas reported the palladation of acetophenone *N,N*-dimethylhydrazone (**61**) at the aliphatic C–H bond using $Pd(PPh_3)_2Cl_2$ and NaOAc in MeCN to furnish palladacycle **63**.[67, 68] When the researchers used Na_2PdCl_4 and NaOAc in MeOH, they observed exclusive palladation at the ortho position of the aromatic ring to give palladacycle **62**.[67] In the ^{1}H NMR spectrum of complex **62**, two *N*-methyl groups gave rise to a singlet at δ 3.09 ppm confirming that the sp^3-hybridized nitrogen atom is not the donor atom (Scheme 6). In contrast, two *N*-methyl substituents of **63** appeared as two singlets, proving diastereotopicity of these two groups and, therefore, Pd coordination with the (sp^3)-N atom. Compound **62** remained unchanged when it was refluxed with NaOAc in MeCN. This observation allowed the authors to conclude that it is not an intermediate in the formation of aliphatic CPC **63**.



Scheme 6. Synthesis of palladacycles **62** and **63** from acetophenone *N,N*-dimethylhydrazone **61**.

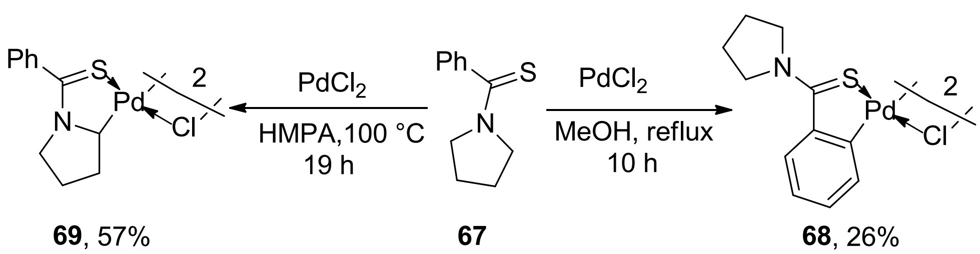
Cinellu et al. reported that the selective palladation of an unactivated (sp^3)C–H bond in the presence of a competing aromatic (sp^2)C–H bond in 6,6′-dimethoxy-2,2′-

bipyridine (**64**) depends on the solvent used.[140] They observed that the use of a protic solvent like AcOH led to metalation at the unactivated (*sp*^{3})C–H bond to give palladacycles **66a,b**.[140] The use of the same Pd reagent in the aprotic solvent toluene led to palladation at the (*sp*^{2})C–H bond to yield complex **65** (Scheme 7).[140]



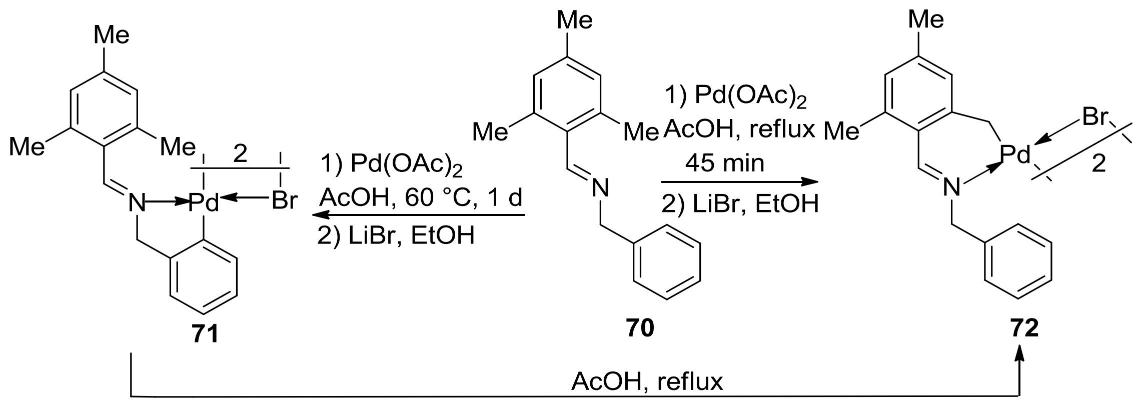
Scheme 7. Solvent effect on the cyclopalladation of preligand **64**.

Dunina et al. observed a similar but opposite effect when they used different solvents in the reaction of 1-thiobenzoylpyrrolidine (**67**) with $PdCl_2$ or K_2PdCl_4.[117] Reaction of **67** with K_2PdCl_4 in the protic solvent MeOH gave CPC **68** with an (*sp*^{2})C–Pd bond, while the use of the aprotic solvent HMPA and $PdCl_2$ led to palladation at (*sp*^{3})C–H bond to furnish CPC **69** (Scheme 8).[117]



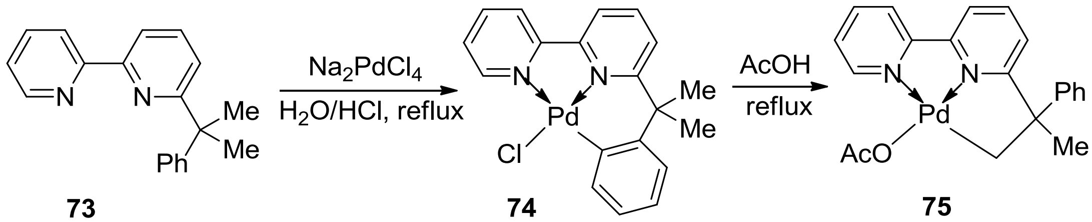
Scheme 8. Solvent effect on the cyclopalladation of preligand **67** by $PdCl_2$.

Both Sales' and Minghetti's groups have shown that regioselectivity of palladation can be governed by using different temperatures.[54, 139] In 1991, Sales et al. studied the palladation of *N*-mesitylbenzylideneamine **70** using $Pd(OAc)_2$. They observed that refluxing the reaction mixture led to metallation at the (sp^3)C–H bond to give palladacycle **72**.[54] When the reaction was carried out at lower temperatures, palladation preferentially took place at the aromatic (sp^2)C–H bond to furnish compound **71** (Scheme 9).[54] These data suggest that complex **72** with the benzylic C–Pd bond is more thermodynamically stable than its anlog **71**.



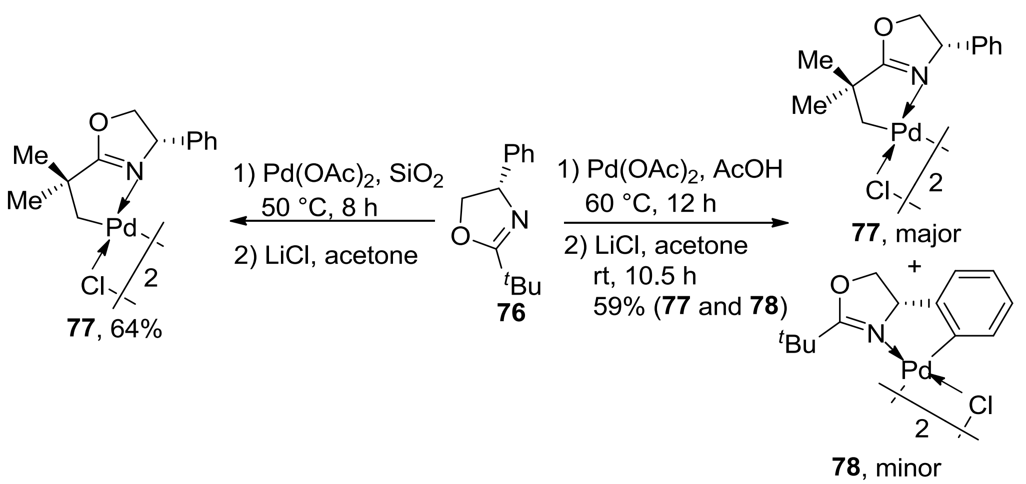
Scheme 9. Temperature effect on the cyclopalladation of preligand **70** using $Pd(OAc)_2$.

The research groups of Sales and Minghetti together with that of Fernandez have investigated the ring size preference in the palladation of (sp^3)C–H bonds.[53, 54, 139] Minghetti et al. obtained the six-membered palladacycle **74** upon reaction of preligand **73** with $Pd(OAc)_2$ in AcOH under reflux.[139] Palladacycle **74** was converted quantitatively to the five-membered-ring analog **75** upon refluxing in AcOH (Scheme 10).[139] This is an example of the general trend that five-membered aliphatic palladacycles appear to be more stable than related six-membered aromatic palladacycles.[167-169]



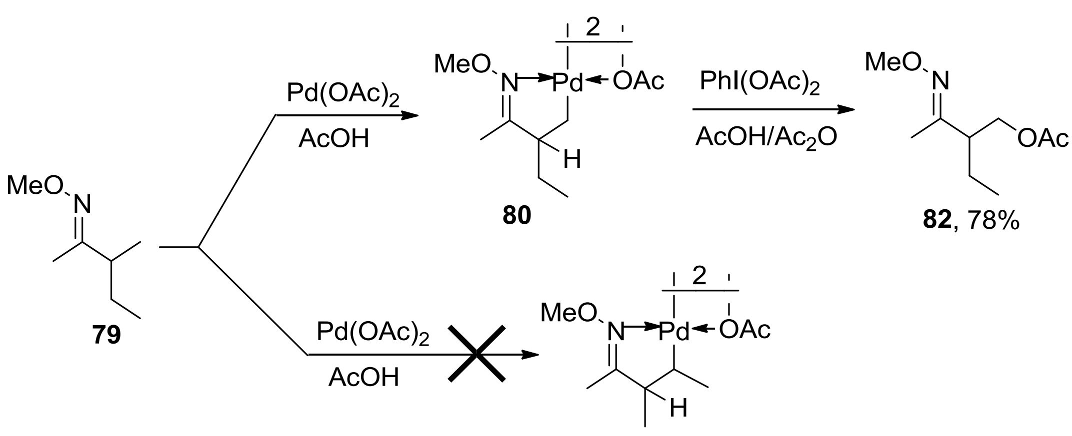
Scheme 10. Effect of reaction conditions on the cyclopalladation of preligand **73**.

In 2004, while studying the palladation of (*R*)-4-phenyl-2-oxazolines using $Pd(OAc)_2$ in AcOH, our research group observed regioselectivity towards the formation of endo-palladacycles derived from imines.[170] Later, our group also investigated reactions of (*S*)-2-*tert*-butyl-4-phenyl-2-oxazoline **76** with Pd(II) salts in an effort to determine whether the endo-effect-driven regioselectivity would lead to metalation at the (sp^3)C–H.[69] This reaction provided endo-palladacycle **77** with the (sp^3)C–Pd as the major product while the alternative exo-palladacycle **78** with an (sp^2)C–Pd bond, was isolated in much lower yield (Scheme 11).[69] It is noteworthy that palladacycle **77** was obtained exclusively when the reaction was performed solvent-free on silica gel (Scheme 11).[18]



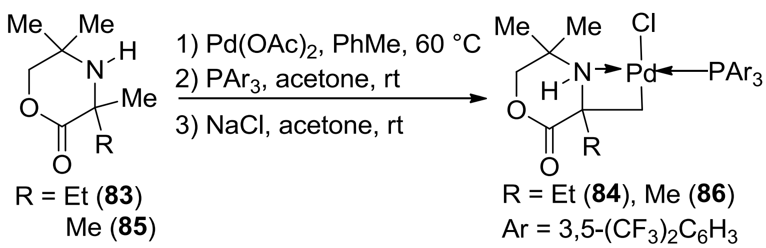
Scheme 11. Palladation of preligand **76**.

As a rule, aliphatic palladations proceed with very high selectivity for 1° (sp^3)C–H bonds especially those in the *tert*-butyl fragment.[167] The reason for such selectivity appears to be due to the possibility of β-hydride elimination in cyclopalladated complexes with 2° and 3° (sp^3)C–Pd bonds. In the case of metalation of the *tert*-butyl group, *β*-elimination is impossible because of the absence of *β*-hydrogens. Sanford et al. has reported the selective palladation and subsequent oxygenation of a 1° (sp^3)C–H bond in the presence of a competing 2° (sp^3)C–H bond in 3-methyl-2-pentanone *O*-methyl oxime **79** (Scheme 12).[171-173] Compound **79** could undergo both 1° (sp^3)C–H bond and 2° (sp^3)C–H bond palladation to form two different five-membered palladacycles; however, no traces of the palladation product at the 2° (sp^3)C–H bond were observed due to a more statistically probable *β*-hydride elimination.[171, 172] Palladation occurred at the 1° (sp^3)C–H bond of the methyl group to give palladacycle **80**, which has just a single *β*-hydrogen.



Scheme 12. Regioselectivity in the palladation of 3-methyl-2-pentanone *O*-methyl oxime.

Recently, McNally et al. reported the cyclopalladation of aliphatic amines using $Pd(OAc)_2$.[19] The amines used in this study (e.g., **83**) have C–H bonds in the positions that could not give rise to conventional five-membered-ring palladacycles.[19] Metalation of these amines led to strained four-membered palladacycles.[19] The effect of β-hydride elimination on selectivity was evident when the researchers selected amine **83**, which could undergo cyclopalladation at an (*sp*^{3})C–H bond of either methyl or ethyl group.[19] Cyclopalladation of amine **83** at one of the three methyl group would give a strained four-membered palladacycle, while metalation at the ethyl group would furnish a conventional five-membered ring.[19] Interestingly, palladation took place at the methyl group to give the four-membered palladacycle **84** (Scheme 13). No product of cyclopalladation at the 1° (*sp*^{3})C–H bond of the ethyl group was obtained.



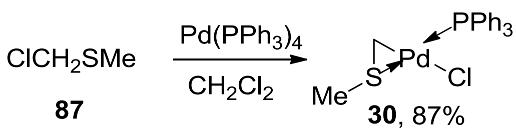
Scheme 13. Selectivity in palladation of aliphatic amines **83** and **85**.

McNally et al. isolated four-membered CPCs by selecting aliphatic amines that possess no C–H bonds in the positions amenable to the formation of five-membered rings (Scheme 13).[19] These four-membered CPCs are the first (and only) examples of their kind.[19, 174, 175] Interestingly, four-membered metalacycles were also obtained when McNally and his collaborators used amines capable of forming five-membered analogs.[19]

I.3.2. Oxidative Addition

Oxidative addition can be used for the synthesis of palladacycles with an (*sp*^{3})C–Pd bond when C–H bond activation is impossible in the preligand. In this method, the two-electron donor group of an alkyl halide oxidatively adds to a Pd(0) or Pd(II) source increasing both its formal oxidation state and coordination number by two.[21] This approach is particuclarly convenient for the preparation of palladacycles with an (sp^2)C–Pd bond.[4]

The synthesis of palladacycles with an (sp^3)C–Pd bond through direct oxidative addition is still a great challenge due to the relative inertness of alkyl halides toward Pd(0) reagents. However, in 1975, Okawara et al. reported the direct oxidative addition of chloromethyl methyl sulfide (**87**) to $Pd(PPh_3)_4$ to give the aliphatic palladacycle **30** in 87% yield (Scheme 14).[35, 36, 176-178]

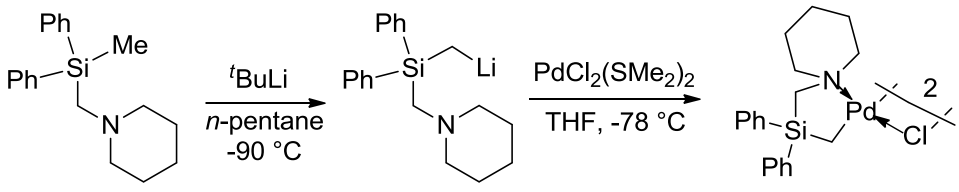


Scheme 14. Synthesis of the aliphatic palladacycle **30** by oxidative addition.

I.3.3. Transmetalation

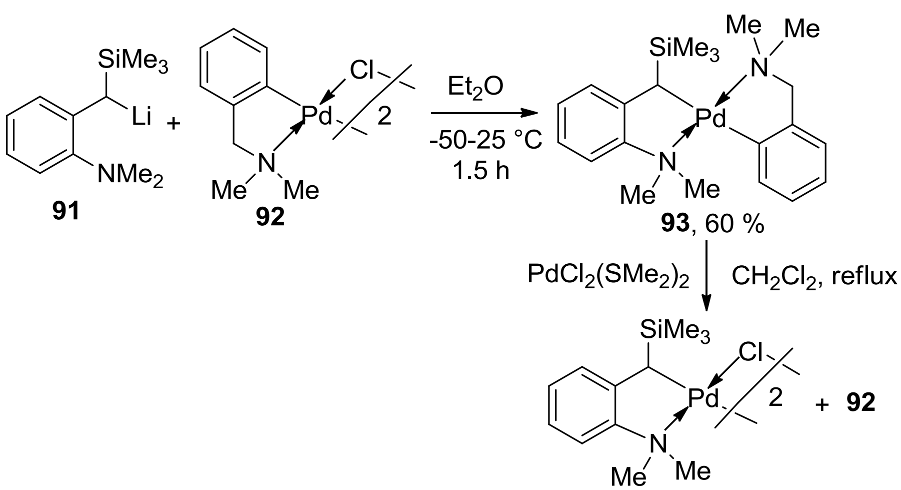
Transmetallation is another method to form a C–Pd bond.[4, 179, 180] In this reaction, Pd replaces a metal within an organometallic compound.[180] Organolithium reagents are the most commonly used to furnish palladacycles, particuclarly those with an (sp^3)C–Pd bond.[48, 180, 181] Tin, silicon and magnesium have also been used, though to a lesser extent.[60, 180, 182-184]

There are several examples of using transmetalation to obtain aliphatic CPCs. Thus, attempts by Strohmann et al. to palladate silane **88** at the 1° carbon using $Pd(OAc)_2$ did not work.[181] Ligand **88** was recovered from the reaction mixture unchanged and palladium black was observed.[181] When silane **88** was treated with ^{t}BuLi in *n*-pentane at -90 °C, metallation took place at the methyl group to give the organolithium derivative **89** in 90% yield. The organolithium reagent **89** was then treated with *trans*-$PdCl_2(SMe_2)_2$ in THF at -78 °C to form the aliphatic dimeric chloro-bridged CPC **90** in 72% yield (Scheme 15).[181]



Scheme 15. Synthesis of the silicon-containing aliphatic *CN*-palladacycle **90** by transmetallation.

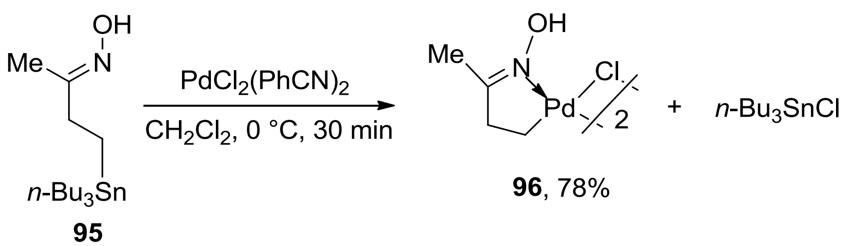
Pfeffer and co-workers have used transmetallation to access the silicon-containing dimeric chloro-bridged CPC **94**, which is difficult to synthesize using other methods.[48, 49] The organolithium reagent **91** did not react with $Pd(SEt_2)Cl_2$.[48] However, the same compound **91** readily underwent transmetalation with the dimeric chloro-bridged *N,N*-dimethylbenzylamine-derived CPC **92** in Et_2O to furnish compound **93** in 60% yield (Scheme 17).[48] Refluxing compound **93** with *trans*-$Pd(SMe_2)Cl_2$ in toluene gave complexes **92** and **94** (Scheme 16).[49]



Scheme 16. Synthesis of the silicon-containing alkyl palladacyle **94** by transmetallation.

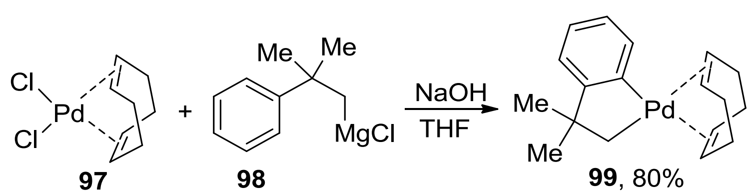
Nishiyama et al. synthesized ketoxime-based aliphatic palladacyles by transmetallation of stannyl and silyl ketoximes (e.g., **95**) with $Pd(PhCN)_2Cl_2$ in CH_2Cl_2.[60] Complex **96** was isolated in 78% yield from the reaction of (*E*)-β-tributylstannyl ketoxime

95 with 1 equiv. of $Pd(PhCN)_2Cl_2$ at 0 °C for 30 min in CH_2Cl_2 (Scheme 17). For comparison, Shaw and his co-workers have reported that direct cyclopalladation of alipahatic oxime derivatives using Pd(II) salts typically takes three days at rt to furnish CPCs with yields up to 70%.[63] This is strong evidence that (sp^3)C–Pd bond is formed faster during transmetallation than in case of C–H bond activation to access ketoxime-based aliphatic palladacycles. However, this transformation suffers significant drawbacks, which are 1) the use of highly poisonous tin derivatives and 2) a laborious synthesis of the tin derivatives prior to transmetallation.



Scheme 17. Synthesis of the ketoxime-based aliphatic palladacyle **96** by transmetallation.

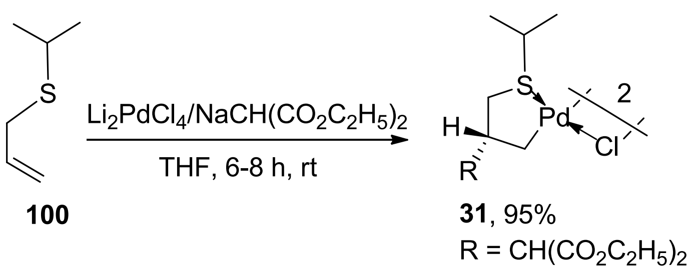
Cámpora et al. have reported the synthesis of *CC*-palladacycle **99** via transmetallation.[183] The Grignard reagent **98** underwent transmetallation by $Pd(COD)Cl_2$ in THF followed by base-catalyzed (sp^2)C–H activation to afford palladacycle **99** in 80% yield (Scheme 18).[183]



Scheme 18. Synthesis of the *CC*-palladacyle **99** by transmetallation.

I.3.4. Nucleophilic Addition

The preparation of palladacycles through nucleophilic addition involves the formation of a carbon-carbon or a carbon-oxygen bond between the *β*-carbon of an allylic amine or sulfide and a nucleophile. This reaction spontaneously results in the formation of a carbon-palladium bond at the δ-carbon of the allylic and homoallylic amine or sulfide. The nucleophile used in this reaction is either an alcohol or a stable enolate ion such as sodiodiethylmalonate; the palladating agent most often used is Li_2PdCl_4. Nucleophilic additions have been used in the synthesis of diverse types of palladacycles including those with an (sp^3)C–Pd bond.[3, 44, 75, 80-83] As mentioned above (Scheme 2), the first CPC with an (sp^3)C–Pd bond was prepared by this method from allylic amines. Later in 1977, Kjonaas et al. expanded the substrate scope in this reaction to include the allylic sulfide **100**.[75, 82] They also found that carbon nucleophiles like sodiodiethylmalonate can also be used in this method (Scheme 19).[75, 82]



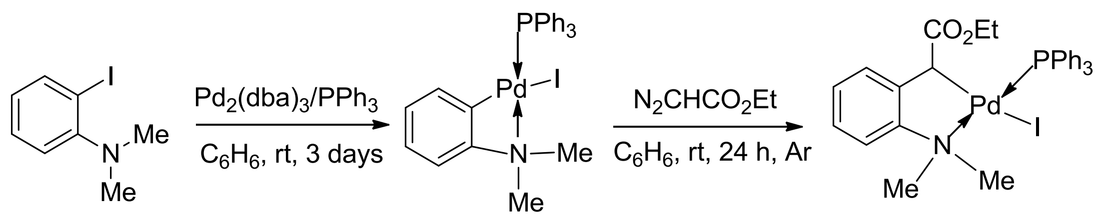
Scheme 19. Synthesis of palladacycle **31** by nucleophilic addition.

I.3.5. Miscellaneous Methods

I.3.5.1. Modification of a Preformed Palladacycle

It is also possible to obtain one palladacycle from another. For example, a preformed (sp^2)C–Pd bonded palladacycle can then undergo a rearrangement or insertion reaction at the C–Pd bond to generate an (sp^3)C–Pd bonded palladacycle.[113, 114, 185, 186] In

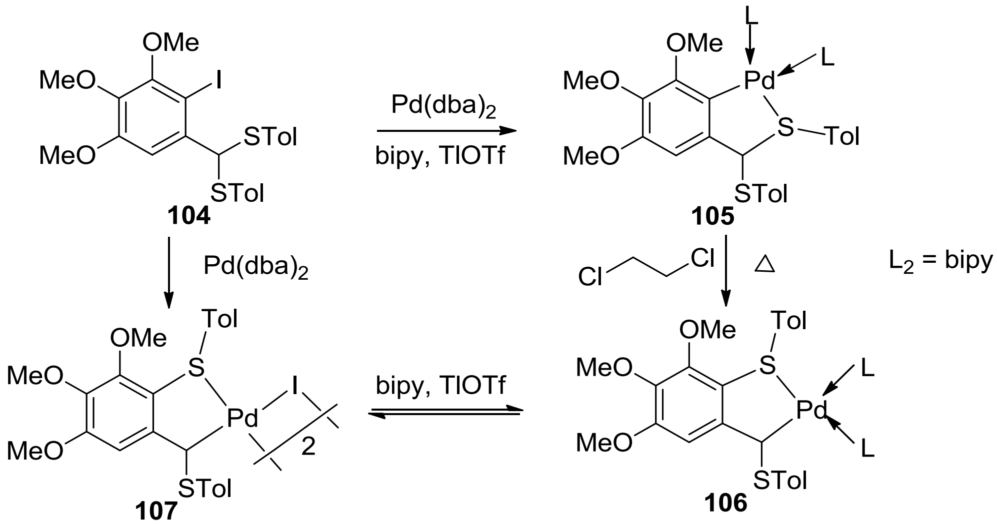
2004, Solé et al. reported the synthesis of azapalladacycle **102** by the oxidative addition of *N*,*N*-dialkyl-2-iodoaniline **101** to $Pd(PPh_3)_4$ or $Pd_2(dba)_3/PPh_3$.[185] As expected, the strained four-membered ring in complex **102** underwent carbene insertion into the C–Pd bond to give the more stable five-membered ring palladacycle **103** (Scheme 20).[185]



101 **102** **103**

Scheme 20. Synthesis of palladacycle **103** by carbene insertion at the C–Pd bond of CPC **102**.

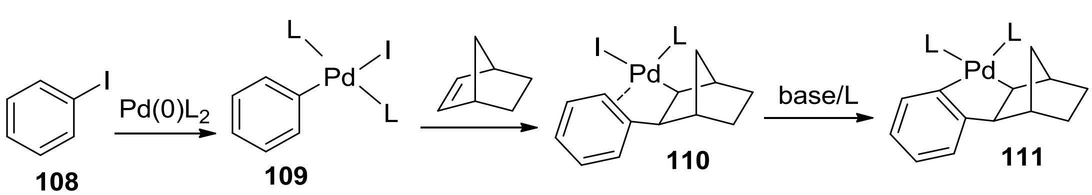
Vicente and his collaborators have reported the unusual rearrangement of ortho-palladated aryldithioacetals.[113, 114] The oxidative addition of aryldithioacetal **104** to $Pd(dba)_2$ gave the unexpected iodine-bridged palladacycle **107** (Scheme 21).[114] When this reaction occurred in the presence of TlOTf and 2,2'-bipyridine (bipy), the expected monomeric product **105** was obtained (Scheme 21).[114] Compound **105** rearranged to palladacycle **106** upon refluxing in 1,2-dichloroethane (Scheme 21).[114] This rearrangement resulted from the cleavage of one (sp^2)C–Pd and one (sp^3)C–S bond and the formation of one (sp^3)C–Pd and one (sp^2)C–S bond.



Scheme 21. Synthesis of palladacycle **107** by a rearrangement of CPC **106**.

I.3.5.2. Modification of a Preformed Pd–Aryl Unit

Oxidative addition of an aryl halide to a Pd(0) source is the first step in another method used for preparation of CPCs.[180] The aryl–Pd compound **109** then reacts with an norbornene followed by treatment with a base to form a *CC*-palladacycle **111**.[180] Catellani et al. have worked extensively on the synthesis of *CC*-palladacycles using this methodology.[126-129, 187] In the example shown in Scheme 16, the first step of this transformation was oxidative addition of phenyl iodide **108** to Pd(0)L_2 to give compound **109**. The subsequent insertion of norbornene into the (sp^2)C–Pd bond of compound **109** provided the stable product **110**. Compound **110** then underwent base-catalyzed intramolecular C–H activation to furnish *CC*-palladacycle **111** (Scheme 22).[126]



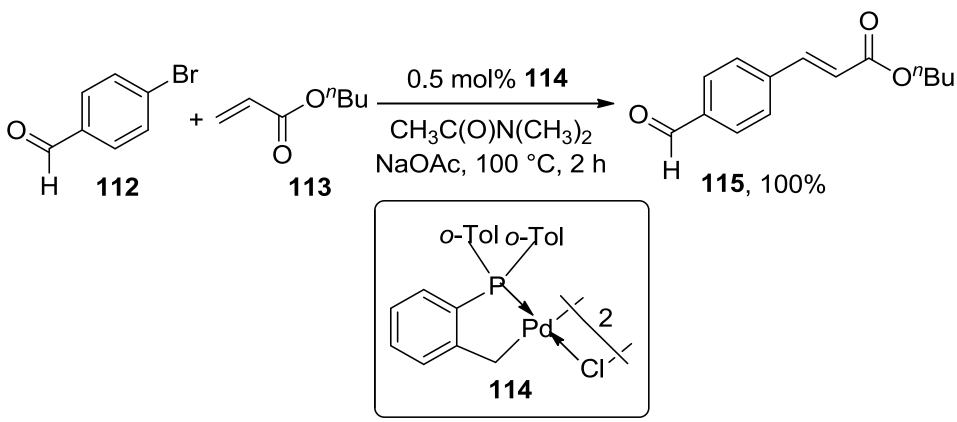
Scheme 22. Synthesis of palladacycle **111** by modification of the preformed Pd–aryl unit **109**.

I.4. Applications of Palladacycles Containing an (sp^3)C–Pd Bond

CPCs containing an (sp^2)C–Pd bond have been used in synthetic organic chemistry as 1) catalysts or precatalysts in the Mizoroki-Heck,[95, 96, 104] Suzuki[57, 92, 96] and other reactions,[92, 101, 188-194] 2) reagents for chiral resolution of racemic ligands,[195] 3) reagents for chiral coordinative derivatizing agents to determine optical activity,[195] 4) chiral auxiliaries,[195] and 5) ligand modifications using reactions at the Pd–C bond.[196] CPCs containing an (sp^3)C–Pd bond have mostly been used as catalysts[92-96, 98, 101, 154, 197] and to a lesser extent in ligand modifications using reactions at the Pd–C bond.[62, 84, 85, 119, 198] To the best of our knowledge, aliphatic CPCs have never been utilized as reagents for chiral resolution of racemic ligands and chiral coordinative derivatizing agents, as well as chiral auxiliaries.

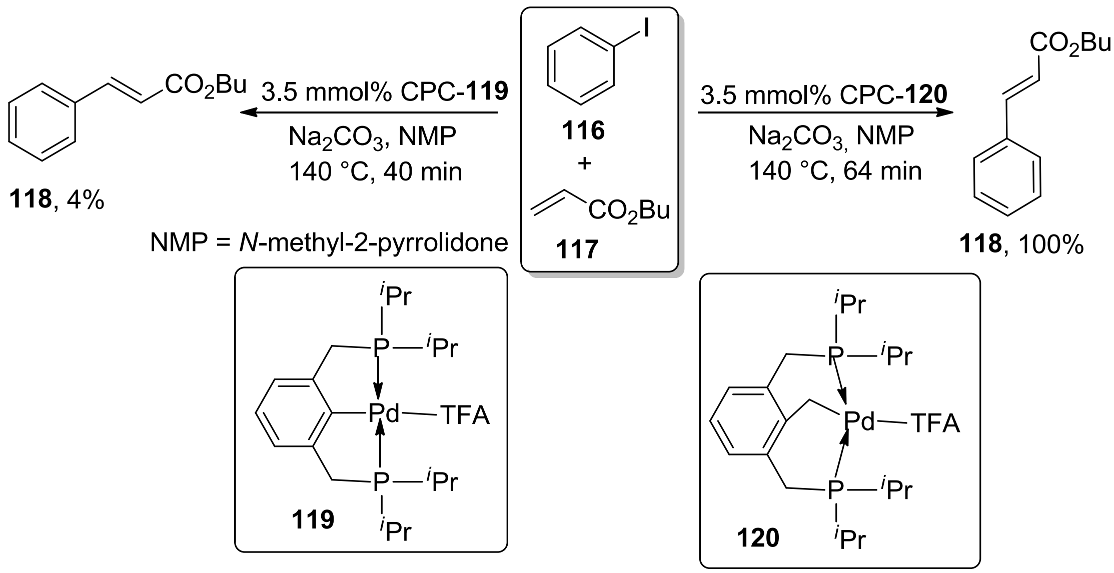
I.4.1. Use as Catalysts or Precatalysts

The first CPC with an (sp^3)C–Pd bond used as a catalyst in cross-coupling reactions is the Herrmann palladacycle **114**.[96] The catalytic activity of complex **114** in the Heck reaction surpassed that of all previously used catalysts in the same transformation.[96] The exceptional stability and a possibility of activating less reactive chloroarenes made this and related complexes target compounds for potential application in industries.[22, 96] Herrmann et al. obtained 100% yield of product **115** when CPC **114** was used as a catalyst in the reaction of 4-bromobenzaldehyde (**112**) with *n*-butyl acrylate (**113**) (Scheme 23).[96] The product yield of this reaction remained the same when the equivalence of the catalysts was reduced to thousand times its initial amount.[96] Kinetic studies showed that the standard catalyst, a mixture of $Pd(OAc)_2$ and triarylphosphine, was deactivated at temperatures above 120 °C due to the breaking of a P–C bond in the phosphine.[96] This led to the deposition of Pd black usually observed in Heck reactions and explained why this catalyst cannot be used for less reactive chloroarenes and deactivated bromoarenes, which are often unreactive under mild reaction conditions and require temperatures above 120 °C.[96, 199] For comparison, thermal gravimetric/mass spectrometric studies of compound **114** indicated that it decomposes only at temperatures above 250 °C; hence it can be used in Heck reactions requiring high temperatures.[96]



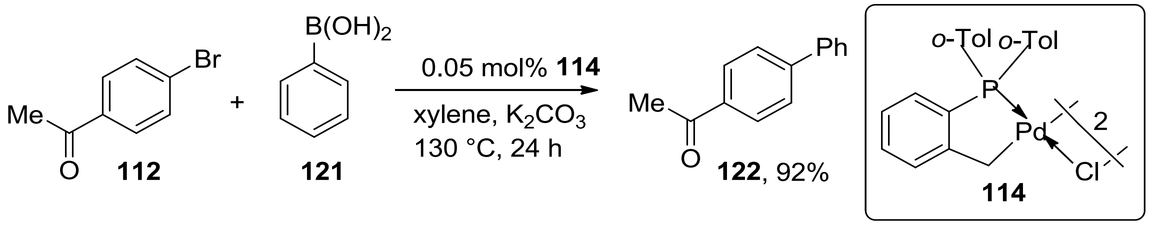
Scheme 23. Catalytic activity of CPC **114** in Heck reaction.

In an effort to compare the catalytic activity of pincer palladacycles with an (sp^3)C–Pd and an (sp^2)C–Pd bond, Milstein and his group used three *PCP* pincer CPCs in a Heck reaction.[200] They reported that iodobenzene (**116**) reacted with *tert*-butyl acrylate (**117**) in the presence of catalytic amounts of the *PCP* pincer complex **119** containing an (sp^2)C–Pd bond to furnish product **118** in 4% yield (Scheme 24).[200] To their surprise, when the *PCP* pincer complex **120** with an (sp^3)C–Pd bond was used, this reaction gave product **118** in 100% yield (Scheme 24).[200] They screened many reagents and reaction conditions, and in each case the *PCP* pincer complex **120** provided better yields of the product than the *PCP* pincer complex **119**.[200] Although both pincer complexes showed very high thermal stability with no decomposition up to 180 °C, CPC **120** had a higher turnover rate.[200] Complex **120** was an effective catalyst even in Heck reactions of nonactivated aryl bromides, in which CPC **119** was not.[200] The researchers concluded that the higher catalytic activity of CPC **120** could be due to electronic factors since the metal center in CPC **120** is more electron rich than in CPC **119**.[200]



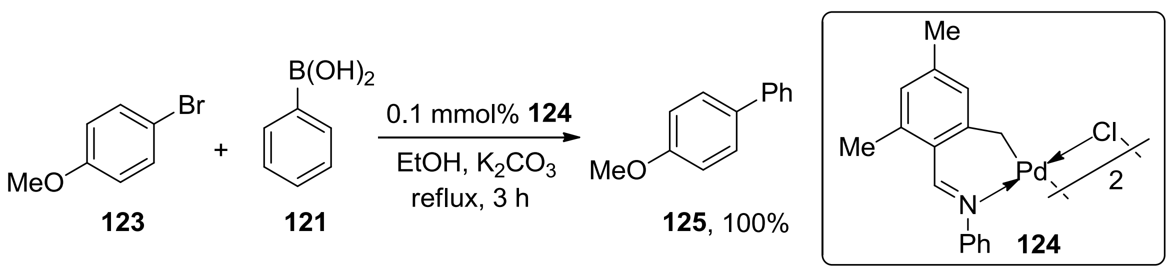
Scheme 24. Catalytic activity of *PCP* pincer CPCs in Heck reaction.

To examine whether the Herrmann palladacycle **114** was also effective in Suzuki reactions, Beller et al. used this complex as a catalyst in cross-coupling reactions of aryl halides with arylboronic acids.[95] These researchers found that 4-bromoacetophenone (**112**) reacted with phenylboronic acid (**121**) in the presence of compound **114** to give the desired 4-acetylbiphenyl (**122**) in yields above 90% (Scheme 25).[95] Complex **114** was also found to be effective in Suzuki reactions with less reactive chloroarenes.[95]



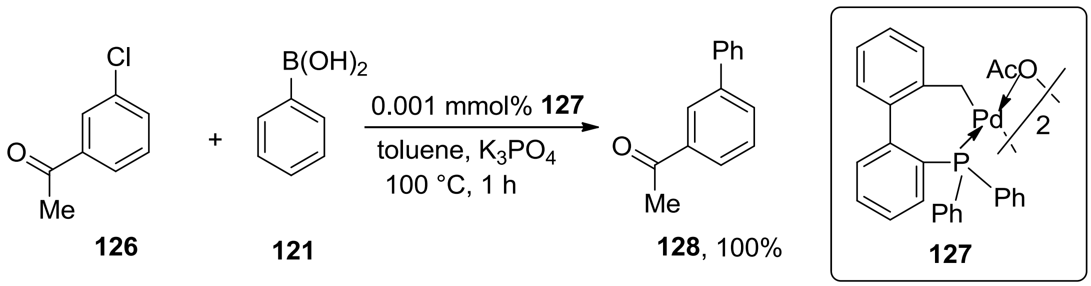
Scheme 25. Catalytic activity of CPC **114** in Suzuki reaction.

Liu and her group have used the imine-derived CPC **124** as a catalyst[57] in a similar Suzuki-Miyaura reaction (Scheme 26).[57] They reported a quantitative yield of the product even though these reactions were carried out in air and protic solvents.[57] The use of activated aryl chlorides like *p*-nitrophenyl chloride and *p*-acetylphenyl chloride both gave 100% yields of the respective products.[57] However, they observed poor conversions for deactivated aryl halides and phenyl chloride.[57, 199] Deactivated aryl halides had electron-donating groups on the benzene ring.[199]



Scheme 26. Catalytic activity of CPC **124** in Suzuki-Miyaura reaction.

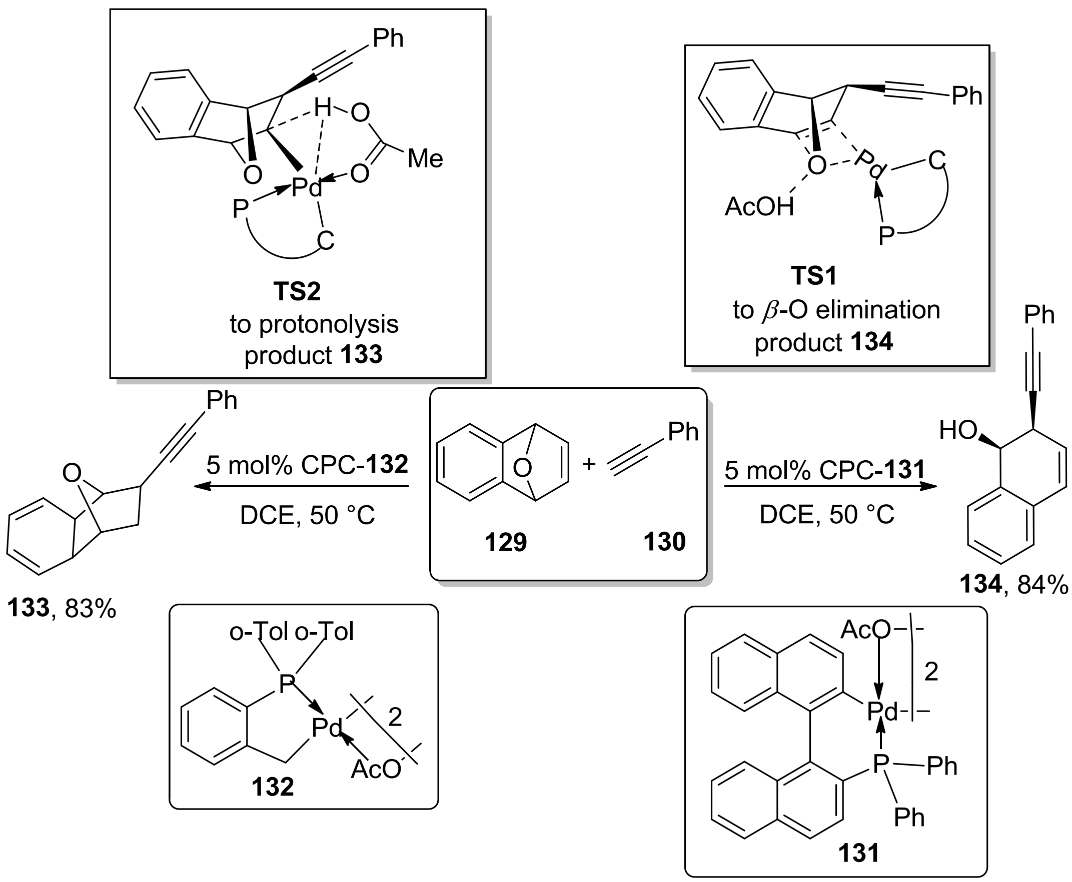
Recently, Joshaghani et al. described the use of the biphenyl-based phosphine-derived CPC **127** as a catalyst in Suzuki couplings (Scheme 27).[93] Previously, the researchers reported high catalytic activity of 2-(diphenylphosphino)-2'-methylbiphenyl in the presence of Pd(0) in several coupling reactions, which they assumed was due to the formation of the palladacycle intermediate **127**.[93] CPC **127** was synthesized and tested as a catalyst for Suzuki cross-coupling reactions.[93] The catalytic activity of CPC **127** improved with increasing reactivity of the aryl chloride used.[93] They observed quantitative yield of the product when highly activated aryl chlorides with electron-withdrawing groups were used.[93] It is worth noting that compound **127** was still effective in the reactions with electron-rich aryl halides like 3-chloroanisole (**126**).[93] They also observed that the catalytic activity of CPC **127** surpassed that of its preligand.[93]



Scheme 27. Catalytic activity of CPC **127** in Suzuki-Miyaura reaction.

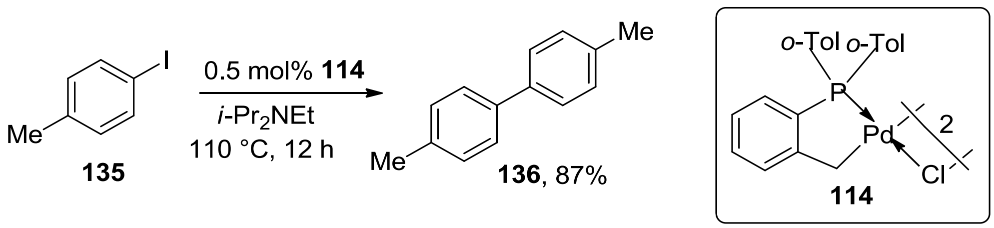
Hou and his group have observed a rather different phenomenon. When *CP*-CPCs containing either an (sp^3)C–Pd or (sp^2)C–Pd bond were used as catalysts in the reaction of oxabicyclic alkenes and terminal alkynes, different products were obtained.[101] When the reaction of 7-oxabenzonorbornadiene (**129**) with phenylacetylene (**130**) was catalyzed by *CP*-CPC **132** containing an (sp^3)C–Pd bond, the cyclic ether **133** was formed as the major product (Scheme 28).[101] A switch to alcohol **134** was observed when *CP*-CPC **131** with an (sp^2)C–Pd bond was used (Scheme 28).[101] DFT calculations showed that this selectivity resulted from the difference in trans effects of the carbon donors in the CPCs.[101] The (sp^3)C atom possess a greater trans effect than the (sp^2)C because the former is a stronger donor.[101] In the transition state (TS1) leading to compound **134**, the O–Pd bond being formed is trans to the (sp^2)C–Pd bond of CPC **131**. This trans-(sp^2)C,O geometry resulted in predominant

β-O elimination. In the transition state TS2 leading to compound **133** the C–Pd bond being broken is trans to the (sp^3)C–Pd bond of CPC **132**. This trans-(sp^3)C,O geometry favored protonolysis.[101]



Scheme 28. Reaction of oxabicyclic alkenes with terminal alkynes using CPCs.

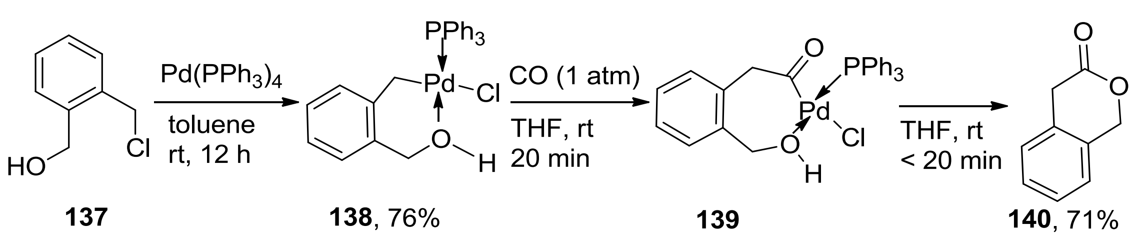
The Herrmann palladacycle has also been used in palladium-catalyzed homocoupling of aryl iodides.[92] Luo et al. observed homocoupling of 4-iodotoluene (**135**) in DMF in the presence of complex **114** to give product **136** in 87% yield (Scheme 29).[92] The yield of the products changed only a little when substituents on the benzene ring were varied.[92] However, the reaction was faster with arenes having electron-withdrawing substituents than with those bearing electron-donating groups.[92]



Scheme 29. Palladium-catalyzed homocoupling of 4-iodotoluene using CPC **114**.

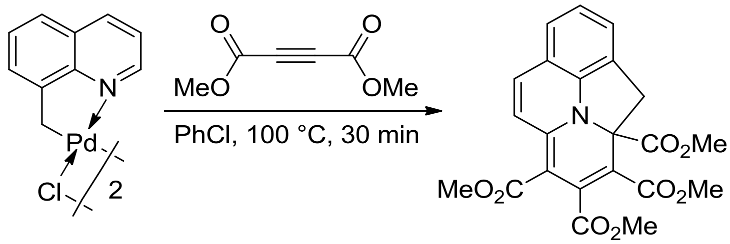
I.4.2. Ligand Modifications Using Reactions at the Pd–C Bond

Similarly to other organometallic compounds, CPCs can react with a number of substrates resulting in ligand modifications. Only a small fraction of these reactions involve CPCs with (*sp*^{3})C–Pd bonds. For example, the research group of Sheppard has reported the synthesis of novel compounds via cyclopalladation of lanosterol and cholesterol.[62] These products could potentially be used as new adjuvant saponins.[62] Holton, R. A. synthesized a prostaglandin by using the cyclopalladation of cyclopentadiene as the first step.[84] Lindsell et al. have utilized reactions at the Pd–C bond of the benzylic CPC **138** to prepare lactone **140**, which is a precursor of pharmaceutical agents.[125] Their lactone synthesis started with the oxidative addition of 2-hydroxymethylbenzyl chloride (**137**) to $Pd(PPh_3)_4$ in toluene to afford CPC **138**.[125] Insertion of CO into the Pd–C bond of CPC **138** gave compound **140** in 71% yield (Scheme 30).[125]



Scheme 30. Synthesis of compound **140** using CPC **138** as a reactant.

Pfeffer et al. have accessed novel heterocyclic compounds containing a bridgehead nitrogen via reactions at the Pd–C bond of the 8-methylquinoline-derived CPC **8**.[198] The researchers reacted CPC **8** with 1 equiv. of dimethyl acetylenedicarboxylate to afford compound **141** in 91% yield (Scheme 31).[198]



8 **141**

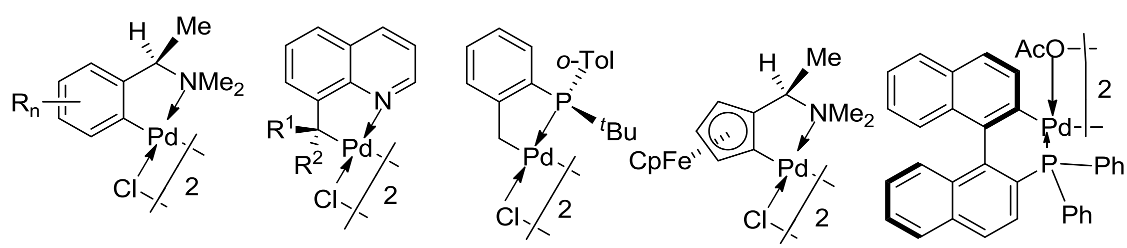
Scheme 31. Synthesis of compound **141** by the ligand modification method.

CHAPTER II

GOALS OF THE STUDY

II. 1. Types of Optically Active Cyclopalladated Complexes

Known optically active CPCs possess either 1) a chiral center,[201] 2) chiral plane,[202] 3) chiral axis[203] or 4) a combination of two chiral elements.[204] The first examples of optically active C*-chiral CPCs were derived from α-arylalkylamines and were reported as early as 1971 (Chart 10).[201, 205] Later in the 1980s, Sokolov et al. introduced the planar chiral 1-dimethylaminoethylferrocene-derived complex **142** (Chart 10).[204, 206] Presently, there are many examples of optically active CPCs, which include both mono- and dinuclear *CN*-, *CS*-, and *CP*-complexes as well as mononuclear *SCS*, *NCN*, *PCP* and *PCN* pincer derivatives. The majority of optically active CPCs reported in literature have an (sp^2)C–Pd bond,[192] although optically active aliphatic CPCs have also been known (Chart 10).[32, 207-209, 133]



(R_C)-**141**, R_n = H, 3,4-benzo, 4,5-benzo

(R_C)-**8,** X = Cl, OAc
R^1 = H, R^2 = Me, ^{i}Pr

(S_PS_P)-**56**

(S_{Pl},R_C)-**142**,
R = H, Me;
Cp = η-C_5H_5

(R_a,R_a)-**131**

Chart 10. Examples of optically active CPC containing 1) a chiral center [(R_C)-**141**, (R_C)-**8**, (S_P,S_P)-**56** and (S_{Pl},R_C)-**142**], 2) chiral plane [(S_{Pl},R_C)-**142**] and 3) chiral axis [(R_a,R_a)-**131**].

II.1.1. Optically Active Cyclopalladated Complexes Containing an (sp^2)C–Pd Bond

Optically active CPCs containing an (sp^2)C–Pd bond are the most abundant group of chiral CPCs and can be differentiated by the type of chirality into those with a chiral plane, chiral center or chiral axis. CPCs with central chirality contain one or more chiral atoms, which can be C, N, P or S. Chart 11 provides examples of C*-chiral CPCs **78** (see Scheme 11) and **141** (Chart 10),[201] C*- and N*-chiral complex **143**,[210] C*- and S*-chiral analog **144**,[211] *CS*-CPC **69** (see Scheme 8)[117] and C*- and P*-chiral CPC **145** (Chart 11).[212] Examples of CPCs with only planar chirality include *CN*-CPCs **146**[213] and **147**[214] (Chart 11). The majory of planar chiral CPCs also contain a chiral center, e.g., **148** and **149** (Chart 11).[214] Phosphapalladacycle **131** derived from binaphthalene exhibits axial chirality (see Chart 10).[203]

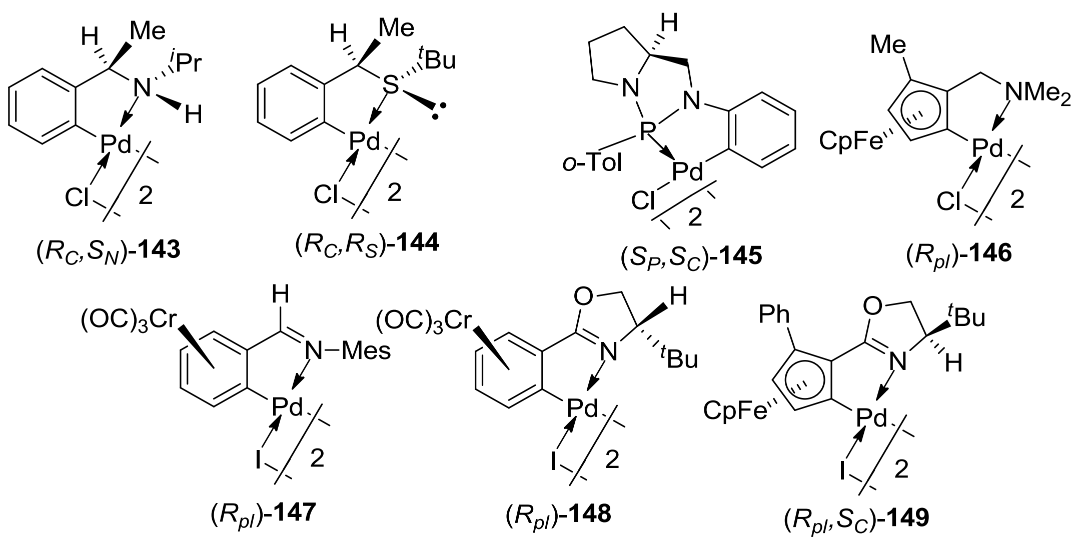
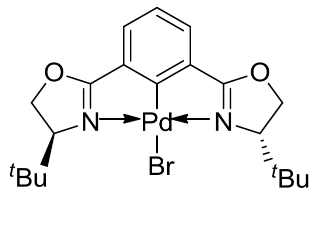


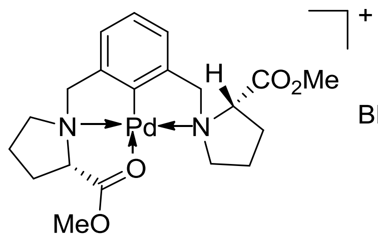
Chart 11. Examples of optically active CPCs with an (sp^2)C–Pd bond.

Pincer CPCs with a stereocenter have been studied by several groups.[215 216 217 133 218 219 194] Examples of these pincer complexes include *CNO*-**44** (see Chart 8),[133] *NCN*-**150**,[215] *NCNO*-**151**,[216] *OCNO*-**152**,[217] *PCP*-**153** and *PCP*-**154**,[219] *PCN*-**155**[194] and *SCS*-

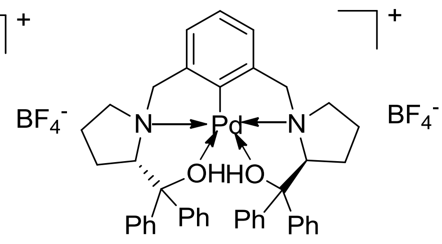
156 (Chart 12).[218] There are also reports of pincer complexes with axial chirality, e.g., *PCP*-**157**[220] as well as complexes with both axial and central chirality, e.g., *NCN*-**158** Chart 12).[221]



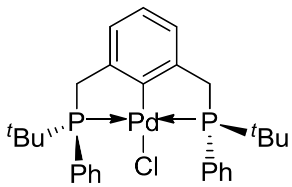
(S_C,S_C)-*NCN*-**150**



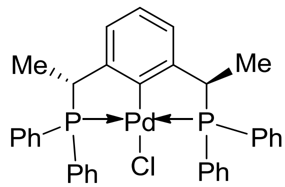
NCNO-**151**



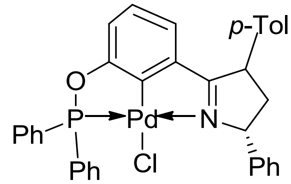
ONCNO-**152**



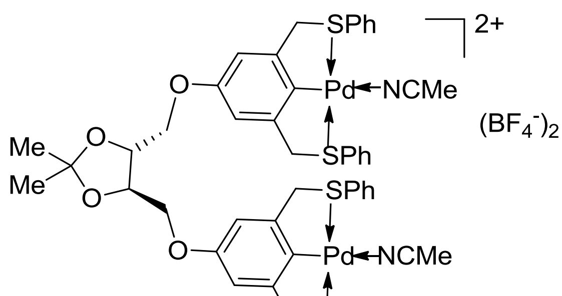
(S_P,S_P)-*PCP*-**153**



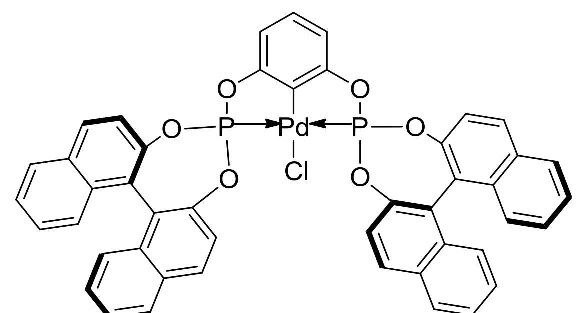
(S_P,S_P)-*PCP*-**154**



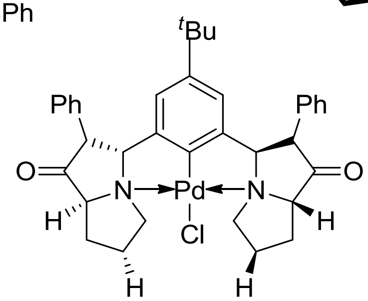
(S_C)-*NCP*-**155**



(R_C,R_C,)-*SCS*-**156**



(R_a,R_a)-*PCP*-**157**

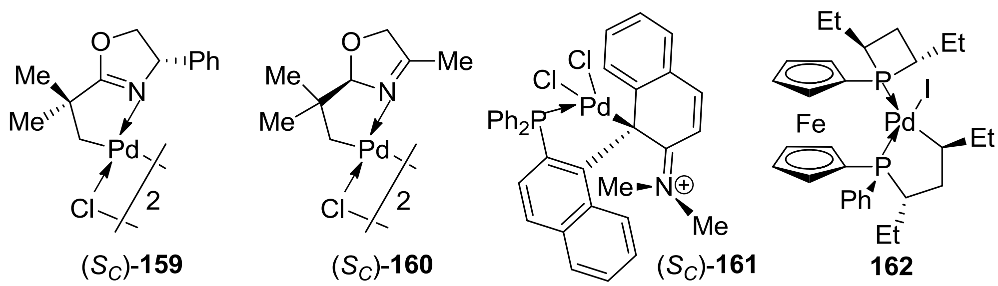


(R_C,S_C,S_a)-*NCN*-**158**

Chart 12. Examples of optically active pincer complexes.

II.1.2. Optically Active Cyclopalladated Complexes with an (sp^3)C–Pd Bond

Most aliphatic CPCs containing a chiral center exist as racemates due to the tedious process of chiral resolution. This is one of the reasons why only a limited number of optically active CPCs of this kind have been known to date. Their examples include phosphapalladacycles **56** (see Scheme 4),[207] **161**[222] and **162**,[223] *CS*-CPC **69** (Scheme 8),[117] *CC*-CPC **38** (Chart 7),[130, 131] pyrazole-derived *CN*-CPC **19** (Chart 2),[23] and oxazoline-based *CN*-CPCs **159** and **160** (Chart 13).[208, 209, 224]



(S_C)-**159** (S_C)-**160** (S_C)-**161** **162**

Chart 13. Examples of optically active complexes containing an (sp^3)C–Pd bond.

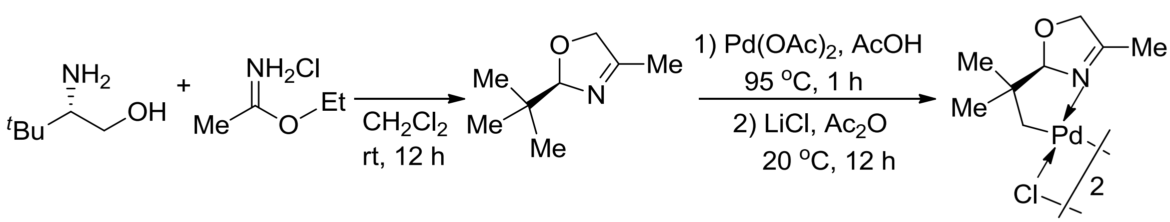
II.2. Synthesis of Optically Active Cyclopalladated Complexes

Two common methods to access optically active CPCs with an (sp^3)C–Pd bond have been reported: 1) cyclometalation of enantiopure preligands[209, 225] and 2) chiral resolution of racemic cyclopalladated complexes.[32, 133] The third approach, enantioselective palladation,[226, 227] has also been used to prepare optically active CPCs, but all of them contain an (sp^2)C–Pd bond.

II.2.1. Cyclopalladation of Enantiopure Preligands

The most straightforward approach for preparation of optically active CPCs is cyclopalladation of preligands derived from naturally occurring optically active compounds. Examples include complexes obtained from (i) 4-substituted 2-oxazolines,[228, 229] which are prepared from readily available enantiopure α-amino alcohols, (ii) derivatives of natural phenols L-(+)-tyrosine and (+)-estrone[230] and (iii) derivatives of L-phenylalanine[231] and (*R*)-2-phenylglycine.[232] Only a small fraction of known enantiomerically pure or scalemic CPCs have an (sp^3)C–Pd bond (see Chart 13).[32, 207-209]

Our research group has also synthesized optically active CPCs via the cyclopalladation of enantiopure preligands. Previously, we studied the cyclopalladation of (*S*)-4-*tert*-butyl-2-methyl-2-oxazoline (**165**).[209] Preligand **165** was synthesized according to a procedure reported by Meyers and Shipman from (S)-*tert*-leucinol and ethylacetimidate hydrochloride (Scheme 32).[225] Reaction of **165** with $Pd(OAc)_2$ in acetic acid gave the exo-palladacycle **160** (Scheme 32).[209] The yield of the product was not high, possibly because 1) the structure of **165** allows only the less favored exo-cyclopalladation and 2) the difficulty associated with the activation of an (sp^3)C–H bond.[209] This is in contrast to the observed endo-cyclopalladation of (*S*)-2-*tert*-butyl-4-phenyl-2-oxazoline and 2-*tert*-butyl-4,4-dimethyl-2-oxazoline previously discussed in this dissertation (see Scheme 3).[208]

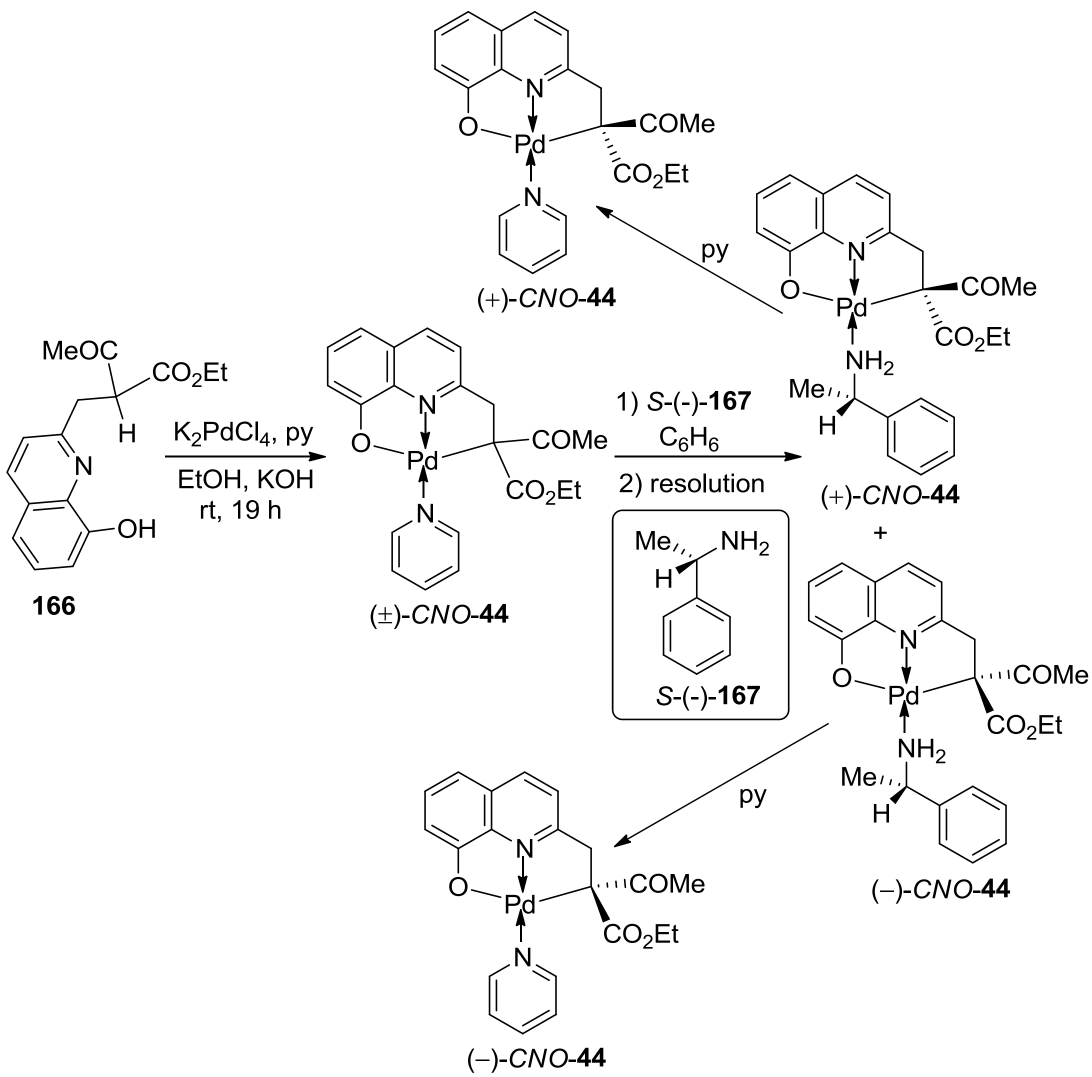


(S_C)-**163** **164** (S_C)-**165**, 79% (S_C)-**160**, 43%

Scheme 32. Synthesis of CPC (S_C)-**160** from (S_C)-**163**.

II.2.2. Synthesis of Optically Active Cyclopalladated Complexes through Chiral Resolution

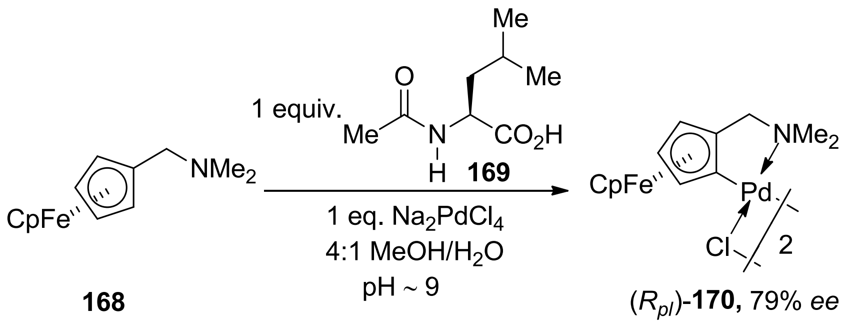
Examples of preparation of optically active aliphatic CPCs using chiral resolution includes synthesis of **56** and **44**. The preparation of enantiomerically pure phosphapalladacycle **56** by chiral resolution using optically active amino acid derivatives was described in Chapter I (see Scheme 4).[32] The pincer *CNO*-complex **44** has also been successfully accessed through chiral resolution.[133] Reaction of compound **166** with K_2PdCl_4 in EtOH followed by addition of pyridine gave *rac*-**44**, which upon stirring with *S*-(-)-1-phenylethylamine furnished a mixture of two diastereomers (Scheme 33).[133] The diastereomeric mixture was separated using column chromatography, and a subsequent ligand exchange with pyridine gave both enantiomers of CPCs **44** (Scheme 33).[133]



Scheme 33. Synthesis of the optically active CPCs **44** by chiral resolution of *rac*-**44**.

II.2.3. Synthesis of Optically Active CPCs through Enantioselective Palladation

All optically active complexes obtained by this method have an (sp^2)C–Pd bond. The synthesis of optically active CPCs via enantioselective palladation was first introduced in 1979 by Sokolov and his research group.[226] In this study, the researchers obtained dimer **170** with 79% ee using 1 equiv. of (*S*)-*N*-acetylleucine (**169**) in the palladation of (dimethylaminomethyl)ferrocene (**170**) by Na_2PdCl_4 (Scheme 34).[226] Recently, Richards and Günay investigated the same reaction in an attempt to confirm the enantioselectivity observed by Sokolov (Scheme 34).[227] To obtain CPC **170**, they used the same reaction conditions described by Sokolov. The product analysis by chiral chromatography provided 96% ee.[227] The research groups of Ryabov and Richards used enantioselective palladation to access other optically active CPCs.[159, 233, 234] To the best of our knowledge, optically active aliphatic CPCs have never been prepared using this method.



Scheme 34. Synthesis of the optically active CPC **170** via enantioselective palladation.

II. 3. Applications of Optically Active Cyclopalladated Complexes

Optically active CPCs have many applications. For example, in asymmetric synthesis, they can play three roles: catalyst/precatalyst,[189, 190, 235-238] chiral auxiliary[239-241] and reactant.[14, 207, 242, 243] Optically active CPCs have also been used in chiral resolution,[244-247] for determination of enantiopurity of amines, phosphines and other substrates possessing ligand properties[248-250] as well as functioning as a reference point for determination of absolute configuration.[245, 246, 251-253] In the majority of the application studies (except for the use of CPCs as chiral catalysts), only a small group of optically active CPCs are commonly employed; they are derivatives of optically active 1-phenylethylamine,[248, 250] 1-(1-naphthyl)ethylamine[205] and 1-(2-naphthyl)ethylamine.[254]

Amongst the optically active CPCs obtained from compounds available in the chiral pool,[255] only CPCs containing the oxazoline moiety were used in applications involving chiral induction, predominantly as catalysts in asymmetric transformations.[256, 257] Moreover, the best results were obtained for quite complex structures, particularly those containing not only the oxazoline ring, but also a planar-chiral moiety.[256, 257] Only a small fraction of known enantiopure or scalemic CPCs have an (sp^3)C–Pd bond,[32, 207-209] and none of them have been used as either resolving agents or catalysts in enantioselective transformations.

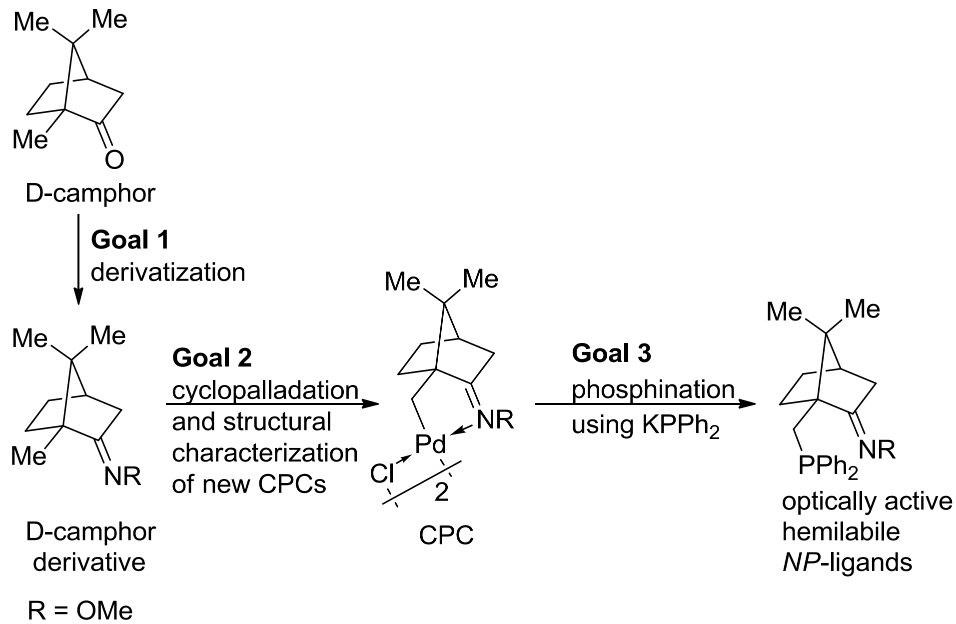
II.4. Goals of the Present Study

As was presented above, enantiopure CPCs have many important applications. However, most of these complexes are derivatives of 1-phenylethylamine and have an (sp^2)C−Pd bond. It is of interest to 1) prepare new types of enantiopure aliphatic CPCs from readily accessible chiral compounds, 2) characterize their structures using available spectrometric methods and 3) study them as chiral inductors in various asymmetric transformations.

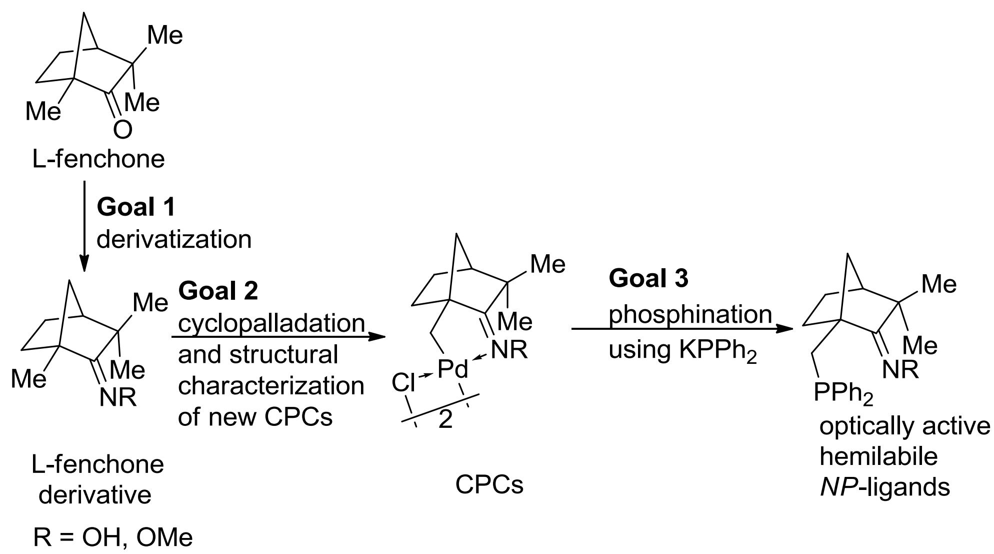
Readily available enantiopure D-camphor and other bicyclic monoterpenoids possess rigid structures that may be an advantageous feature in asymmetric reactions; therefore, CPCs based on compounds of this type are important research targets. If new CPCs based on inexpensive compounds from the chiral pool become available, applications of metallacycles in catalysis can be broadened and enriched. In this dissertation, we proposed and studied the synthesis, structural pecularities and applications of new enantiopure CPCs derived from D-camphor and L-fenchone. Among various possible applications of the new camphor- and fenchone-based CPCs, we selected and investigated their transformations using $KPPh_2$.

Recently, our research group[14, 15] and others[258, 259] have shown that $LiPPh_2$ and $KPPh_2$ are capable of reacting with aromatic CPCs at the C–Pd bond to give hemilabile *NP*-ligands containing an (sp^2)C−P bond. *NP*-, *PP*- and *SP*-bidentate ligands are efficient catalysts in a number of reactions. New types of chiral hemilabile *NP*-, *PP*- and *SP*-ligands obtained from inexpensive and naturally optically active compounds can greatly broaden and enrich the applications of these compounds in catalysis. In this dissertation, we proposed and studied the synthesis of new enantiopure *NP*- and other bidentate ligands through the reaction of aliphatic CPCs with $KPPh_2$. Bidentate ligands having an (sp^2)C−P bond have primarily been synthesized using lithium-mediated substitution.[260-262]

The specific goals of the present study are: (1) to prepare D-camphor and L-fenchone derivatives capable of forming cyclopalladated complexes; (2) to synthesize and structurally characterize new enantiopure CPCs based on D-camphor- and L-fenchone derivatives and (3) to investigate a possibility of the *NP*-ligand preparation by reactions of aliphatic CPCs with $KPPh_2$ (Schemes 35 and 36).



Scheme 35. Proposed synthesis and applications of D-camphor-derived CPCs.



Scheme 36. Proposed synthesis and applications of L-fenchone-derived CPCs.

CHAPTER III

RESULTS AND DISCUSSION

III.1. Synthesis of CPCs

III.1.1. Oxime of D-Camphor

There are a few reports about CPCs based on D-camphor; however, their structures are either quite complex (see structures **171** and **172** in Chart 14)[263] or the bornane carbon framework is not a part of the metalacycle (compound **173**).[264] In 1983, Constable et al. reported unsuccessful attempts to cyclopalladate D-camphor oxime (HL) (**174a**) using Na_2PdCl_4.[265] The main product of the reaction was the corresponding coordination complex, $PdCl_2(HL)_2$. Attempts to convert the coordination complexes $PdCl_2(HL)_2$ and $PdI_2(HL)_2$ to their cyclopalladated analogs by heating in high-boiling solvents were also unsuccessful.[265] For comparison, the oximes of 2,2-dimethylcyclohexanone and related substrates undergo cyclopalladation using the same palladating reagent in high yields.[64]

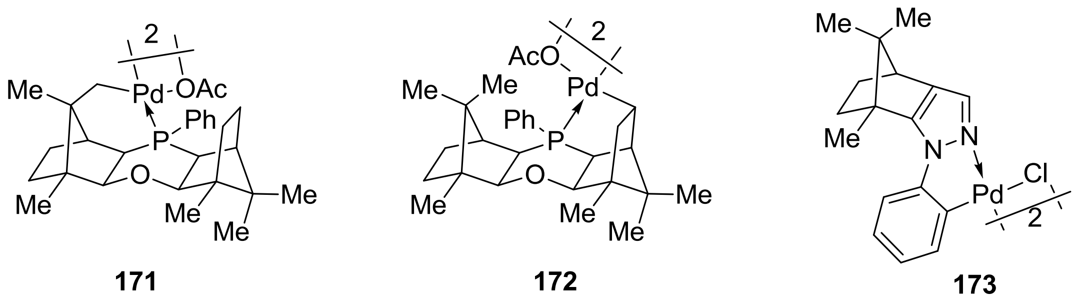
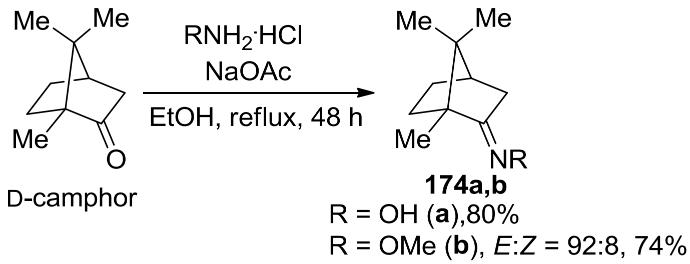


Chart 14. Known CPCs containing the D-camphor carbon framework.

The Sanford group reported $Pd(OAc)_2$-catalyzed C–H bond oxygenation of *O*-methyl camphor oxime (**174b**) using $K_2S_2O_8$ in a mixture of AcOH and Ac_2O (100 ºC, 12 h, 63%)[172] or $PhI(OAc)_2$ in AcOH (100 ºC, 12 h, 75%).[172, 173] The same year, Thu et al. disclosed the results of the $Pd(OAc)_2$-catalyzed amidation of the same camphor derivative using $K_2S_2O_8$ and H_2NCOR (R = *p*-ClC_6H_4) and resulting in the conversion of the 1-methyl group to 1-CH_2NHSO_2R (80 ºC, 14–20 h, 93%).[266] Both groups suggested that the reactions preceded through the formation of a cyclopalladated intermediate; however, no attempts were made to isolate it.

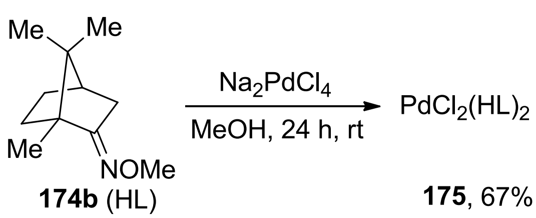
*Synthesis of Compounds **174-178** and Spectral Characterization*

On the basis of the aforementioned literature data, *O*-methyl camphor oxime **174b** was chosen as a simple preligand for synthesis. First, attempts were made to obtain oxime **174b** following the procedure, according to which a solution of D-camphor, methoxyamine hydrochloride and pyridine in isopropanol was refluxed for 7 h.[267] The ^{1}H NMR spectrum of the reaction mixture showed that only ca. 10% of D-camphor was converted to the oxime. The Booth method,[268] following which a mixture of D-camphor, methoxyamine hydrochloride and pyridine was stirred at rt for 48 h, was also unsuccessful in our hands. When a mixture of D-camphor, methoxyamine hydrochloride and NaOAc in ethanol was refluxed for 5 h following the procedure by Kumar and Verma,[269] the desired product was prepared in 25% yield. When two-fold excess of methoxyamine hydrochloride and NaOAc was used and the reaction time was increased to 24 h, the pure product was isolated in 74% yield (Scheme 37). According to the ^{1}H NMR, the prepared oxime was a 92:8 mixture of two geometrical isomers. Refluxing $HONH_2$.HCl with D-camphor and NaOAc in EtOH for 48 h gave preligand **174a** in 80% yield. The structure of **174a** was confirmed using [1]H and [13]C NMR spectra.



Scheme 37. Preparation of oxime **174** from D-camphor.

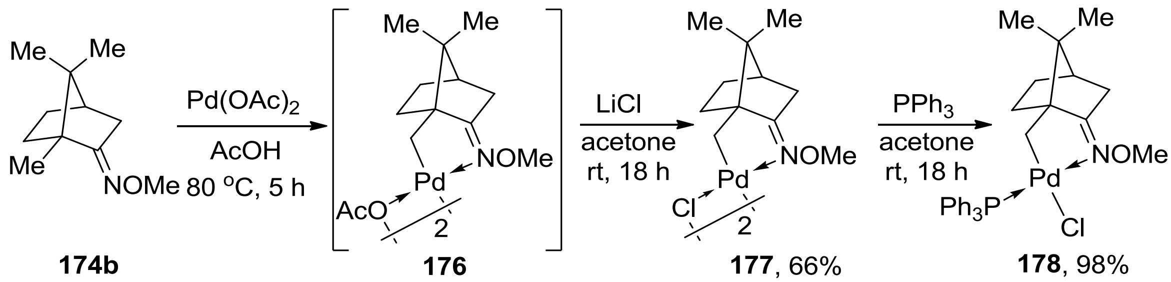
The coordination complex $PdCl_2(HL)_2$ (**175**) was prepared as a reference compound before attempting the cyclopalladation of the oxime. The coordination complex **175** was isolated in 67% yield by stirring camphor oxime **174b** with 0.5 equiv of Na_2PdCl_4 at rt for 18 h (Scheme 38). According to the NMR spectroscopy data, the compound was a mixture of two isomers in ca. 9:1 ratio, possibly due to the presence of *E* and *Z* isomers in the starting oxime, although the existence of trans/cis forms of the complex in the solution cannot be excluded.



Scheme 38. Preparation of the coordination complex **175**.

Cyclopalladation of oxime **174b** was first tested with equimolar amounts of Na_2PdCl_4 and NaOAc by stirring the reagents in abs. MeOH at rt. Analytical TLC and [1]H NMR spectrum of the product indicated that this reaction gave only complex **175** (33% yield). Repeating this reaction at reflux for 6 h still showed only the coordination complex.

An equimolar mixture of camphor oxime **174b** and $Pd(OAc)_2$ was then stirred in glacial acetic acid at 80 °C for 5 h. After treatment with LiCl, the chloro-bridged CPC **177** was obtained in 66% yield (Scheme 39). The dimeric complex was converted to the mononuclear triphenylphosphine adduct **178** in 98% yield by stirring a 2:1 mixture of PPh_3 and CPC **177** in acetone at rt (Scheme 39).



Scheme 39. Preparation of dimeric and mononuclear complexes **177** and **178**.

The proposed structures of the obtained coordination and cyclopalladated complexes **175**, **177** and **178** were supported by NMR spectroscopy. Signal assignment in the ^{1}H and ^{13}C NMR spectra was done using DEPT, COSY and HMQC spectra. Purity and elemental composition of the compounds were proven by satisfactory elemental analysis.

The ^{1}H NMR spectra of the free oxime and the coordination complex contained four 3H singlets confirming the presence of one methoxy and three methyl groups in their structures. The striking difference between the two spectra was a significant downfield shift of the singlet belonging to the 1-Me group of complex **175** from δ 1.02 to 2.42 ppm. Such downfield shifts of some signals in the spectra of coordination complexes in comparison to those of free ligands have been observed earlier[56, 111, 270, 271] and can be explained by the position of the corresponding hydrogens above or below the $PdCl_2N_2$

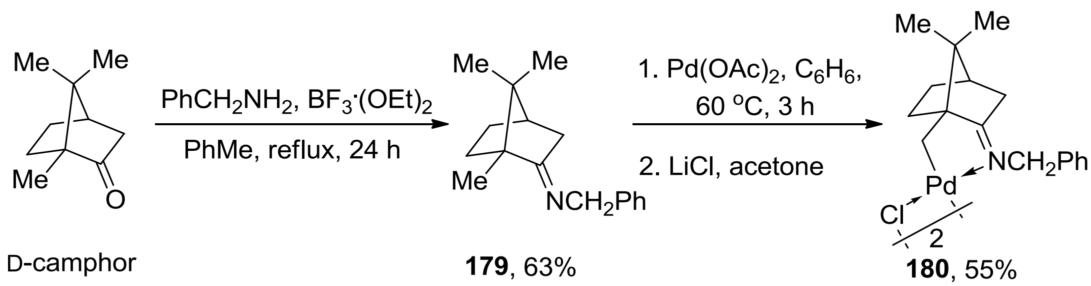
plane of the coordination complex.[272] Such positioning of the C–H bond is considered a possible step of cyclopalladation.[23]

As expected, ^{1}H NMR spectra of the cyclopalladated derivatives **176** and **178** had signals of only two methyl groups instead of three (in addition to the singlet of the NOMe fragment). Each of the two diastereotopic hydrogens in the $PdCH_2$ group provided a doublet (or a doublet of doublets due to $^{3}J_{H,P}$ for one of the hydrogens in complex **178**): ^{2}J = 8 Hz at 2.22 and 2.58 ppm for **177** and ^{2}J = 10 Hz at 0.53 and 1.86 ppm for **178**. The observed coupling constants and chemical shift values are similar to those reported previously for other dimeric CPCs and PPh_3 derivatives with the (sp^3)C–Pd bond.[208, 209]

It is noteworthy that the ^{1}H and ^{13}C NMR spectra in C_6D_6 of the dimeric CPC **177** showed doubling of some signals (in a 5:3 ratio). This can be explained by the presence of two geometrical isomers, cis and trans. Such isomerism is well known for dimeric CPCs[25, 273] including those with the (sp^3)C–Pd bond.[23]

The ^{1}H, ^{13}C and ^{31}P NMR spectra[23] of the mononuclear CPC **178** had one set of signals that suggests the existence of only one isomer in a solution. This complex appears to have the trans-*P,N* geometry as practically all known PPh_3 adducts of *CN*-cyclopalladated complexes. The 1D NOE experiment with the irradiating frequency corresponding to the resonance frequency of the ortho hydrogens of the PPh_3 ligand (δ 7.78 ppm) showed a positive enhancement of the signal at 1.86 ppm, which belongs to one of the hydrogens of the CH_2Pd fragment. Also, the ^{1}H NMR signal of one of the hydrogens of the CH_2Pd group (δ 0.53 ppm) appeared as a doublet of doublets with $^{2}J_{HH}$ = 10 Hz and $^{3}J_{HP}$ = 8 Hz. A similar value of the $^{3}J_{HP}$ coupling constant observed for only one of the two hydrogens of the CH_2PdP fragment was reported for a related PPh_3 complex with trans-*P,N* geometry proven by X-ray crystallographic study.[209]

When the cyclopalladation *O*-methyl camphor oxime (**174**) was achieved in our lab, we learned that Kuchin et al. just published the cyclopalladation of a closely related derivative of camphor, *N*-benzylimine **179** (Scheme 40).[274, 275] When our work was compared with Kuchin's, we concluded that their spectral data and ours were similar (Scheme 40).[274, 275]



Scheme 40. D-Camphor-derived palladacycle **180** with the (*sp*^{3})C−Pd bond.

*X-ray Crystallographic Study of CPC **177***

The X-ray single crystal study of complex **177** unambiguously proved its dimeric and cyclopalladated structure. The molecular structure of the compound and the numbering scheme are presented in Fig. 3. Several crystallographic studies of chloro-bridged dimeric five-membered *CN*-CPCs with the (*sp*^{3})C–Pd bond have been reported, including structures **90**, **181**–**184**, which will be used for comparison (Chart 15).[63, 181, 276, 277] Only one of these studies describes the molecular structure of a cyclopalladated oxime with a (*sp*^{3})C–Pd bond (**184**); that oxime was obtained from *tert*-butyl methyl ketone.[63]

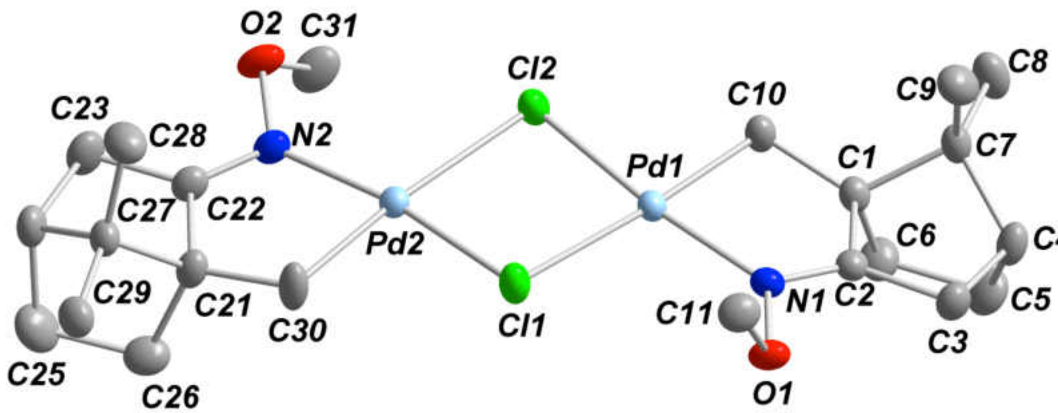


Figure 3. ORTEP drawing of the molecular structure of CPC **177**. Thermal ellipsoids are shown at the 50% probability level.

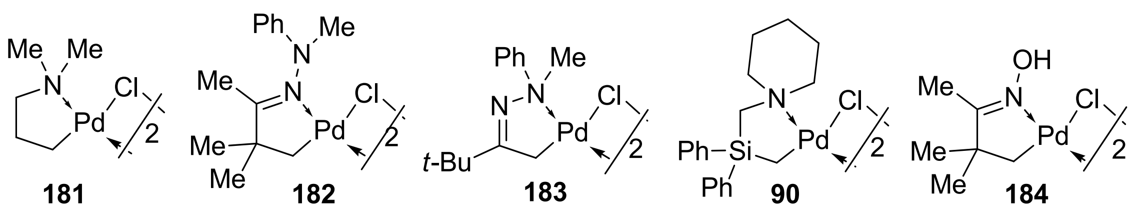


Chart 15. Examples of chloro-bridged dimeric *CN*-CPCs with the (sp^3)C–Pd bond and a known molecular structure.

Complex **177** crystallizes from hexane/dichloromethane in the orthorhombic crystal system and in the space group $P2_12_12_1$. The dimeric molecule consists of two independent halves, which are slightly different in their structural parameters. The structure showed trans geometry of the cyclopalladated ligands typical for the majority of known chloro-bridged *CN*-CPCs with a five-membered palladacycle in solid state. The Pd_2Cl_2 ring in **177** is almost planar as in many other chloro-bridged *CN*-CPCs with trans-configuration. Four torsion angles in the Pd_2Cl_2 ring are between 7.28 and 7.89 Å. The Pd…Pd distance in the complex is 3.500 Å, which is similar to those reported for *CN*-CPCs with trans-geometry.[278] For comparison, the closest analog **184** has very rare cis ligand geometry in solid state and displays a significant bending of the Pd_2Cl_2 ring that results in an unusually short Pd…Pd distance of 2.99 Å.[63]

The Pd–Cl bond trans to the metalated carbon is longer, 2.4996 Å, than that trans to the nitrogen, 2.3311 Å (Δ 0.1685 Å), (here and later, the given values represent the average of two numbers obtained for each half of the dimeric molecule). Similar findings were reported for trans complexes **90**, **181**–**183**, in which the Pd–Cl bond length differences are 0.188, 0.156, 0.128 and 0.162 Å, respectively.[181, 276, 277] For three representative chloro-bridged dimeric *CN*-CPCs with (i) the (sp^2)C–Pd bond, (i) a five-membered palladacycle and (iii) trans ligand geometry, the difference between two Pd–Cl bonds (cis and trans to the aromatic carbon) has also been observed, although that difference is smaller, 0.1053, 0.125 and 0.131 Å.[4, 170, 228, 279] These data reflect a stronger trans influence of (i) the carbon donor atom compared to nitrogen and (ii) the (sp^3)C atom compared to (sp^2)C.

The (sp^3)C–Pd bond length in **177** is 2.019 Å. This value is within the range reported for complexes **90**, **181**–**184** (1.959–2.034 Å). The (sp^2)N–Pd bond in **177** is a little bit longer than the (sp^3)C–Pd bond, 2.037 Å, as it is reported for other chloro-bridged dimeric *CN*-CPCs with the (sp^2)N and (sp^2)C donor atoms and trans geometry of cyclopalladated ligands.[170, 228, 279, 280] For comparison, in complexes **182** and **184**, the (sp^2)N–Pd bond lengths are 1.996(13) and 1.986(1) Å, respectively.[63, 277]

In complex **177**, the bite angles C(10)-Pd-N(1) and C(30)-Pd(2)-N(2) are 82.14(10) and 82.39(10)^o, respectively. This value falls in the range reported for compounds **181**–**183**: 84.5(1), 80.7(7) and 82.9(6) ^{o}, respectively.[276, 277] In complex **183** with a silicon atom in the metalacycle, the angle reaches 86.81(9)^o.[181] For comparison, the C-Pd-N angle for chloro-bridged CPCs with the (sp^2)N and (sp^2)C donor atoms varies from 80.3 to 81.2^o;[170, 228, 279] for the corresponding complexes with (sp^3)N and (sp^2)C, the C-Pd-N bite angle is slightly larger, 80.6−82.8^o.[278, 280]

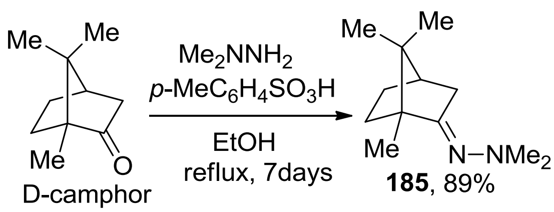
Both palladium atoms in complex **177** are nearly in square-planar coordination with a slight tetrahedral distortion. The angle between the planes {N(1)Pd(1)C(10)} and {Cl(1)Pd(1)Cl(2)} is only 0.56°; the angle between the corresponding planes {N(2)Pd(2)C(30)} and {Cl(1)Pd(2)Cl(2)} is just slightly bigger, 3.26°. It appears that such almost ideal square-planar geometry is a characteristic feature of aliphatic palladacycles.[209]

Two metalacycles of dimer **177** can be described as slightly twisted envelopes with C(10) and C(21) serving as the envelope flaps. To estimate the distortion of each metalacycle from planarity, the sum of absolute values of intrachelate torsion angles was used as was proposed by Dunina.[281] For one of the rings in CPC **177**, the sum is 65.67° with the average angle of 13.13°. For the second metalacycle, the sum is 31.7° with the average angle of 6.34°. The closely related dimer **181** displays a significantly higher distortion of the metalacycle with the sum of torsion angles equal to 158°, with an average angle of 31.6°.[276] For comparison, chloro-bridged *CN*-CPCs with the (sp^2)C and (sp^3)N donor atoms have the sum of intrachelate torsion angles in the range of 99–135.5°.

III.1.2. *N,N*-Dimethylhydrazone of D-Camphor

The *N,N*-dimethylhydrazone of D-camphor (**185**) was first reported by Chelucci et al. in 1986 in their study of pyridoannelation of hindered ketones.[282] As mentioned before, aliphatic CPCs containing the hydrazone directing group have been investigated by Cardenas et al.[67, 68] There are no literature reports on the attempted cyclopalladation of compound **185** or its involvement in palladium-catalyzed reactions.

Preligand **185** was synthesized as a single isomer (^{1}H and ^{13}C{^{1}H} NMR data) in 89% yield following the published procedure by Chelucci et al.[282, 283] D-Camphor, *N,N*-dimethylhydrazine and a catalytic amount of 4-toluenesulfonic acid were refluxed for seven days in ethanol to give product **185** in 89% yield (Scheme 41). The product of this reaction can exist as two geometric, *E/Z*, isomers. According to ^1H and $^{13}C\{^1H\}$ NMR data, the hydrazone was isolated as a single geometric isomer. To determine whether the compound has either E or Z geometry, an NOE test was carried out. Irradiation of the protons on the NMe_2 group during the NMR experiment showed positive NOE for the endo hydrogen on C(3). Based on this observation, it could be concluded that compound **185** has the E geometry.



Scheme 41. Synthesis of camphor *N,N*-dimethylhydrazone **185**.

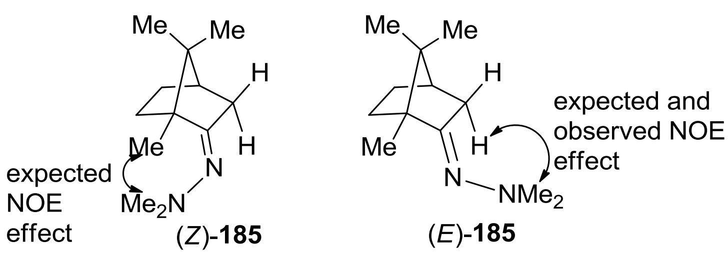
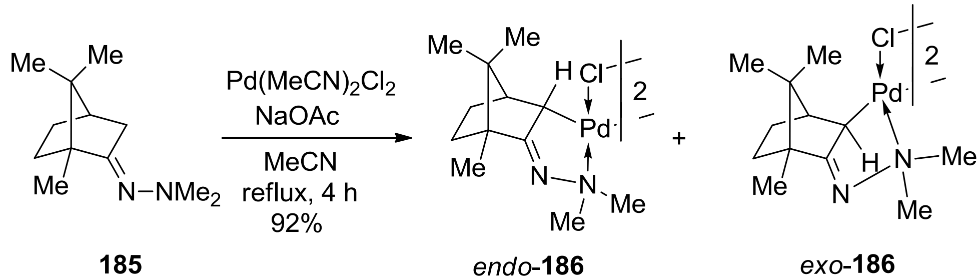


Figure 4. Expected and observed NOE effect upon irradiation of the NMe_2 group on **185**.

Cyclopalladation of the camphor hydrazone **185** was attempted using a variety of conditions; the successful results are summarized in Table 1. All reactions in AcOH resulted in deprotection of the carbonyl group to give camphor. Palladation of **185** using $Pd(OAc)_2$ in MeCN or toluene furnished the desired product **186**, although in low yields. The yield of compound **186** was increased to 72% when Na_2PdCl_4 was used in the presence of the weak base NaOAc in MeCN. The best yield (92%) of the cyclopalladated complex was achieved with $Pd(MeCN)_2Cl_2$/NaOAc in MeCN (Scheme 42).



Scheme 42. Cyclopalladation of camphor *N,N*-dimethylhydrazone **185**.

Table 1. Cyclopalladation of camphor *N,N*-dimethylhydrazone **185**.

Entry	Pd source/base	Rxn temp. (°C)	Rxn time (h)	Solvent	Yield of **186** (%)
1	$Pd(OAc)_2$	reflux	4	MeCN	44
2	Na_2PdCl_2/AcONa	reflux	4	MeCN	72
3	$Pd(OAc)_2$	60	6	PhMe	46
4	$Pd(CH_3CN)_2Cl_2$/NaOAc	reflux	4	MeCN	92

Cyclopalladation of **185** occurred at the methylene group. This conclusion was made based on the ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of CPC **186** which showed signals of the three methyl groups on the camphor moiety in addition to the nonequivalent methyl groups on the (sp^3)N atom. This suggested that palladation takes place at C(3) (the methylene carbon) and the (sp^3)N atom is coordinated to the Pd center leading to the possibility of endo/exo palladation. The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of product **186** were complex. This complexity is not only due to possible formation of endo and exo isomers but also cis and trans isomers (Chart 16). In addition, conformational flexibility of *trans*- and *cis*-**186** is plausible, resulting in three diastereomers for each conformation. This was observed by Perera et al. for complexes of molybdenum derived from 3-diphenylphosphino-(1*R*)-(+)-camphor dimethylhydrazone.[284]

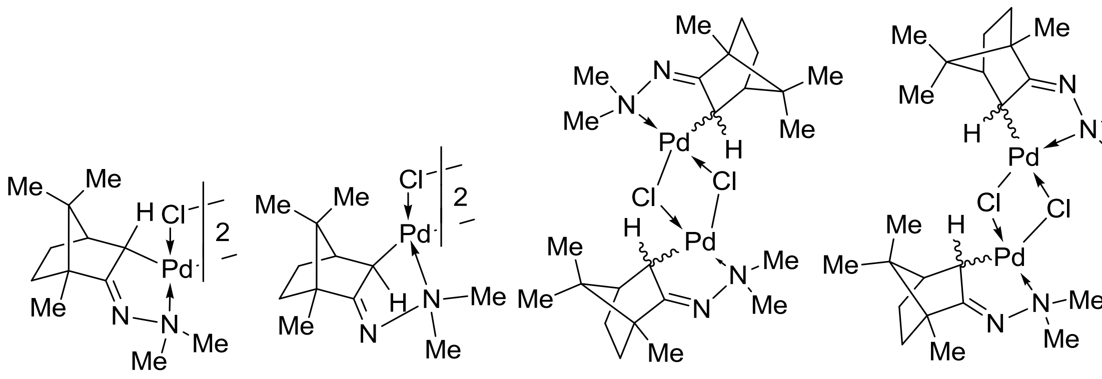
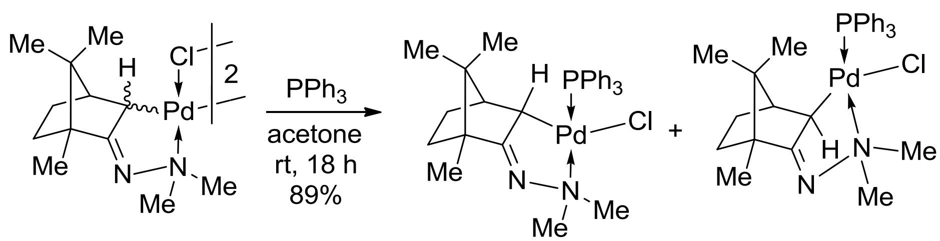


Chart 16. Possible isomers of CPC **186**.

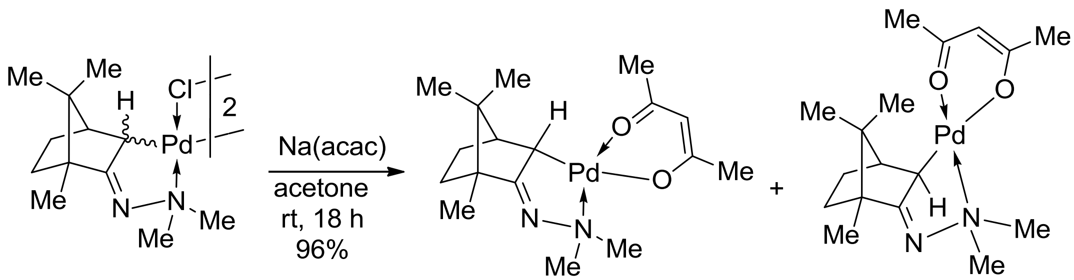
Repeated attempts to get only one isomer by varying the reagents and reaction conditions gave the same mixture (^{1}H and ^{13}C{^{1}H} NMR data). All efforts to separate the isomers by preparative thin-layer chromatography (TLC) using different eluents were unsuccessful. The mixture of CPCs was refluxed in MeOH in the hope that it would isomerize to give a single isomer, but instead deprotection of the carbonyl group occurred to give D-camphor. Refluxing CPCs **186** over 6 h in aprotic solvents like MeCN and toluene also led to the breakdown of the complex with the deposition of Pd black. Separation of CPCs **186** by recrystallization using common solvents was unsuccessful.

Because the ^{1}H and ^{13}C{^{1}H} NMR spectra for the dimeric complex **186** were difficult to interpret, it was reacted with 2 equiv. of PPh_3 in acetone to give the mononuclear triphenylphosphine adduct **187** (Scheme 43). The ^{1}H and ^{13}C{^{1}H} NMR spectra of complexes **187** showed a mixture of two stereoisomers in a 1:1 isomeric ratio, one with an endo C−Pd bond (*endo*-**187**) and the other with an exo C−Pd bond (*exo*-**187**, Scheme 43). Attempts to separate the isomers by preparative TLC using different eluents were also unsuccessful. Similar to dimers **186**, deprotection of the carbonyl group occurred to give D-camphor when the mixture of complexes **187** was refluxed in MeOH. Refluxing complexes **187** in aprotic solvents like MeCN and toluene also led to the breakdown of the complex with the deposition of Pd black. Separation of CPCs **187** by recrystallization using common organic solvents failed.



Scheme 43. Reaction of camphor *N,N*-dimethylhydrazone CPC **186** with PPh_3.

There are many reports of the conversion of dimeric CPCs to their mononuclear adducts by reaction with Na(acac).[74, 285-289] Na(acac) was prepared by slow addition of a solution of NaOH to acetylacetone. CPC-**186** was also converted to the mononuclear acetylacetonate adducts *endo*- and *exo*-**188** in 96% yield by stirring with 3 equiv. of Na(acac) in $CHCl_3$ (Scheme 44). The yield of *endo*- and *exo*-**188** was similar to those reported in the literature (80–98%). The ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra of product **188** showed a mixture of two diastereomers, which differ by stereochemistry at C(3) (Scheme 44). Attempts to separate the two isomers using preparative TLC were unsuccessful.



Scheme 44. Reaction of the camphor *N,N*-dimethylhydrazone CPC **186** with Na(acac).

The best ratios of *endo*- and *exo*-**188**, 83:17 for the former and 19:81 for the latter, were obtained using preparative TLC (silica gel, 1:2 ethyl acetate–hexane). The 83:17 mixture of endo and exo complexes were left in $CDCl_3$ for 3 weeks resulting to a 3:2 ratio of endo and exo complexes which suggested a slow isomerization of the former compound to the latter. The two isomers can be differentiated by a distinct ^{1}H NMR signal of the hydrogen bonded to C(3). The singlet at δ 3.99 ppm was assigned to isomer *exo*-**188** with the endo hydrogen at C(3) since no coupling is expected between hydrogens of C(3) and C(4). The exo hydrogen of C(3) in isomer *endo*-**188** was coupled with both the hydrogen of C(4) and the exo hydrogen of C(5) providing a triplet at δ 4.82 ppm with a coupling constant of 3.5 Hz. These data point to the fact that *endo*-**188** has C–Pd bond in endo position, while *exo*-**188** is the exo isomer as shown in scheme 44. The identity of the endo isomer could further be confirmed by comparing the ^{1}H NMR signals of the three methyl groups of the camphor fragment as they appear in three compounds: preligand **185** and complexes *endo*- and *exo*-**188**. The three methyl groups of the camphor moiety of the endo isomer are arranged in a similar pattern to those of the preligand **185** while those in the exo isomer are not. The interaction of the acac ligand with (pro-*S*)-Me at C(7) in the exo isomer led to a downfield shift of its ^{1}H NMR signal.

*X-ray Crystallographic Study of CPC **186***

The X-ray single crystal study of complex **186** unambiguously proved its dimeric and cyclopalladated structure. The molecular structure of the compound and the numbering scheme are presented in Fig. 4. To the best of our knowledge, there are no reported crystal structures for *CN*-CPCs with a 2° (sp^3)C–Pd bond. However, several crystallographic studies of chloro-bridged dimeric five-membered *CN*-CPCs with 1° (sp^3)C–Pd bonds have been reported, including structures **90**, **177**, **181**–**184**, which will be used for comparison (Chart 17).[63, 181, 276, 277] Only two of these studies describe the molecular structure of a cyclopalladated hydrazone with a (sp^3)C–Pd bond (**182**, **183**); these hydrazones were obtained from *tert*-butyl methyl ketone.[277]

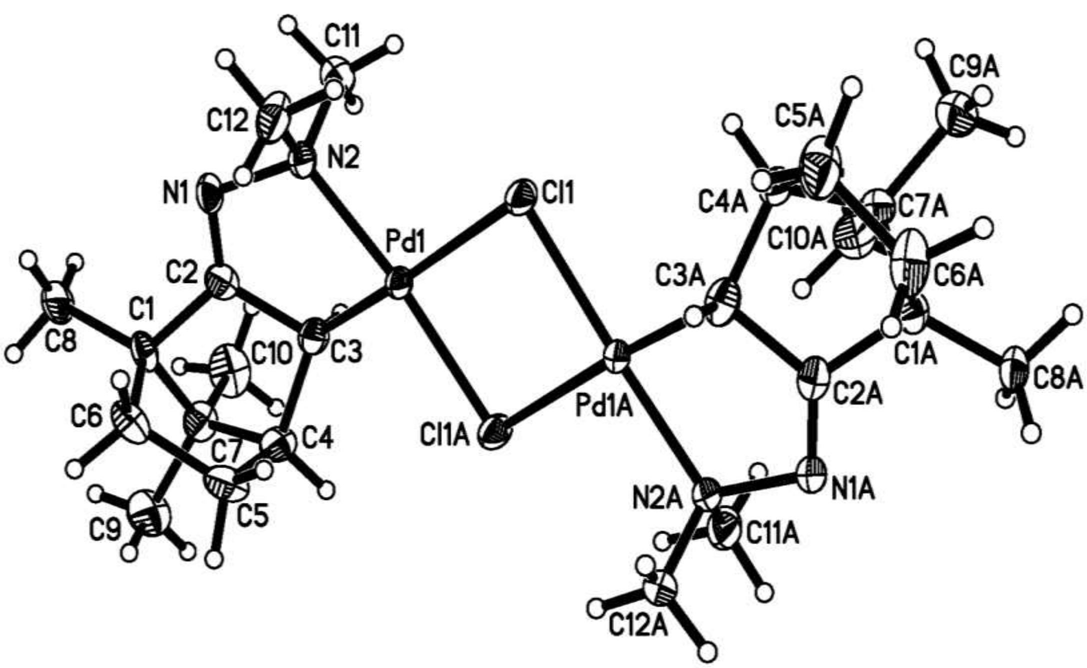


Figure 5. ORTEP drawing of the molecular structure of CPC **186**. Thermal ellipsoids are shown at the 50% probability level.

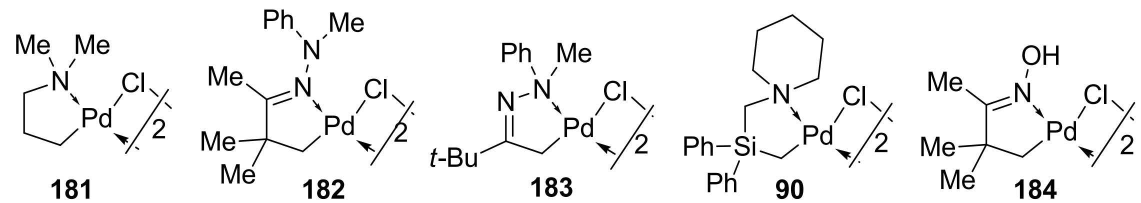


Chart 17. Examples of chloro-bridged dimeric *CN*-CPCs with an (sp^3)C–Pd bond and a known molecular structure.

Complex **186** crystallizes from hexane/dichloromethane in the monoclinic crystal system and in the space group $P2_1$. The dimeric molecule consists of two independent halves, which are slightly different in their structural parameters. The structure showed trans geometry of the cyclopalladated ligands typical for the majority of known chloro-bridged *CN*-CPCs with a five-membered palladacycle in solid state. The Pd_2Cl_2 ring in **186** is almost planar as in many other chloro-bridged *CN*-CPCs with trans configuration. Four torsion angles in the Pd_2Cl_2 ring are between 2.17 and 2.38 Å. The Pd…Pd distance in the complex is 3.466 Å, which is similar to those reported for *CN*-CPCs with trans-geometry.[278] For comparison, the closest analog **177** has a Pd…Pd distance of 3.500 Å while another close analog, **184**, possesses very rare cis ligand geometry in solid state and displays a significant bending of the Pd_2Cl_2 ring that results in an unusually short Pd…Pd distance of 2.99 Å.[63]

The Pd–Cl bond trans to the metalated carbon is longer, 2.4906 Å (here and later, the given values represent the average of two numbers obtained for each half of the dimeric molecule), than that trans to the nitrogen, 2.3374 Å (Δ 0.1532 Å). Similar findings were reported for trans complexes **90**, **177**, **181**–**183**, in which the Pd–Cl bond length differences are 0.188, 0.169, 0.156, 0.128 and 0.162 Å, respectively.[181, 276, 277] For three representative chloro-bridged dimeric *CN*-CPCs with (i) the (sp^2)C–Pd bond, (ii) a five-membered palladacycle and (iii) trans ligand geometry, the difference between two Pd–Cl bonds (cis and trans to the aromatic carbon) has also been observed, although that difference is smaller, 0.1053, 0.125 and 0.131 Å.[4, 170, 228, 279] These data reflect a stronger trans influence of (i) the carbon donor atom compared to nitrogen and (ii) the (sp^3)C atom compared to (sp^2)C.

The (sp^3)C–Pd bond length in complex **177** is 1.982 Å. This value is within the range reported for complexes **90**, **177**, **181**–**184** (1.959–2.034 Å). The (sp^3)N–Pd bond (2.078 Å) in **186** is a little bit longer than the (sp^3)C–Pd bond (1.982 Å), as it is reported for other chloro-bridged dimeric *CN*-CPCs with the (sp^2)N and (sp^3)C or (sp^3)N and (sp^3)C donor atoms and trans-geometry of cyclopalladated ligands.[17, 170, 228, 279, 280] For comparison, in complexes **177**, **182** and **184**, the (sp^2)N–Pd bond lengths are 2.037(2) 1.996(13) and 1.986(1) Å, respectively [63, 277] while in complex **183** the (sp^3)N–Pd bond length is 2.063(1) Å.[277]

In complex **186**, the bite angles C(3)-Pd(1)-N(2) and C(3A)-Pd(1A)-N(2A) are equivalent, 80.8(2)°. This value falls in the range reported for compounds **177**, **181**–**183**: 82.27(10), 84.5(1), 80.7(7) and 82.9(6) °, respectively.[17, 276, 277] In complex **183** with a silicon atom in the metalacycle, the angle reaches 86.81(9)°.[181] For comparison, the C-Pd-N angle for chloro-bridged CPCs with the (sp^2)N and (sp^2)C donor atoms varies from 80.3 to 81.2°;[170, 228, 279] for the corresponding complexes with (sp^3)N and (sp^2)C, the C-Pd-N bite angle is slightly larger, 80.6−82.8°.[278, 280]

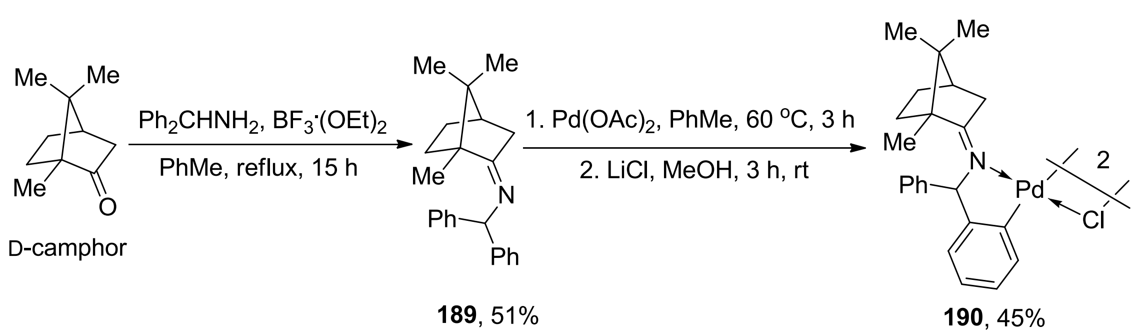
Both palladium atoms in complex **186** are nearly in square-planar coordination with a slight tetrahedral distortion. The angle between the planes {N(2)Pd(1)C(3)} and {Cl(1)Pd(1)Cl(1A) is only 6.02°; the angle between the corresponding planes

{N(2A)Pd(1A)C(3A)} and {Cl(1)Pd(1A)Cl(1A)} is just slightly bigger, 3.60°. It appears that such almost ideal square-planar geometry is a characteristic feature of aliphatic palladacycles.[209]

Two metalacycles of dimer **177** can be described as slightly twisted envelopes with C(10) and C(21) serving as the envelope flaps. To estimate the distortion of each metalacycle from planarity, the sum of absolute values of intrachelate torsion angles was used as was proposed by Dunina.[281] For one of the rings in CPC **177**, the sum is 65.67° with the average angle of 13.13°. For the second metalacycle, the sum is 31.7° with the average angle of 6.34°. The closely related dimer **181** displays a significantly higher distortion of the metalacycle with the sum of torsion angles equal to 158°, with an average angle of 31.6°.[276] For comparison, chloro-bridged *CN*-CPCs with the (*sp*^{2})C and (*sp*^{3})N donor atoms have the sum of intrachelate torsion angles in the range of 99–135.5°.

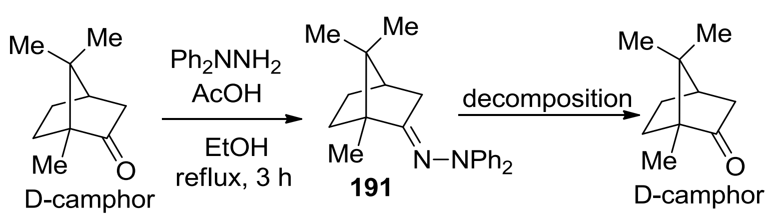
III.1.3. *N,N*-Diphenylhydrazone of D-Camphor

Previously, Kuchin et al. synthesized CPC **190** from camphor *N*-benzylimine **189** using $Pd(OAc)_2$ in toluene at 60 °C. Preligand **189** can undergo either palladation at the (*sp*^{2})C of the phenyl group or at the (*sp*^{3})C of the camphor moiety. This research group observed regioselective metalation at the (*sp*^{2})C of the phenyl group of camphor *N*-benzylimine **189** to give CPC **190** in 45% yield (Scheme 45).[274, 275, 290]



Scheme 45. D-Camphor-derived palladacycles with the (*sp*^{2})C−Pd bond.

It was of interest to investigate regioselectivity of cyclopalladation for the related preligand, *N,N*-diphenylhydrazone of D-camphor **191**. There are no literature reports on *N,N*-diphenylhydrazone of D-camphor **191**. Attempts were made to obtain hydrazone **191** following the published procedure for the synthesis of the phenylhydrazone of D-camphor **192** by Schantl et al.[291] According to their procedure, *N,N*-diphenylhydrazine, D-camphor and a catalytic amount of AcOH were refluxed for 3 h in ethanol (Scheme 46). ^{1}H NMR spectrum of the reaction mixture indicated the presence of the product in ca. 70% yield, but upon purification the *N,N*-diphenylhydrazone of D-camphor completely decomposed to D-camphor.

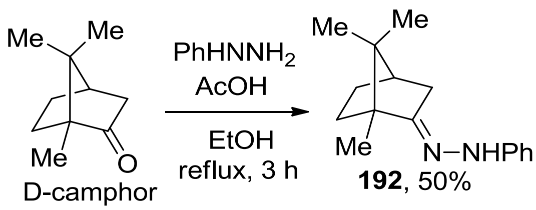


Scheme 46. Synthesis of camphor *N,N*-diphenylhydrazone **191**.

III.1.4. Phenylhydrazone of D-Camphor

The phenylhydrazone of D-camphor (**192**) was synthesized in 50% yield following the published procedure by Schantl et al.[291] According to their procedure, D-camphor, phenylhydrazine and a catalytic amount of AcOH were refluxed for 3 h in ethanol (Scheme 47). The structure of the phenylhydrazone product was confirmed using ^{1}H NMR spectroscopy. As the authors mentioned, elevated temperatures or traces of acids readily converted phenylhydrazone **192** to D-camphor. It is worth noting that we observed decomposition of this compound immediately after purification even at rt as the brown oily product was turning green. All attempts to cyclopalladate the freshly prepared compound

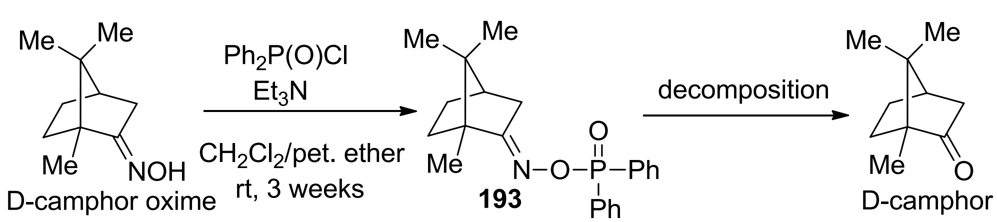
192 using Na_2PdCl_2/AcONa, $Pd(OAc)_2$ or $Pd(CH_3CN)_2Cl_2$/NaOAc at rt in aprotic solvents such as MeCN and toluene failed due to too rapid decomposition of the preligand to the starting carbonyl compound.



Scheme 47. Synthesis of camphor phenylhydrazone **192**.

III.1.5. *O*-(Diphenylphosphinyl)oxime of D-Camphor

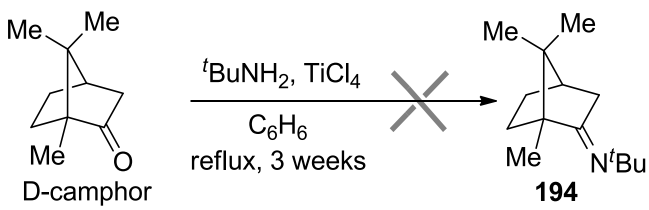
The aim of this work was to access a chiral aliphatic *CP*-palladacycle based on D-camphor. The presence of a phosphorus atom in the desired CPC allows one to use ^{31}P NMR spectroscopy for characterization. There are no reports of *O*-(diphenylphosphinyl) oxime of D-camphor **193** in literature. The synthesis of the acetone analog has been reported by the research groups of Harger and Jennings.[292-294] According to their procedure, diphenylphosphinic chloride, D-camphor oxime and Et_3N were stirred at rt in CH_2Cl_2/petroleum ether for three weeks (Scheme 48). The ^1H NMR spectrum of the reaction mixture showed ca. 91% conversion to product **193**; however, several attempts to isolate this compound in pure form were unsuccessful.



Scheme 48. Synthesis of *O*-(diphenylphosphinyl)oxime of D-camphor **193**.

III.1.6. *tert*-Butylimine of D-Camphor

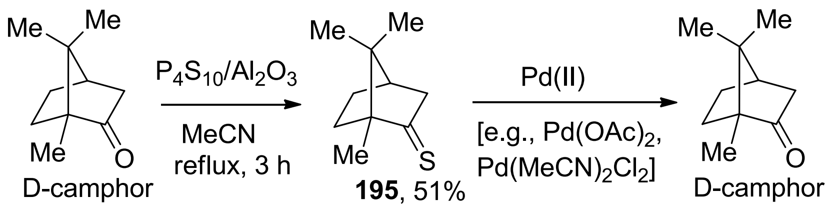
The *tert*-butylimine of D-camphor **194** has not been reported in literature. $TiCl_4$ has been shown to be a very effective catalyst for the condensation of sterically hindered ketones and alkyl amines to furnish *N*-alkylimines.[295-297] Based on this information, D-camphor, *tert*-butylamine and $TiCl_4$ were refluxed in benzene for three weeks (Scheme 49). Analysis of the reaction mixture using ^{1}H NMR spectroscopy showed no conversion to the product.



Scheme 49. Failed attempt to obtain *tert*-butylimine of D-camphor **194**.

III.1.7. Thiocamphor

A sulfur-containing D-camphor derivative **195** was synthesized in order to attempt preparation of the corresponding *CS*-palladacycle. Since there was a report of the cyclopalladation of thioketones,[117] we decided to obtain thioketone **195** (also known as thiocamphor). Attempts to synthesize this compound by refluxing D-camphor with Lawesson's reagent in toluene were unsuccessful.[298] The reaction gave a complex mixture that was difficult to separate. The Polshettiwar and Kaushik procedure, according to which D-camphor and P_4S_{10}/Al_2O_3 were refluxed in MeCN for 2 h, gave thiocamphor in 51% yield (Scheme 50).[299] The structure of thiocamphor **195** was confirmed using ^{1}H NMR spectroscopy. All attempts to cyclopalladate thiocamphor using Na_2PdCl_2/AcONa, $Pd(OAc)_2$ or $Pd(CH_3CN)_2Cl_2$/NaOAc led to the formation of D-camphor.



Scheme 50. Synthesis and the failed cyclopalladation of thiocamphor **195**.

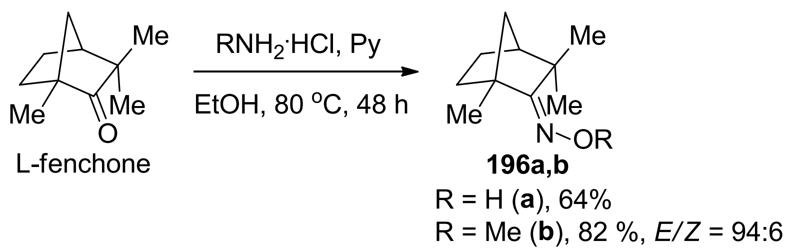
III.1.8. Oxime of L-Fenchone

After succeeding to synthesize and cyclopalladate D-camphor *O*-methyloxime, we decided to try a closely related bicyclic derivative, L-fenchone. Since there is not a single report in the literature on the cyclopalladation of any L-fenchone derivative or their involvement in palladium-catalyzed reactions, we thought that it would be interesting to study their cyclopalladation. The rigidity of inexpensive and naturally optically active L-fenchone could be an advantageous feature in cyclopalladation and subsequently in the applications of the fenchone based CPCs.

Preparation of CPCs Based on L-Fenchone Oximes and their Spectral Characterization

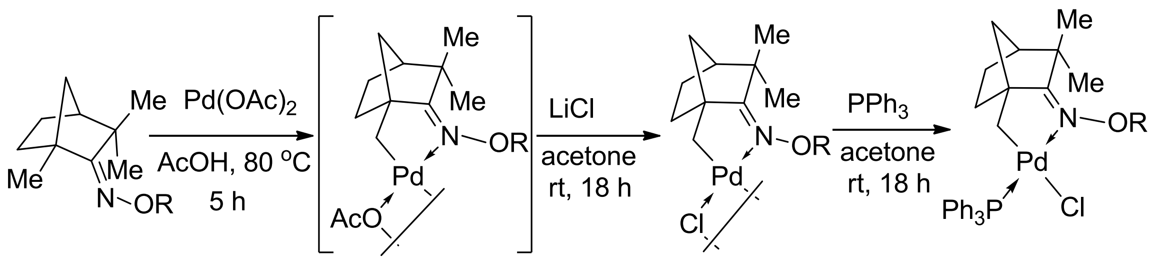
Readily available and inexpensive L-fenchone was converted to two preligands: oxime **196a** and its *O*-methyl derivative **196b** (Scheme 51). Oximes **196b** were synthesized using the Kumar and Verma procedure[269] according to which a mixture of L-fenchone, methoxyamine hydrochloride and NaOAc in ethanol was refluxed for 48 h furnishing the desired product in ca. 50:50 isomeric ratio. All attempts to get a single isomer or predominantly one isomer ratio did not work. Palladation of oxime **196b** using $Pd(OAc)_2$ in AcOH with the hope that isomerization would occur during this process instead gave an inseparable mixture of CPCs. The Jennequin procedure was used to prepare compound **196a** according to which a mixture of L-fenchone, hydroxylamine hydrochloride ($HONH_2{\cdot}HCl$) and pyridine was refluxed in EtOH for 48 h to afford oxime **196a** in 64%

yield .[267] The ^{1}H and ^{13}C NMR spectra of **196a** contained only one set of signals suggesting that the oxime was in the form of one isomer. When $HONH_2 \cdot HCl$ was replaced with its *O*-methyl analog, oxime **196b** was isolated in 82% yield. The ^{13}C NMR spectrum of **196b** contained two sets of signals; the 94:6 ratio of two geometric isomers was determined by integration of two MeO signals in the ^{1}H NMR spectrum.



Scheme 51. Preparation of preligands **196a,b** from L-fenchone.

Cyclopalladation of oximes **196a,b** was accomplished using the same reagent and conditions as reported for the preparation of CPC **177**[17]: $Pd(OAc)_2$, AcOH, 80 °C, 5 h.[55, 60] The dimeric acetato-bridged complexes **197a,b** were converted in situ to their chloro-bridged analogs **198a,b** using LiCl in acetone. In a separate reaction, the latter complexes were converted to mononuclear derivatives **199a,b** using PPh_3 as a monodentate auxiliary ligand (Scheme 52). Chemical composition and purity of complexes **198a,b** and **199a,b** as well as the fenchone derivative **196b** were confirmed by satisfactory elemental analysis.



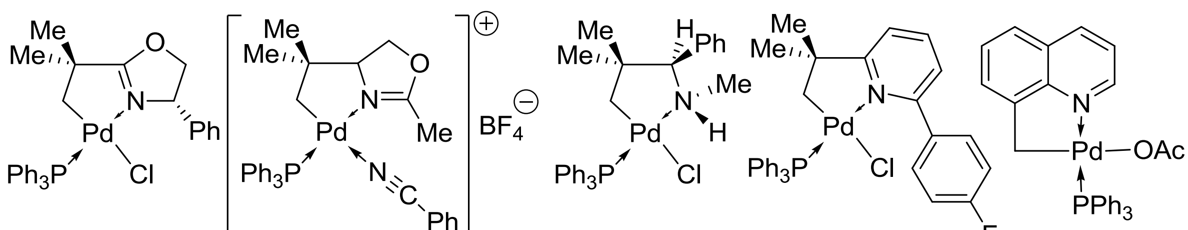
Scheme 52. Preparation of L-fenchone-derived CPCs **198a,b**.

Cyclopalladation of preligands **196a,b** and the proposed structures of new complexes **198a,b** were supported by NMR spectroscopy. The ^{1}H NMR spectra of oxime **196a**[300] and its *O*-methyl derivative **196b** contained three 3H singlets in the region of 1.20−1.35 ppm assigned to the methyl groups at positions 1 and 3. In the ^{1}H NMR spectra of complexes **198a,b**, one of the three singlets in that region was replaced by two one-proton signals with the chemical shifts between 2.15 and 2.80 ppm. Compared to oximes **196a,b**, the DEPT spectra of dimers **198a,b** contained one more CH_2 signal (at 24.6 ppm for **198a** and at 25.8 ppm for **198b**). For comparison, the ^{1}H NMR signals of two diastereotopic hydrogens of the $PdCH_2$ group in the camphor-derived complexes **177** and **180** appeared at 1.55 and 2.59 ppm (**180**) and 1.89 and 2.41 ppm (**177**); the $^{13}C\{^{1}H\}$ NMR signal of the carbon bonded to the metal in complexes **177** and **180** was observed at 30.2 and 29.9 ppm, respectively.[17, 275] $^{13}C\{^{1}H\}$ NMR spectra of dimers **198a,b** in $CDCl_3$ contained only one set of signals suggesting that these complexes exist in solution as one isomer. For comparison, the $^{13}C\{^{1}H\}$ NMR spectra of the camphor-derived dimeric complex **177** in $CDCl_3$ and C_6D_6 contained two sets of signals signifying the existence of this complex in solution as a mixture of cis and trans isomers.[17]

^1H, $^{13}C\{^1H\}$ and $^{31}P\{^1H\}$ NMR spectra of mononuclear CPCs **199a,b** in $CDCl_3$ contained only one set of signals suggesting that these complexes are single geometric isomers in solutions. The $^{13}C\{^1H\}$ NMR signals assigned to the carbon of the $PdCH_2$ fragment in compounds **199a,b** appeared as singlets at 32.8 and 33.0 ppm. The fact that these signals appeared as singlets ($^3J_{C,P} \approx 0$ Hz) may be indicative of the cis position of PPh_3 relative to the methylene group bonded to the palladium.[24] For comparison, the *sp*^{3}-hybridized carbons bonded to the metal in the PPh_3 derivatives of **177** and **180** of trans geometry provided singlets in the $^{13}C\{^1H\}$ NMR spectra at 35.1 and 27.0 ppm, respectively.[17, 275] As reported for related PPh_3 derivatives with the (*sp*^{3})C−Pd bond and proven trans-*N,P* geometry,[76, 208, 209] one of the two ^1H NMR signals of the $PdCH_2$ group in **199a,b** appeared as a doublet ($^2J_{H,H}$ = 10.1 and 10.7 Hz, respectively), while the other hydrogen gave a doublet of doublets due to additional splitting on the phosphorus atom ($^3J_{H,P}$ = 7.2 and 9.0 Hz, respectively). One of the two hydrogens of the $PdCH_2$ fragment in both complexes **199a,b** provided a signal in a significantly higher field (at 1.09 ppm for **199a** and 0.84 ppm for **199b**) compared to the other hydrogen (2.28 and 2.16 ppm, respectively). The significant signal shift to a higher field for one of the two hydrogens of the $PdCH_2$ group in the ^1H NMR spectra of the PPh_3 adducts **199a,b** suggests that the hydrogen is under the influence of magnetic anisotropy caused by phenyl groups of the PPh_3 auxiliary ligand.[301-303] This, in turn, suggests trans-*N,P* geometry of complexes **199a,b**. For comparison, both ^1H NMR signals of the $PdCH_2$ group in the chloro-bridged CPCs **198a,b** were observed above 2.15 ppm. To note, the chemical shift of the signals in the $^{31}P\{^1H\}$ NMR spectra of **199a,b** (19.70 and 20.32 ppm relative to $P(OEt)_3$, respectively) is within the range reported for related mononuclear CPCs with the (sp^3)C−Pd bond, the PPh_3 auxiliary ligand, and proven trans-*N,P* geometry.[76, 208, 209, 304]

X-ray Structural Analysis of Complexes ***199a,b***

Cyclopalladated structure of complexes **199a,b** and their trans-*N,P* geometry were unambiguously proven by X-ray crystallographic studies. Molecular structures of the complexes and the numbering schemes are presented in Figures 5 and 6. Crystal, data collection, and refinement parameters for **199a,b** are presented in Table 15–20. The data obtained for complexes **199a,b** are compared to those reported for dimer **177**[17] and the closely related five-membered *CN*-palladacycles **200−204** containing the (sp^3)C−Pd bond and PPh_3 as the auxiliary ligand (Chart 18).[74, 76, 208, 209, 304]



200 **201** **202** **203** **204**

Chart 18. Examples of PPh_3 adducts of *CN*-CPCs with the (sp^3)C−Pd bond and a known molecular structure.

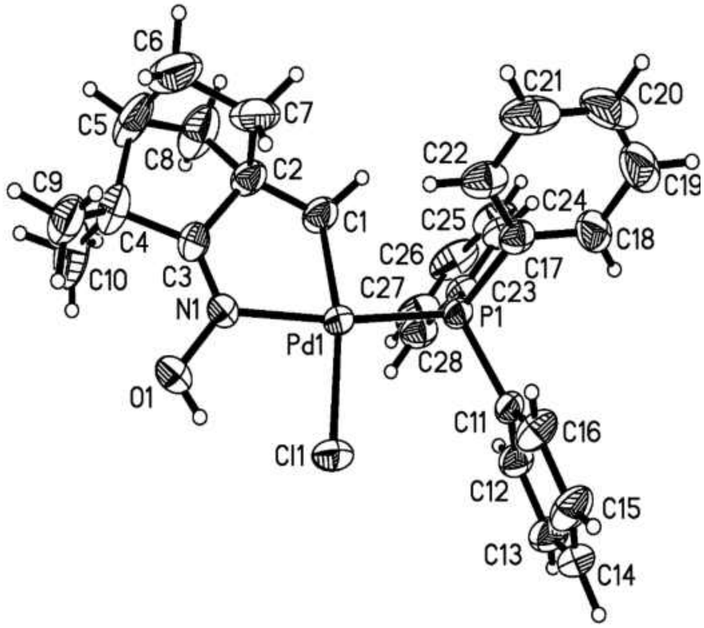


Figure 6. ORTEP drawing of the molecular structure of complex **199a**. Thermal ellipsoids are shown at the 50% probability level.

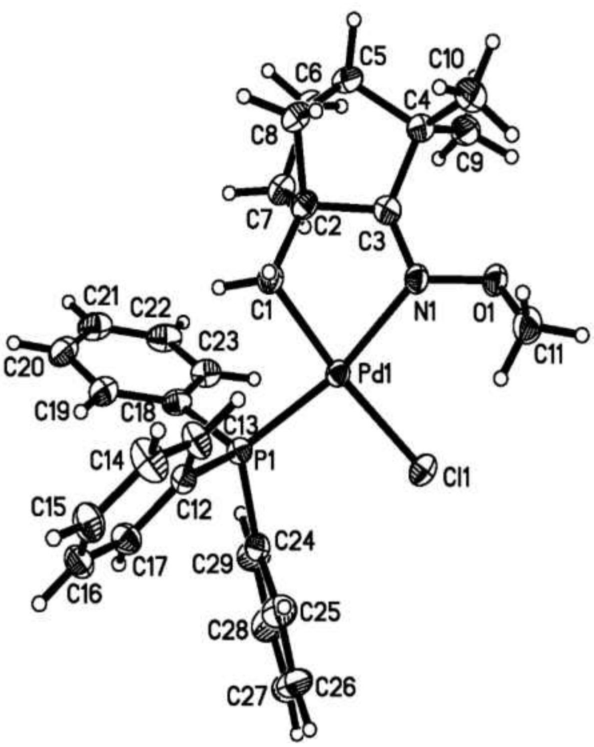


Figure 7. ORTEP drawing of the molecular structure of complex **199b**. Thermal ellipsoids are shown at the 50% probability level.

Bond lengths in **199a,b** are similar to those reported for related complexes.[17, 74, 76, 208, 209, 304] It is noteworthy that the C−Pd bond (2.063 Å) in complex **199b** is the longest among those found in the related complexes (2.000–2.051 Å). Interestingly, the Pd−N bond (2.115 Å) in the same complex **199b** is also the longest among the camphor- and fenchone-derived CPCs **177** and **199a,b**. The Pd−P bond (2.2218 and 2.2250 Å, respectively) in **199a,b** are the shortest among the related *CN*-palladacycles chosen for the comparison (2.2340–2.2563 Å).

The values of the C(1)-Pd-N angle (81.43° and 79.25°, respectively) in both complexes **199a,b** fall in the range of reported values for related compounds (78.15–83.43 °).[17, 74, 76, 208, 209, 304] Other bond angles in **199a,b** are also similar to those found in complexes **177** and **200−203**.

The palladium atom in complexes **199a,b** has square-planar coordination with a slight distortion. In both compounds, the torsion angles Pd-N-C(1)-P, Pd-C(1)-P-Cl, Pd-P-Cl-N and Pd-Cl-N-C(1) have the same sign; therefore, the distortion can be described as pyramidal. The distance from the mean plane {PClC(1)N} to the metal in **199a,b** is 0.049 and 0.075 Å, respectively, indicating that the distortion is greater in **199b**. The angle between the planes {NPdC(1)} and {PPdCl} is equal to 4.3° in **199a** and 6.8° in **199b**. For comparison, the angle between planes {NPdC(1)} and {PPdCl} in the reported mononuclear complexes **200** and **201** is equal to 7.7° (the average for four independent molecules) and 2.9°, respectively.[208, 209]

Palladacycle's conformation in complexes **199a,b** can be described as a slightly twisted envelope with the Pd atom serving as the envelope flap. The sum of absolute values of intrachelate torsion angles in the palladacycle of **199a** is found to be 93.50° with the average angle value of 18.70°. The metalacycle in **199b** is more distorted than that in **199a**: the sum of absolute values of intrachelate torsion angles in palladacycle **199b** is equal to 123.24° with the average angle value of 24.65°. These values suggest that distortion of palladacycles **199a,b** from planarity is about average compared to related palladacycles.[17] For example, for the closely related dichloro-bridged dimer **177**, the sum of the intrachelate torsion angles in palladacycle is 48.69° (the average for two palladacycles in the dimer), while the angle sum in the palladacycle of complex **200** is found to be 97.56°. The most distorted palladacycle appears to be in complex **201**,[209] where the sum of intrachelate torsion angles reaches 171.24°.

A notable feature of the crystal structure of complex **199a** is the participation of the OH fragment in an intramolecular hydrogen bond with the Cl acceptor. There are two other reports of hydrogen bonding involving the oxime group in camphor-derived Pd(II) complexes.[265, 305] One of these two studies describes the molecular structure of the coordination complex $PdCl_2L_2$, L = camphor oxime.[265] The authors drew attention to two hydrogen bonds involving one of the two Cl atoms and both hydroxyl groups suggesting that such a geometry makes the cyclopalladation difficult as it is impossible for the carbon atom of CH_3(7) to approach the metal. All attempts to palladate camphor oxime with halogen-containing Pd salts were unsuccessful.[265] Our own attempts to synthesize a CPC from this oxime using $Pd(AcO)_2$ also failed. This makes the cyclopalladation of the closely related fenchone oxime **196a** especially rewarding.

III.2. Reactions of KPPh2 with CPCs having the (sp3)C–Pd Bond

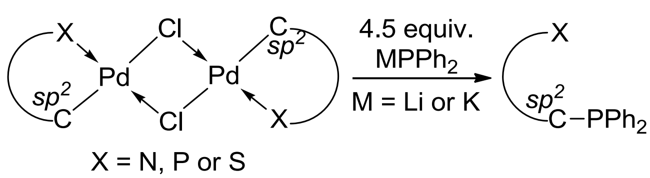
Stoichiometric and catalytic transformations using palladium and other transition-metal derivatives are rightfully considered a cornerstone of organic and organometallic chemistry. During the last decade, a variety of atom-economical Pd-catalyzed C–H bond functionalization reactions have gained recognition as a powerful and versatile synthetic approach.[306-317] Most recently, the focus of these investigations has shifted toward aliphatic C–H bond activation[220, 306, 307, 318-321] because possible synthetic applications appear to be more diverse and, therefore, more useful. However, metal-catalyzed reactions at the (sp^3)C–H bond are difficult to achieve in comparison to those at the (sp^2)C–H bond[171, 306, 317] due to the absence of both empty low-energy orbitals and filled high-energy orbitals that facilitate interaction with orbitals from the metal.[306, 322] To attain the C–H bond activation by a metal and to increase the regioselectivity of this process, a directing heteroatom or auxiliary is introduced into in the substrate structure.[317, 323-329] As a result, the first step in many Pd-catalyzed C–H bond functionalization reactions is the formation of a palladacycle.[330] Additionally, it has been noted that many examples of C–H bond activation, including cyclopalladation reactions, appear to occur under thermodynamic control; therefore, the outcome is dependent on the relative stability of the palladacycle and the strength of the nascent C–Pd bond.[331] By analogy with data previously reported for Rh complexes,[331] (sp^2)C–Pd bonds are expected to be stronger then (sp^3)C–Pd bonds; this may explain frequently observed[4, 8, 332] (with rare exceptions)[47, 51, 54, 63, 76, 136, 139, 208, 333] regioselective aromatic cyclopalladation in the presence of a competing aliphatic fragment. Besides the C–Pd bond forming step, a typical catalytic cycle includes the reaction of this bond with a second reagent. Therefore, investigating possible Pd-catalyzed C–H bond functionalization transformations by a certain reagent, it is important to consider the reactivity of the corresponding C–Pd bond toward that chemical. The fact that palladacycles are intermediates of the auxiliary-directing Pd-catalyzed C–H bond functionalization reactions warrants further studies of stoichiometric reactions of cyclopalladated complexes (CPCs), particularly those with the (sp^3)C–Pd bond.

Despite the abundance of reported reactions at the C–Pd bond of palladacycles,[137, 196, 334] there are only a limited number of transformations involving the (sp^3)C–Pd bond. Moreover, most of these infrequent studies describe reactions at the benzylic position. The earliest examples of reactions at the (sp^3)C–Pd bond of CPCs were reported by the Pfeffer group.[56, 335, 336] They investigated mono- and bis-insertions of hexafluorobutyne and other electron-deficient alkynes into the C–Pd bond of various *CN*-CPCs including dimeric complexes obtained from *N,N*-dimethyl-*o*-toluidine. Later, the same group reported reactions of benzyl isocyanide with several *CS*-CPCs, including one with a benzylic C–Pd bond and one with an aliphatic C–Pd bond (derived from methyl 2,2-dimethylphenyl sulfide and *tert*-butyl phenyl sulfide, respectively).[112] The same CPCs were also tested in reactions with CO at rt; however, only the complex obtained from *tert*-butyl phenyl sulfide provided a new insertion product.[112] The authors noted that (i) the yields of the isocyanide insertion products were comparable for all studied CPCs regardless of the hybridization of the carbon atom bonded to the metal and (ii) *CS*-palladacycles were more reactive towards insertion reactions of isocyanides and CO compared to *CN*-analogs.

In 1984, Carr and Sutherland studied the iodination of an aliphatic five-membered *C,N* palladacycle with I_2.[65] Later, chlorinations using Cl_2[337] and Et_3BnNCl[137] were reported for one *C,N* and one *C,S* complex, respectively. In 2005, the Yu group described the iodination of 2,4-di-*tert*-butyl-2-oxazoline with I_2 using stoichiometric and catalytic amounts of $Pd(OAc)_2$.[338] The CPC used in the Yu study was first synthesized by Balavoine and Clinet, who reacted the complex with methyl vinyl ketone, MeI, *n*-BuI, allyl iodide and CO with and without MeOH to give substituted oxazolines with new C–C bonds. However, no information was provided about the products formed in these reactions except for the yields.[25]

Several research groups reported oxidation of *CN*-CPCs obtained from oximes with bulky alkyl substituents.[59, 61, 339, 340] The formation of an (sp^3)C–(sp^2)C bond was observed in the reaction of Me_3SnPh with a *CP*-palladacycle having a benzylic C–Pd bond.[341] All of these reports suggest that palladacycles with benzylic and aliphatic (sp^3)C–Pd bonds can be used in the same reactions as analogous (sp^2)C–Pd-bonded CPCs; however, no proper comparison of their reactivity can be made because of the limited data available.

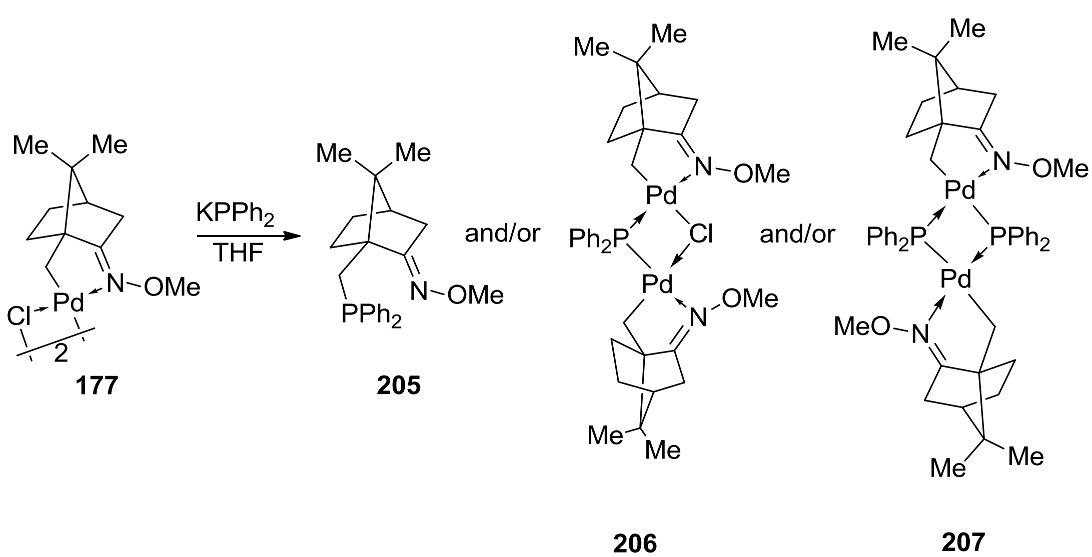
Our group[14, 15, 342] and others[243, 258, 259] have investigated reactions of CPCs with lithium and potassium phosphides to form aminophosphines and related bidentate ligands (Scheme 53). All CPCs used in these studies contained an (sp^2)C–Pd bond. In this section of the dissertation, we report our data on reactivity of *CN-, CP-* and *CS*-palladacycles with an (sp^3)C–Pd bond toward $KPPh_2$ and compare these results with the those reported for the (sp^2)C–Pd-bonded CPCs in the same reaction.



Scheme 53. Formation of bidentate ligands by reacting $MPPh_2$ with dimeric CPCs containing an (sp^2)C–Pd bond.

Previously, we showed that both $LiPPh_2$ and $KPPh_2$ are capable of reacting with dimeric chloro-bridged CPCs.[14, 15] However, the outcome of the $LiPPh_2$ reactions with CPCs was highly sensitive to the phosphide structure in the solution, which in turn, depended on the preparation method, concentration and age of the chemical. $KPPh_2$ in a solution appears to exist only in a monomeric form, and reactivity of the commercial reagent and the one prepared in our lab from $ClPPh_2$ and K was proven to be the same. In the present investigation, we used only commercially available $KPPh_2$ as a phosphide source.

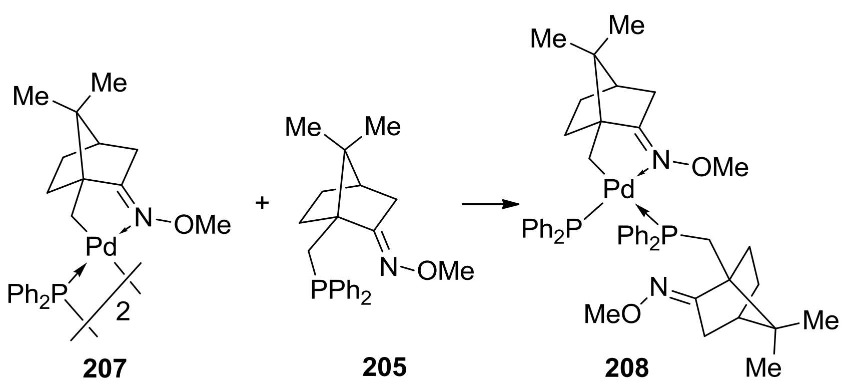
The dimeric dichloro-bridged *CN*-CPC **177** derived from *O*-Me camphor oxime[17] was chosen as a model complex for our study. Complex **177** reacted with 4.5 equiv. of $KPPh_2$ in THF at rt for 18 h to give the desired *NP*-ligand **205** in 21% yield (Scheme 54). The conditions used for this transformation were the same as those previously reported in reactions with CPCs derived from aromatic substrates,[14, 15, 342] but the obtained yield of the phosphine was less than half.[14, 15] Increasing the reaction temperature to 40 °C resulted in 5% yield of **205**. Considering that the bidentate ligand **205** might be coordinated to the metal, 1,2-bis(diphenylphosphino)ethane was added at the end of the room temperature reaction to release the *NP*-ligand in its free form. The yield, indeed, was improved, but not significantly (28%).



Scheme 54. Reaction of CPC **177** with $KPPh_2$.

In an attempt to improve the yield of the camphor-based phosphine **205** and learn more about this reaction, the dimeric CPC **177** was reacted in THF with 1 equiv. of $KPPh_2$ (corresponds to a 1:2 ratio of Pd and PPh_2). As in the previously reported reactions of CPCs with 1 equiv. of $KPPh_2$,[15] no phosphine **205** was formed and only complex **206** was isolated (Scheme 54). The best yield of this complex (31%) was obtained when the reaction time was shortened to 1 h.

Then, the reaction of CPC **177** with 4.5 equiv. of $KPPh_2$ was performed using the standard conditions (THF, 18 h, rt) with a modified purification procedure. Use of ethyl acetate instead of halogenated solvents allowed for isolation of the unstable complex **207** (24%), which presumably has a dimeric structure with two PPh_2 bridges. Phosphine **205** was obtained from the same reaction in 17% yield. Further chromatographic purification of complex **207** using CH_2Cl_2 provided several compounds, some of which were isolated in a pure form or identified using $^{31}P\{^1H\}$ NMR data. The μ-Cl-μ-PPh_2 complex **206** and $HP(O)Ph_2$ were obtained in 16% and 5% yield, respectively, and phosphine **205** was detected by $^{31}P\{^1H\}$ NMR (<5% yield). The $^{31}P\{^1H\}$ NMR spectrum of one of the fractions contained the singlet of complex **207** at δ -64.7 ppm [in C_6D_6 relative to $P(OEt)_3$] and two doublets, δ 21.8 and 113.5 ppm, J_{PP} = 36 Hz. We hypothesize that these doublets belong to compound **208**, which can be formed by reacting free phosphine **205** with complex **207** (Scheme 55). The $^{31}P\{^1H\}$ NMR chemical shift of 123.2 ppm has been reported for complexes with the PAr_2 group as a terminal ligand bonded to Pd(II)[343] (*cf.* the chemical shift of -7.8 ppm for the terminal PPh_2 ligand bonded to Pt),[344, 345] while the chemical shifts in a range of 20–35 ppm are typical for tertiary phosphines bonded to Pd(II) as terminal ligands.[342, 346] The value of the coupling constant suggests that there are two phosphorus atoms in complex **208** that are cis to each other. Also, the values of the ^{31}P NMR chemical shifts and the coupling constant of compound **208** are remarkably similar to the analogous complex **209** (Figure 8), which was previously isolated and fully characterized (including a satisfactory elemental analysis).[347] According to the transphobia concept,[348, 349] complexes of type **208** and **209** are expected to have a terminal PPh_2 group cis to the CH_2 fragment of the cyclopalladated ligand. Thus, we suggest that the diphosphido-bridged complexes of type **207** can a) slowly produce the corresponding *N,P* ligands (in this case **205**) as a result of reductive elimination and b) react with other ligands, including compound **205**, to form mononuclear complexes of type **208** and **209**.



Scheme 55. Proposed reaction of dimer **207** with phosphine **205**.

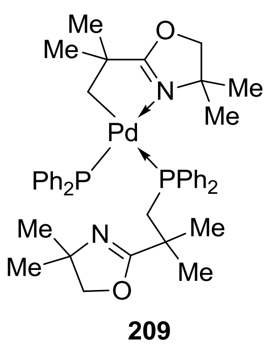


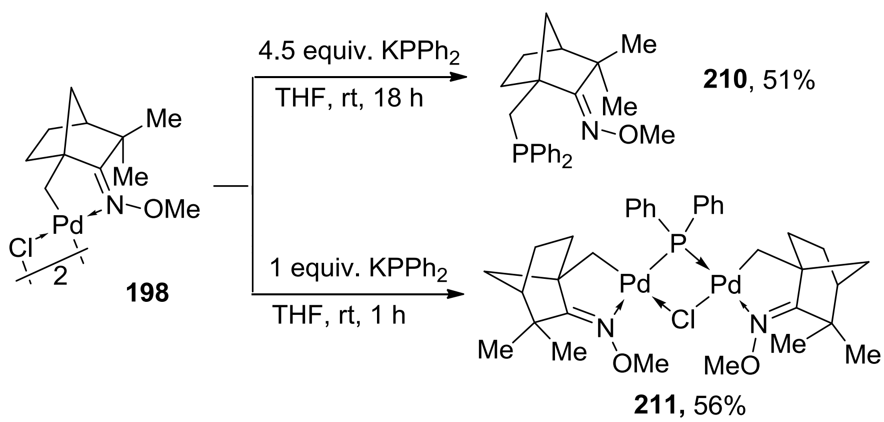
Figure 8. Structure of complex **209**.

To test whether the μ-Cl-μ-PPh_2 complex **206** could be converted to its di-μ-PPh_2 analog **207** and/or phosphine **205**, it was reacted with 1 equiv. of $KPPh_2$. Two compounds were isolated after preparative TLC: free *N,P* ligand **205** in 23% yield and complex **207** in 14% yield. It is noteworthy that the μ-Cl-μ-PPh_2 CPC obtained from *N,N*-dimethylbenzylamine can also be converted to the corresponding free aminophosphine in 38% yield by reacting with $LiPPh_2$.[342]

Next, we studied whether the free phosphine could be obtained directly from the di-μ-PPh_2 CPC **207** by reacting it with 2.5 equiv. of $KPPh_2$ in THF. To our surprise, after 18 h at rt, no free phosphine **205** was detected in the $^{31}P\{^1H\}$ NMR spectrum of the reaction mixture. Chromatographic separation of the reaction mixture allowed for 31% recovery of the starting complex **207**. Carrying out the same reaction over 36 h provided no free phosphine either. In the third experiment, which lasted 96 h, the non-coordinated *NP*-ligand **205** was finally isolated in 27% yield. Therefore, the di-μ-PPh_2 CPC **207** can be converted to compound **205** by reaction with $KPPh_2$; however, this produces the *NP*-ligand much more slowly than the direct reaction of CPC **177** with 4.5 equiv. of $KPPh_2$ in THF. In another experiment, the di-μ-PPh_2 dimer **207** was treated with 2 equiv. of LiCl before addition of 2.5 equiv. of $KPPh_2$. The $^{31}P\{^1H\}$ NMR spectrum of the reaction mixture after 18 h at rt already contained the signal of non-coordinated phosphine **205** suggesting that the reaction of complex **207** with $KPPh_2$ to give phosphine **205** is faster in the presence of chloride ions.

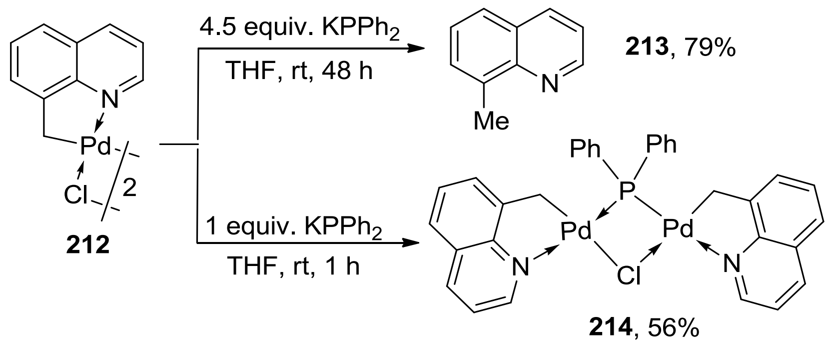
The $^{31}P\{^1H\}$ NMR spectra of the sample from the reaction of CPC **177** with 4.5 equiv. of $KPPh_2$ (rt, 18 h) had signals of free phosphine **205**, complex **207**, PPh_2PPh_2 and its monoxide, as well as several compounds, which we could not identify, including two complexes apparently having two different P atoms cis to each other and separated by two bonds (J_{PP} = 30–40 Hz). The formation of PPh_2PPh_2 and its monoxide was also observed in all other reactions of CPCs with metal phosphides.

Encouraged by our results for the camphor-based complex **177**, we tested the fenchone-derived CPC **198**[353] in reactions with $KPPh_2$. The reaction of CPC **198** with 4.5 equiv. of $KPPh_2$ in THF furnished the enantiopure *NP*-ligand **210** (δ -37.1 ppm) in 51% yield (Scheme 57). Using 1 equiv. of $KPPh_2$, CPC **198** was converted to the μ-Cl-μ-PPh_2-bridged derivative **211** (δ 2.2 ppm) in 56% yields (Scheme 57). ^{1}H, ^{13}C{^{1}H} and ^{31}P{^{1}H} NMR data for complex **211** suggest that this and other μ-Cl-μ-PPh_2-bridged CPCs reported in the literature,[14, 15, 342] as well as the others described in this study, exist in solutions as single isomers with trans-*N,P* geometry.



Scheme 56. Reactions of the fenchone-derived CPC **198** with $KPPh_2$.

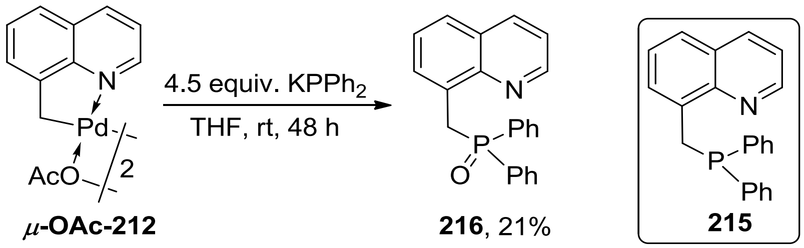
The 8-methylquinoline-derived complex **212**[42] studied next differs from the previously used CPCs **177** and **198** by having a benzylic carbon bonded to the metal. Reactions of CPC **212** with 4.5 equiv. of $KPPh_2$ at rt gave only 8-methylquinoline (Scheme 58). The isolation of free preligands was previously reported in $KPPh_2$ reactions with CPCs containing an (sp^2)C–Pd bond[14] as well as in the Pd-catalyzed phosphination reactions of aryl triflates with PPh_3.[354] The formation of such products can be explained by β-hydride elimination of the alkoxide-containing Pd(II) intermediate,[14] which could be formed after the adventitious cleavage of a C–O bond in THF by the phosphide.[342]



Scheme 57. Reactions of CPCs **212** with $KPPh_2$.

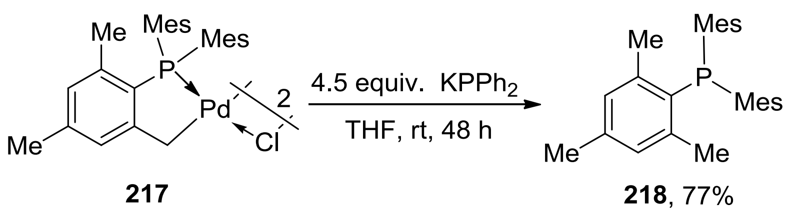
When 1 equiv. of $KPPh_2$ was used in the reaction, the μ-Cl-μ-PPh_2-brigded derivative **214** was isolated in 56% (Scheme 58). The $^{31}P\{^1H\}$ NMR spectrum of complex **214** had a singlet at δ 10.2 ppm [$CDCl_3$ relative to $P(OEt)_3$] and matched the data for this complex prepared by a different method.[347]

Complex **212** had a limited solubility in THF. To test if the more soluble complex ***μ*-OAc-212** could provide the phosphination product **215**, the reaction of this CPC with 4.5 equiv. of $KPPh_2$ at rt was carried out. Preparative TLC provided a mixture of the desired product **215** and its oxide **216**. In the next experiment, air was bubbled through the reaction mixture for 18 h before preparative TLC. The change in the work-up resulted in the isolation of compound **216** in 21% (Scheme 59). This reaction is the first example of converting acetato-bridged CPCs to the corresponding phosphines (or phosphine oxides) using metal phosphides.



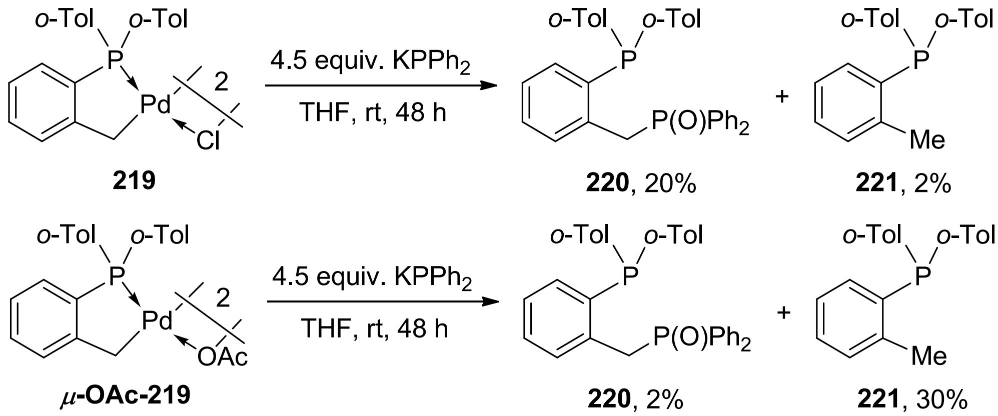
Scheme 58. Reaction of CPC ***μ*-OAc-212** with 4.5 equiv. of $KPPh_2$.

It was of interest to investigate $KPPh_2$ reactivity toward CPCs with donor atoms other than nitrogen such as trimesitylphosphine-derived complex **217**[103] containing a benzylic C–Pd bond. This compound reacted with 4.5 equiv. of $KPPh_2$ at rt to provide only the free preligand **218** (Scheme 60).



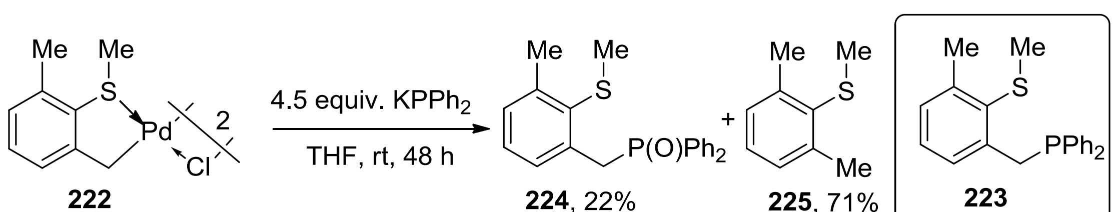
Scheme 59. Formation of compound **218** in the reaction of CPC **217** with $KPPh_2$.

Reactions of $KPPh_2$ with two tri-*ortho*-tolylphosphine-derived complexes, dichloro-bridged dimer **219** and its acetato-bridged analog ***μ*-OAc-219**[31] were investigated as well. In all experiments with these two CPCs, air was bubbled into the reaction mixtures before purification to ensure oxidation of the phosphine product. Reaction of complex **219** furnished phosphine oxide **220** in 20% yield (Scheme 61). In contrast to the $KPPh_2$ reactions with the 8-methylquinoline-derived CPCs, the use of ***μ*-OAc-219** instead of its chloro-bridged analog provided only traces of the phosphination product **220**. It is worth mentioning that, according to ^{31}P NMR data, only one of the two phosphino groups in the product was oxidized. In both reactions, along with compound **220**, tri-*ortho*-tolylphosphine **211** was isolated as well (Scheme 61).



Scheme 60. Reaction of complexes **219** and ***μ*-OAc-219** with $KPPh_2$.

Finally, the reactivity of the *CS*-CPC **222**[111] was studied. This complex reacted with 4.5 equiv. of $KPPh_2$ to provide the phosphination product **223** in low yield. Because of the rapid conversion of **223** to the corresponding oxide **224** during purification, the crude product was oxidized before preparative TLC. The best yield of the phosphine oxide was 22%. It is noteworthy that a significant amount of the free sulfide **225** was isolated in all reactions of CPC **222** (Scheme 62).



Scheme 61. Reaction of CPC **222** with $KPPh_2$.

2.2. Structure confirmation

According to the literature,[355, 356] non-coordinated tertiary phosphines provide $^{31}P\{^1H\}$ NMR signals in the -70 to +70 ppm interval (relative to H_3PO_4), diphenyl-substituted tertiary phosphines give signals with negative chemical shift values, and signals of phosphine oxides usually have positive chemical shift values between 10 and 30 ppm. The spectra of the synthesized phosphines **205** and **210** contained a single peak at -23.2 and -37.1 ppm [relative to $P(OEt)_3$], respectively. These phosphines were slowly, within a week, oxidized by oxygen in air to give corresponding phosphine oxides with $^{31}P\{^1H\}$ NMR signals at δ 15.1 and 15.0 ppm, respectively. $^{31}P\{^1H\}$ NMR spectra of phosphine oxides **216** and **224** exhibited singlets at δ 16.5 and 15.0 ppm, respectively, whereas the spectrum of product **9f** with two phosphorus atoms contained two doublets at δ -45.1 and 15.4 ppm ($^4J_{P,P}$ = 9.2 Hz).

^1H and $^{13}C\{^1H\}$ NMR signals of the CH_2P fragment in compounds **205** and **210** and **226**, **216**, **220** and **224** displayed $J_{H,P}$ and $J_{C,P}$ coupling constants. Diastereotopic hydrogens of the CH_2P group in **205** and **210** and **226** (Figure 9) provided two doublets of doublets between δ 2.15 and 3.06 ppm. The ^1H NMR signal of the benzylic CH_2 group bonded to the phosphorus atom in phosphine oxides **216**, **220** and **224** appeared as a doublet between δ 4.00 and 4.56 ppm. It is noteworthy that the values of the coupling constant $^2J_{H,P}$ for phosphines **205** and **210** were 3.5 and 4.1 Hz, while those for phosphine oxides **226**, **216**, **220** and **224** were much larger: 16.0, 14.2, 9.6 and 14.1 Hz, respectively. The difference in the values of coupling constants when comparing phosphines to phosphine oxides was especially noticeable in $^{13}C\{^1H\}$ NMR spectra. The CH_2P group in phosphines **205** and **210** gave a doublet at δ 27.5 and 30.7 ppm with $^1J_{C,P}$ equal to 18 and 13 Hz, respectively. The $^{13}C\{^1H\}$ NMR signal of the same group in phosphine oxides **226**, **216**,

220 and **224** appeared between δ 27.3 and 36.6 ppm and displayed the coupling constant $^{1}J_{C,P}$ in a range of 67−73 Hz. The oxidation of the phosphino group in compounds **226**, **216**, **220** and **224** was also confirmed by IR spectroscopy. IR spectra of these compounds had an absorption band at 1187−1199 cm^{-1} assigned to the stretching vibrations of the P=O group.[357] The elemental composition of phosphines **205** and **210** and phosphine oxides **213**, **221** and **225** was confirmed by HRMS data.

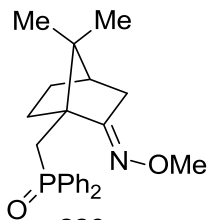


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Figure 9. Oxide of **205**.

Pd(II) complexes with both a chloro and phosphido bridge are rather uncommon in the literature.[15, 342, 358-361] Moreover, there are only two known cyclopalladated complexes of this type. They were obtained from *N,N*-dimethylbenzylamine[15, 342] and its α-*tert*-butyl-derivative.[361] Three isomers can be predicted for such complexes; however, it was shown that in the solid form[361] and in a solution,[342] they exist as syn isomers with the trans-*N,P* ligand configuration. The μ-Cl-μ-PPh_2 Pd(II) complex (**206**) obtained in this study presumably have a syn configuration with the PPh_2 bridging ligand trans to both nitrogen atoms. The $^{31}P\{^{1}H\}$ NMR spectra of CPC **206** in $CDCl_3$ exhibited a singlet at δ 4.9 ppm, respectively. In the $^{13}C\{^{1}H\}$ NMR spectra of this complex, the signal of the CH_2Pd fragment appeared as a doublet ($^{2}J_{C,P}$ = 2.2 Hz) at 19.4 ppm. For comparison, the reported complex of this type synthesized from *N,N*-dimethylbenzylamine provided the ^{31}P NMR signal at δ 25.1 ppm ($^{2}J_{C,P}$ = 1.8 Hz).[342] The ^{1}H NMR spectra of complex **206** confirmed a

1:2 ratio of the PPh_2 group and cyclopalladated ligands in it structure. The elemental composition and purity of this compound was confirmed by satisfactory elemental analysis.

Di-μ-PPh_2 complexes of Pd(II) and especially Pt(II) are well known.[362-366] However, to the best of our knowledge, only one cyclometallated derivative of this type has been reported, the Pt(II) complex derived from 7,8-benzoquinoline.[367] Unfortunately, only the X-ray crystallographic data for this compound are available. The $^{31}P\{^1H\}$ NMR spectra of known di-μ-PPh_2 Pd(II) complexes usually have the signals of the bridging PPh_2 group between -100 and -140 ppm.[362, 363, 365, 368] In the present study, we were able to isolate complex, **207**, which presumably have dimeric cyclopalladated structure with two bridging PPh_2 ligands. The ^1H NMR spectrum of the oxazoline-derived analog of complex **207** previously synthesized in our lab suggests a 1:1 ratio of the PPh_2 fragment and the cyclopalladated ligand. The $^{31}P\{^1H\}$ NMR spectrum of the same compound in $CDCl_3$ exhibited a lone singlet at δ -85.1 ppm (-72.5 ppm in C_6D_6), which suggests the anti configuration of the cyclopalladated ligands. The $^{13}C\{^1H\}$ NMR signal of the CH_2Pd fragment in oxazoline-derived analog of complex **207** appeared at δ 42.2 ppm as a triplet with $J_{C,P}$ equal to 55.1 Hz. Regrettably, the camphor-derived complex **207** could not be obtained in the pure form to allow its complete characterization by NMR spectroscopy. The ^1H NMR spectrum of this compound was too complex to assign all signals; however, the signal integration suggested a 1:1 ratio of the PPh_2 fragment and the cyclopalladated ligand. The only reliable spectroscopic data for this complex that can be reported are its $^{31}P\{^1H\}$ NMR signal at δ -64.8 ppm in C_6D_6 and -76.9 ppm in $CDCl_3$.

CONCLUSIONS

As a result of the experimental work, all three major goals (see page 47) have been accomplished.

1. Enantiopure D-camphor *O*-methyloxime, L-fenchone oximes and camphor *N,N*-dimethylhydrazone were synthesized according to published procedures in 64–89% yield from readily available compounds in the chiral pool. Structures of these preligands were confirmed using NMR spectroscopy.

2. Direct cyclopalladation of D-camphor *O*-methyloxime, L-fenchone oximes and camphor *N,N*-dimethylhydrazone with $Pd(OAc)_2$ and/or $Pd(MeCN)_2Cl_2$, afforded new optically active aliphatic cyclopalladated complexes in 49–92% yield. NMR spectral and single crystal X-ray crystallographic studies were used to confirm the presence of an (sp^3)C–Pd bond in the complexes.

3. Phosphination reactions of new complexes derived from the *O*-methyloximes of D-camphor and L-fenchone as well as other dimeric *CN*-, *CP*- and *CS*-CPCs with an (sp^3)C–Pd bond were investigated. Using 4.5 equiv. of $KPPh_2$, CPCs were converted to the corresponding phosphines or phosphine oxides in 20–51% yield. When CPCs reacted with 1 equiv. of $KPPh_2$, unique mono-chloro-mono-phosphido-bridged CPCs were isolated in 31–56% yield.

CHAPTER VI

EXPERIMENTAL

VI.1. General Methods and Materials

Routine ^{1}H (500 MHz) and $^{13}C\{^{1}H\}$ (126 MHz) as well as DEPT, COSY, and HSQC NMR spectra were recorded on a Bruker AVANCE 500 NMR spectrometer. Chemical shifts are reported in ppm with $SiMe_4$ as an internal standard (^{1}H and ^{13}C) or $P(OEt)_3$ as an external standard (^{31}P). Spin-spin coupling constants, J, are given in Hz. Spectra were recorded in $CDCl_3$ unless stated otherwise. IR spectra were recorded on a Perkin Elmer Spectrum 400 FT-IR/FT-FIR Spectrometer. Melting points were measured on a Laboratory Devices Mel-Temp apparatus and are uncorrected. Optical rotations were measured at rt on a Rudolph Autopol III automatic polarimeter in a 1-dm tube. Elemental analyses were carried out by Atlantic Microlabs Inc., Norcross, GA. Analytical TLC was performed on Whatman silica gel 60 (F_{254}) 250 precoated plates. Preparative TLC was carried out using 200 × 250 mm glass plates with an unfixed layer of Merck silica gel 60 (230 mesh) containing ca. 5% of silica gel with fluorescent indicator (Aldrich). Compounds were visualized on TLC plates using UV light (254 nm) and/or iodine stain. Methoxyamine hydrochloride, hydroxylamine hydrochloride and L-(-)-fenchone were purchased from Acros Organics Co., PPh_3 from Eastman Kodak, D-camphor {$[\alpha]_D = +44.1^{o}$ (c = 10.0, EtOH)} from Fisher Scientific. These reagents were used as purchased as their purity was confirmed by ^{1}H NMR spectroscopy. $Pd(OAc)_2$ purchased from Aldrich was purified by dissolving in hot benzene, filtering the solution and removing the solvent on a rotavapor. NaOAc and $Pd(OAc)_2$ were dried in vacuum prior to use. Benzene, CH_2Cl_2, hexane and ethyl acetate were distilled over CaH_2. Toluene and THF were dried by refluxing over K/benzophenone ketyl and distilled under Ar immediately before starting a reaction. These reagents were used as purchased. The enantiometric purity of L-(-)-fenchone was 97%, $[\alpha]^{24}_{D}$ - 48.9 (neat). Other chemicals were acquired from Sigma-Aldrich Co. and were used without purification unless indicated.

VI.2. Preparation of D-Camphor Derivatives and Their Cyclopalladation

Compounds **174b**, **185**, **191**, **192** and **195** were synthesized using published procedures.[269, 282, 283, 291, 299] The NMR spectra of the obtained compounds matched those reported in the literature.

VI.2.1. Synthesis and Characterization of New Compounds

(1*R*,4*R*)-1,7,7-Trimethylbicyclo[2.2.1]heptan-2-one *O*-Methyloxime (D-Camphor *O*-Methyloxime (174b). Enantiopure D-camphor (0.2000 g, 1.314 mmol) was added to a solution of methoxylamine hydrochloride (0.3007 g, 3.600 mmol) and sodium acetate (0.4676 g, 5.700 mmol) in water (1.2 mL). Ethanol (2 mL) was added, and the mixture was refluxed for 48 h. The mixture was then filtered to remove any solid residue, and ethanol was evaporated under reduced pressure to get an oily residue. The crude product was purified by extraction using CH_2Cl_2 (5 mL × 3). The combined organic layers were dried over Na_2SO_4. After filtration, the solvent was removed on a rotavapor to obtain the pure product as a colorless oil in 74% (0.1744 g, 0.9625 mmol). According to the ^{1}H NMR spectrum, the product was a mixture of two geometric isomers in a ratio of 92:8. R_f 0.60 (100:1 hexane–acetone); $[\alpha]^{22}_{D}$ -29.7, $[\alpha]^{22}_{546}$ -42.7, $[\alpha]^{22}_{435}$ -67.9 (*c* 0.781, EtOH). IR (film, ν, cm^{-1}): 1654 and 1667 (C=N), 1045 (N-O). ^{1}H NMR (*δ*, ppm) [63]: 0.80 (s, 3H,

CH_3), 0.91 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.22 (ddd, 1H, $^2J_{5endo,5exo}$ = 12.8, $^3J_{5endo,6endo}$ = 9.3, $^3J_{5endo,4}$ = 4.2, H(5endo)), 1.45 (ddd, 1H, $^2J_{6endo,6exo}$ = 14.5, $^3J_{6endo,5endo}$ = 9.3, $^3J_{6endo,5exo}$ = 4.4, H(6endo)), 1.69 (td, 1H, $^2J_{6exo,6endo}$ = $^3J_{6exo,5exo}$ = 12.0, $^3J_{6exo,5endo}$ = 4.3, H(6exo)), 1.82 (m, 1H, H(5exo)), 1.86 (t, 1H, $^3J_{4,5exo}$ = $^3J_{4,3exo}$ = 4.3, H(4)), 1.98 (d, 1H, $^2J_{3endo,3exo}$ = 18.1, H(3endo)), 2.47 (dt, 1H, $^2J_{3exo,3endo}$ = 18.1, $^3J_{3exo,4}$ = $^4J_{3exo,5exo}$ = 4.3, H(3exo)), 3.73 (minor isomer) and 3.82 (major isomer) (two s, 3H, OCH_3). $^{13}C\{^1H\}$ NMR (δ, ppm): 11.2, 18.6, 19.5 (three CH_3), 27.4 (CH_2, C(5)), 32.9 (CH_2, C(6)), 33.6 (CH_2, C(3)), 43.8 (CH, C(4)), 48.1 and 51.6 (two quat. C, C(1) and C(7)), 61.2 (OCH_3), 169.2 (C=N).

(1*R*,4*R*)-Dichlorobis{2-(methoxyimino)-1,7,7-trimethylbicyclo[2.2.1]heptane}palladium(II) (175). To a small, one-neck round-bottomed flask containing a magnetic stirring bar and camphor oxime **174b** (0.0245 g, 0.135 mmol), Na_2PdCl_4 (0.0206 g, 0.0700 mmol) was added. Abs. MeOH (1 mL) was added as well, and the flask was covered with a stopper. After stirring the mixture at rt for 18 h, MeOH was removed on a rotavapor. The red-brown crude product was purified using preparative TLC (silica gel, 5:1 hexane–acetone). The pure product was isolated as a yellow powder in 67% yield (0.0168 g, 0.0468 mmol). Mp: 180–182 °C; R_f 0.36 (99:1 benzene–acetone); $[\alpha]^{22}_D$ +50.3, $[\alpha]^{22}_{546}$ +44.4 (*c* 0.0510, EtOH). IR (Nujol mull, ν, cm^{-1}): 1655 (C=N). ^1H NMR (δ, ppm): 0.84 (minor isomer) and 0.87 (major) (two s, 3H, CH_3), 0.94 (minor) and 0.98 (major) (two s, 3H, CH_3), 1.22 (m, 1H, H(5endo)), 1.81–1.99 (m, 4H, H(5exo, 6endo, 6exo, 4)), 2.29 (d, 1H, $^3J_{3endo,3exo}$ = 18.5, H(3endo)), 2.42 (s, 3H, CH_3), 2.80 (m, 1H, H(3exo)), 4.20 (major) and 4.51 (minor) (two s, 3H, OCH_3). $^{13}C\{^1H\}$ NMR (δ, ppm): 14.8, 19.2, 20.4 (three CH_3), 27.2 (CH_2, C(5)), 32.4 (CH_2, C(6)), 38.6 (CH_2, C(3)), 43.5 (CH, C(4)), 50.3 (C, C(7)), 55.4 (C, C(1)), 62.5 (OCH_3, C(10)), 188.0 (C=N).

Anal. Calcd for $C_{22}H_{38}Cl_2N_2O_2Pd$: C, 48.94; H, 7.09; N, 5.19. Found: C, 48.94; H, 7.18; N, 5.21%.

(1*S*,4*R*)-Di-*μ*-chlorobis{[2-(methoxyimino)-7,7-dimethylbicyclo[2.2.1]heptyl]methyl-*C*,*N*}dipalladium(II) (177). To a 10-mL one-neck round-bottomed flask containing a magnetic stirring bar, camphor oxime **174b** (0.0797 g, 0.440 mmol), $Pd(OAc)_2$ (0.0987 g, 0.440 mmol) and glacial acetic acid (19 mL) were added. The resulting mixture was stirred at 80 °C for 5 h. The solvent was removed under reduced pressure to give a brown oily residue of the crude acetate-bridged analog of **176.** Abs. acetone (19 mL) was added to the crude product followed by introduction of LiCl (0.0746 g, 1.76 mmol). The mixture was stirred at rt for 18 h. The solution was then filtered through celite (h = 1 cm), and the flask with the filtrate was placed on a rotavapor to remove acetone. The crude product was purified using preparative TLC (silica gel, 99:1 benzene–acetone). The pure product was isolated as an orange-yellow powder in 66% yield (0.0936 g, 0.145 mmol). Mp: 204–206 °C; R_f 0.56 (99:1 benzene–acetone); $[\alpha]^{22}_{D}$ -164, $[\alpha]^{22}_{546}$ -201, $[\alpha]^{22}_{435}$ -307 (*c* 0.100, EtOH). IR (Nujol mull, ν, cm^{-1}): 1662 (C=N). ^{1}H NMR (δ, ppm): 0.80 (s, 3H, CH_3), 0.93 (s, 3H, CH_3), 1.32 (t, 1H, $^2J_{5endo,5exo}$ = $^3J_{5endo,6endo}$ = 9.4, H(5endo)), 1.89 (m, 4H, H(5endo), H(6endo), PdCH^A, H(3exo)), 2.06 (m, 1H, H(6exo)), 2.14 (t, 1H, $^3J_{4,3exo}$ = $^3J_{4,5exo}$ = 4.0, H(4)), 2.41 (m, 2H, $^2J_{3endo,3exo}$ = 18.1, $^3J_{3exo,4}$ = 4.0, H(3exo), PdCH^B), 3.78 (s, 3H, OCH_3). $^{13}C\{^1H\}$ NMR (δ, ppm): 18.3 and 19.6 (two CH_3), 26.7 (CH_2, C(5)), 31.9 (CH_2, C(6)), 33.3 (CH_2, C(3)), 46.7 and 66.4 (two quat. C, C(1) and C(7)), 47.6 (CH, C(4)), 62.2 (OCH_3), 193.6 (C=N). ^{1}H NMR (C_6D_6, δ, ppm): 0.42 (s, 3H, CH_3), 0.56 (s, 3H, CH_3), 0.74 (ddd, 1H, $^2J_{5endo,5exo}$ = 12.5, $^3J_{5endo,6endo}$ = 9.2, $^3J_{5endo,6exo}$ = 4.2, H(5endo)), 1.34 (m, 1H, H(5exo)), 1.43 (d, 1H, $^2J_{3exo,3endo}$ = 19.0, H(3endo)), 1.47 (t, 1H, $^3J_{4,5exo} = {}^3J_{4,3exo} = 4.0$, H(4)), 1.51 (m, 1H, H(6endo)), 1.71 (ddd, 1H $^2J_{6endo,6exo} = 13.0$, $^3J_{6exo,5exo} = 9.2$, $^3J_{6exo,5endo} = 4.2$, H(6exo)), 1.96 (dt, 1H, $^2J_{3endo,3exo} = 18.8$, $^3J_{3exo,4} = {}^3J_{3exo,5exo} = 4.0$, H(3exo)), 2.22 (d, 1H, $^2J_{H,H} = 8.0$, $PdCH^A$), 2.58 (d, 1H, $^2J_{H,H} = 8$, $PdCH^B$), 3.79 (s, 3H, OCH_3). Minor isomer: 2.06 and 2.42 (two br. s, $PdCH^A$ and $PdCH^B$), 3.87 (s, 3H, OCH_3). The isomer ratio in C_6D_6 solution was 5:2. $^{13}C\{^1H\}$ NMR (C_6D_6, δ, ppm): 16.7 and 18.1 (two CH_3), 25.3 (CH_2, C(5)), 30.5 (CH_2, C(6)), 31.8 (CH_2, C(3)), 45.0 and 65.0 (two quat. C, C(1) and C(7)), 46.2 (CH, C(4)), 60.9 (OCH_3), 191.0 (C=N). Anal. Calcd for $C_{22}H_{36}Cl_2N_2O_2Pd_2$: C, 41.01; H, 5.63; N, 4.35. Found: C, 41.02; H, 5.69; N, 4.38%.

(1*S*,4*R*)-Chloro{[2-(methoxyimino)-7,7-dimethylbicyclo[2.2.1]heptyl]methyl-*C*,*N*}(triphenylphosphine-*P*)palladium(II) (178). To a 25-mL round-bottomed flask containing a magnetic stirring bar and CPC **177** (0.0148 g, 0.0230 mmol), abs. acetone (8 mL) and PPh_3 (0.0121 g, 0.0460 mmol) were added. The resulting mixture was stirred at rt for 18 h. The solvent was removed under reduced pressure to give a pale-yellow residue. The crude product was purified using preparative TLC (silica gel, 1:2 ethyl acetate–hexane). The pure product was isolated as a pale yellow powder in 98% yield (0.0263 g, 0.0450 mmol). Mp 198–200 °C; R_f 0.40 (1:2 ethyl acetate–hexane); $[\alpha]^{22}_D$ -237, $[\alpha]^{22}_{546}$ -277, $[\alpha]^{22}_{435}$ -462 (*c* 0.0730, EtOH). IR (Nujol mull, ν, cm^{-1}): 1662 (C=N). ^1H NMR (δ, ppm): 0.53 (dd, 1H, $^2J_{H,H} = 10$, $^3J_{H,P} = 8$, $PdCH^A$), 0.56 (s, 3H, CH_3), 0.84 (s, 3H, CH_3), 1.29 (ddd, 1H, $^3J_{6endo,5endo} = 12.5$, $^2J_{5endo,5exo} = 9.5$, $^3J_{5endo,6exo} = 4.2$, H(5endo)), 1.61 (td, 1H, $^2J_{6exo,6endo} = {}^3J_{6endo,5endo} = 12.5$, $^3J_{6endo,5exo} = 4.2$, H(6endo)), 1.80 (m, 1H, H(5exo)), 1.86 (d, 1H, $^2J_{H,H} = 10$, $PdCH^B$), 1.96 (ddd, 1H, $^2J_{6exo,6endo} = 12.5$, $^3J_{6exo,5exo} = 9.3$, $^3J_{6exo,5endo} = 4.2$, H(6exo)), 2.02 (d, 1H, $^2J_{3endo,3exo} = 18.7$, H(3endo)), 2.07 (t, 1H, $^3J_{4,5exo} = {}^3J_{4,3exo} = 4.3$, H(4)), 2.49 (dt, 1H, $^2J_{3exo,3endo} = 18.7$, $^3J_{3exo,4} = 4.3$, $^4J_{3exo,5exo} = 3.5$, H(3exo)), 4.12 (s, 3H,

OCH_3), 7.40 (m, 9H, *m*- and *p*-PPh), 7.74 (m, 6H, *o*-PPh). $^{13}C\{^1H\}$ NMR (δ, ppm): 18.2 and 20.2 (two CH_3), 27.0 ($PdCH_2$)), 27.2 (CH_2, C(5)), 33.4 (CH_2, C(3)), 33.5 (CH_2, C(6)), 47.2 (CH, C(4)), 48.1 (C, C(7)), 63.3 (OCH_3), 66.0 (C, C(1)), 128.5 (d, $^3J_{C,P}$ = 10.1, *m*-PPh), 130.7 (d, $^4J_{C,P}$ = 2.4, *p*-PPh), 131.7 (d, $^1J_{C,P}$ = 51.6, *ipso*-PPh), 135.1 (d, $^2J_{C,P}$ = 11.3, *o*-PPh), 192.2 (C=N). $^{31}P\{^1H\}$ NMR (*δ*, ppm): 20.4. Anal. Calcd for $C_{29}H_{33}ClNOPPd$: C, 59.60; H, 5.69; N, 2.40. Found: C, 59.83; H, 5.68; N, 2.48%.

Complexes 188. To a 25-mL round-bottomed flask containing a magnetic stirring bar and the CPC of camphor *N,N*-dimethylhydrazone (0.0385 g, 0.0574 mmol), chloroform (12 mL) and Na(acac) (0.0216 g, 0.0177 mmol) were added. The resulting mixture was stirred at rt for 18 h. The solvent was removed under reduced pressure to give a pale yellow residue. The crude product was purified using preparative TLC (silica gel, 1:2 ethyl acetate–hexane) to give the pure product **188** as a pale yellow powder (0.0538 g, 0.0900 mmol, 96%).

(1*R*,3*S*,4*S*)-Chloro{[2-(*N,N*-dimethylhydrazono)-1,7,7-trimethylbicyclo[2.2.1]heptyl]methylenyl-*C,N*}(acetylacetonate-*O,O*)palladium(II) (*endo*-188). Mp: 120–122 °C; R_f 0.80 (2:1 hexane–ethyl acetate). IR (ν, cm^{-1}, mineral oil): 1656 (C=N). ^1H NMR (*δ*, ppm): 0.91, 0.93, 1.08 (three s, 9H, $3CH_3$), 1.31 (ddd, 1H, $^3J_{5endo,6endo} \approx 13$, $^2J_{5endo,5exo} \approx 9.2$, $^3J_{5endo,6exo} = 4.0$, H(5endo)), 1.70 (m, 1H, H(5exo)), 1.75 (m, 1H, H(6endo)), 1.87 (s, 3H, acac CH_3), 1.89 (m, 1H, H(6exo)), 1.91 (s, 3H, acac CH_3), 2.02 (t, 1H, $^3J_{4,5exo} \approx {}^3J_{4,3exo} \approx 4.3$, H(4)), 2.66, 3.02 (two s, 6H, $2NCH_3$), 4.82 (t, 1H, $^3J_{4,PdCH} \approx {}^4J_{PdCH,5exo} \approx 3.5$, PdCH), 5.22 (s, 1H, acac CH). $^{13}C\{^1H\}$ NMR (*δ*, ppm): 11.2, 20.0, 21.3 (three CH_3), 26.3 (CH_2, C(5)), 27.7, 28.7 (two CH_3, (acac)), 37.2 (CH_2, C(6)), 48.3 (PdCH)), 48.4 (C, C(7)), 48.9 (CH, C(4)), 51.92, 51.94 (two NCH_3), 53.0 (C, C(1)), 99.9 (CH, (acac)), 186.2, 188.1 (two C, (acac)), 200.3 (C=N). Anal. Calcd for $C_{17}H_{28}N_2O_2Pd$: C, 51.19; H, 7.08; N, 7.02. Found: C, 50.89; H, 6.89; N, 7.03%.

(1*R*,3*R*,4*S*)-Chloro{[2-(*N,N*-dimethylhydrazono)-1,7,7-trimethylbicyclo[2.2.1]heptyl]methylenyl-*C,N*}(acetylacetonate-*O,O*)palladium(II) (*exo*-188). Mp: 120–122 °C; R_f 0.75 (2:1 hexane–ethyl acetate). IR (ν, cm^{-1}, mineral oil): 1656 (C=N). ^1H NMR (δ, ppm): 0.89, 0.99 (two s, 6H, $2CH_3$), 1.33 (ddd, 1H, $^3J_{5endo,6endo} \approx$ 11.8, $^2J_{5endo,5exo} \approx 8.9$, $^3J_{5endo,6exo} = 2.9$, H(5endo)), 1.42 (s, 3H, CH_3), 1.69 (t, 1H, $^3J_{4,5exo} \approx$ $^3J_{4,3exo} \approx 3.4$, H(4)), 1.76 (m, 2H, H(5exo), (6endo)), 1.888 (s, 3H, acac CH_3), 1.891 (m, 1H, H(6exo)), 1.893 (s, 3H, acac CH_3), 2.66, 3.04 (two s, 6H, $2NCH_3$), 3.99 (s, 1H, PdCH), 5.21 (s, 1H, acac CH). $^{13}C\{^1H\}$ NMR (δ, ppm): 12.1, 20.7, 21.3 (three CH_3), 27.9, 28.6 (two CH_3, (acac)), 29.3 (CH_2, C(5)), 30.9 (CH_2, C(6)), 46.8 (CH, C(4)), 46.9 (CH, PdCH)), 50.7 (C, C(7)), 51.5 (C, C(1)), 52.1, 52.5 (two NCH_3), 99.9 (CH, (acac)), 186.3, 188.0 (two C, (acac)), 198.6 (C=N). Anal. Calcd for $C_{17}H_{28}N_2O_2Pd$: C, 51.19; H, 7.08; N, 7.02. Found: C, 50.89; H, 6.89; N, 7.03%.

VI.3. Preparation of L-Fenchone Derivatives and Their Cyclopalladation

(1*R*,4*S*)-1,3,3-Trimethylbicyclo[2.2.1]heptan-2-one oxime (196a). To a solution of hydroxylamine hydrochloride (0.5483 g, 7.891 mmol) in abs. EtOH (10 mL) was added L-(-)-fenchone (0.4290 g, 2.818 mmol). Pyridine (0.60 mL, 7.5 mmol) was then added dropwise and the mixture was refluxed for 48 h. The mixture was filtered, and ethanol from the filtrate was evaporated under reduced pressure. 1M aq. HCl solution (30 mL) was added to the oily residue, and the product was extracted with Et_2O (3 × 5 mL). The combined organic layers were dried over Na_2SO_4. After filtration, the solvent was removed on a rotavapor to obtain the pure product as a white powder (0.3041 g, 1.818 mmol, 64%). Mp:

149–151 °C (lit. data 150-153 ºC [14]); $[\alpha]^{24}_{D}$ +3.00 (*c* 0.406, EtOH); R_f 0.53 (100:1 hexane–acetone). IR (ν, cm^{-1}, mineral oil): 1682 (C=N). ^{1}H NMR (δ, ppm): 1.22 (s, 3H, CH_3(8)), 1.30, 1.33 (two s, 3H each, CH_3(9exo) and CH_3(9endo)), 1.34 (m, 1H, H(7A)), 1.45 (m, 1H, H(6endo)), 1.55 (m, 2H, H(6exo), H(5endo)), 1.72 (d, $^{2}J_{7A,7B}$ = 10.5 Hz, 1H, H(7B)), 1.79 (m, 1H, H(5exo)), 1.82 (d, $J \approx 1$ Hz, 1H, H(4)), 8.61 (br s, 1H, OH). $^{13}C\{^{1}H\}$ NMR (δ, ppm): 17.1 (CH_3(8)), 22.2, 22.9 (CH_3(9exo) and CH_3(9endo)), 25.2 (CH_2, C(5)), 34.2 (CH_2, C(6)), 43.2 (CH_2, C(7)), 44.2 (quat. C, C(3)), 48.6 (CH, C(4)), 50.1 (quat. C, C(1)), 172.5 (C=N). HRMS: $[M + H]^+$ calcd for $C_{10}H_{18}NO$ 168.1388, found 168.1449.

(1*R*,4*S*)-1,3,3-Trimethylbicyclo[2.2.1]heptan-2-one O-Methyloxime (196b). This compound was synthesized using the procedure described for oxime **196a** in 82% yield (3.197 g, 17.63 mmol) using methoxylamine hydrochloride (5.000 g, 59.87 mmol), L-(-)-fenchone (3.255 g, 21.38 mmol) and pyridine (4.7 mL, 58 mmol) and abs. EtOH (50 mL). According to the ^{1}H NMR spectrum, the product was a mixture of two geometric isomers in a ratio of 94:6. Bp: 86–88 °C; $[\alpha]^{24}_{D}$ -20.0, $[\alpha]^{24}_{546}$ -35.0, $[\alpha]^{24}_{435}$ -67.0 (*c* 1.04, EtOH); R_f 0.66 (100:1 hexane–acetone). IR (ν, cm^{-1}, mineral oil): 1655 (C=N). ^{1}H NMR (δ, ppm): 1.22, 1.23, 1.25 (three s, 9H, 3CH_3), 1.31 (dd, $^{2}J_{7A,7B}$ = 10.0, $^{3}J_{7,4}$ = 1.2, 1H, H(7A)), 1.43 (m, 1H, H(6endo)), 1.54 (m, 2H, H(6exo), H(5endo)), 1.70 (dq, $^{2}J_{7A,7B}$ = 10.0, $^{3}J_{4,7B} \approx {}^{4}J_{5exo,7B} \approx {}^{4}J_{5endo,7B} \approx 1.8$ Hz; 1H, H(7B)), 1.78 (m, 2H, H(5exo), H(4)), 3.71 (minor isomer) and 3.75 (major isomer) (two s, 3H, OCH_3). $^{13}C\{^{1}H\}$ NMR (δ, ppm): 17.2, 22.5, 23.4 (three CH_3), 25.3 (CH_2, C(5)), 34.4 (CH_2, C(6)), 43.4 (CH_2, C(7)), 48.6 (CH, C(4)), 44.6 and 49.9 (two quat. C, C(1) and C(3)), 61.0 (OCH_3), 172.6 (C=N). Anal. Calcd for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 72.59; H, 10.35; N, 7.78%.

(*S,S*)-Di-*μ*-chlorobis{[2-(hydroxyimino)-3,3-dimethylbicyclo[2.2.1]heptyl]methyl-*C,N*}dipalladium(II) (198a). To a 25-mL one-neck round-bottomed flask containing a magnetic stirring bar, fenchone oxime **196a** (0.0527 g, 0.315 mmol), $Pd(OAc)_2$ (0.0707 g, 0.315 mmol) and glacial acetic acid (5.6 mL) were added at rt. The resulting mixture was stirred at 80 °C for 5 h. The solvent was removed under reduced pressure to give a brown oily residue of the crude acetate-bridged dimer **197a**. HPLC-grade acetone (5.6 mL) was added to the crude acetate-bridged dimer followed by introduction of LiCl (0.0534 g, 1.26 mmol). The mixture was stirred at rt for 18 h. The solution was then filtered through celite (h = 1 cm), and the flask with the filtrate was placed on a rotavapor to remove acetone. The crude product was separated into several fractions using preparative TLC (silica gel, 9:1 toluene–ethyl acetate). Complex **198a** was isolated as an orange-yellow powder in 65% yield (0.0189 g, 0.0307 mmol). Mp: 189–191 °C; $[\alpha]^{24}_{D}$ -57, $[\alpha]^{24}_{546}$ -70 (*c* 0.30, CH_2Cl_2); R_f 0.56 (9:1 toluene–ethyl acetate). ^1H NMR (δ, ppm): 1.20 (s, 3H, CH_3), 1.27 (s, 3H, CH_3), 1.39 (d, $^2J_{7A,7B}$ = 9.9, 1H, H(7A)), 1.59–1.71 (m, 2H, H(6endo), 5(endo)), 1.80–1.87 (m, 2H, H(7B), H(5exo)), 1.95 (m, 1H, H(6exo)), 2.14 (s, 1H, H(4)), 2.29 (d, 1H, $^2J_{A,B}$ = 8.8, $PdCH^A$), 2.76 (d, 1H, $^2J_{A,B}$ = 8.8, $PdCH^B$), 7.60 (br s, 1H, OH). $^{13}C\{^1H\}$ NMR (δ, ppm): 21.3 and 22.4 (two CH_3), 24.6 (CH_2, PdC) [24], 25.2 (CH_2, C(5)), 34.0 (CH_2, C(6)), 41.0 (CH_2, C(7)), 43.9 and 65.6 (two quat. C, C(1) and C(3)), 54.1 (CH, C(4)), 190.4 (C=N). Anal. Calcd for $C_{20}H_{32}Cl_2N_2O_2Pd_2$: C, 38.98; H, 5.23; N, 4.55. Found: C, 39.23; H, 5.23; N, 4.55%.

(*S,S*)-Di-*μ*-chlorobis{[2-(methoxyimino)-3,3-dimethylbicyclo[2.2.1]heptyl]methyl-*C,N*}dipalladium(II) (198b). This compound was isolated as an orange–yellow powder in 49% yield (0.1453 g, 0.2255 mmol) using the procedure described for complex **198a** and the following reagents: fenchone *O*-methyloxime **196b** (0.3164 g, 1.745 mmol), $Pd(OAc)_2$ (0.3918 g, 1.745 mmol) and LiCl (0.2960 g, 6.981 mmol). Mp: 202–204 °C; $[\alpha]^{22}_{D}$ -172, $[\alpha]^{22}_{546}$ -226, (*c* 0.416, CH_2Cl_2); R_f 0.56 (9:1 toluene–ethyl acetate). ^{1}H NMR (δ, ppm): 1.19, 1.21 (two s, 6H, 2CH_3), 1.38 (d, $^2J_{7A,7B}$ = 10.2, 1H, H(7A)), 1.63 (m, 1H, 5(endo)), 1.74 (m, 1H, H(6endo)), 1.81 (m, 2H, H(7), H(5exo)), 2.01 (m, 1H, H(6exo)), 2.08 (d, J = 3.5, 1H, H(4)), 2.17 (br. s, 1H, $PdCH^A$), 2.58 (br. s, 1H, $PdCH^B$), 3.78 (s, 3H, OCH_3)). $^{13}C\{^1H\}$ NMR (δ, ppm): 22.4 and 23.3 (two CH_3), 25.3 (CH_2, C(5)), 25.8 (PdC) [24], 33.9 (CH_2, C(6)), 41.3 (CH_2, C(7)), 44.6 and 64.9 (two quat. C, C(1) and C(3)), 53.7 (CH, C(4)), 62.4 (OCH_3), 198.6 (C=N). Anal. Calcd for $C_{22}H_{36}Cl_2N_2O_2Pd_2$: C, 41.01; H, 5.63; N, 4.35. Found: C, 41.28; H, 5.52; N, 4.28%.

(*S*,*S*)-Chloro{[2-(hydroxyimino)-3,3-dimethylbicyclo[2.2.1]heptyl]methyl-*C*,*N*} (triphenylphosphine-*P*)palladium(II) (199a). To a 50-mL round-bottomed flask with a magnetic stirring bar, a solution of complex **198a** (0.0505 g, 0.0820 mmol) in acetone (32 mL) and PPh_3 (0.0430 g, 0.164 mmol) were added. The resulting mixture was stirred at rt for 18 h. The solvent was removed under reduced pressure to give a white residue. The crude product was purified using preparative TLC (silica gel, 1:2 ethyl acetate–hexane). The pure complex was isolated as a white powder in 99% yield (0.0921 g, 0.0164 mmol). Mp: 148–150 °C; $[\alpha]^{22}_{D}$ -76.0, $[\alpha]^{22}_{546}$ -96.0, $[\alpha]^{22}_{435}$ -212 (*c* 0.366, EtOH); R_f 0.65 (2:1 hexane–ethyl acetate). ^{1}H NMR (δ, ppm): 1.09 (dd, 1H, $^2J_{H,H}$ = 10.1, $^2J_{H,P}$ = 7.2, $PdCH^A$), 1.22 (d, 1H, $^2J_{7A,7B}$ = 10.4, H(7A)), 1.27, 1.29 (two s, 6H, 2CH_3), 1.52 (m, 1H, H(6endo)), 1.58 (m, 1H, H(5endo)), 1.76 (br. d, 1H, $^2J_{7A,7B}$ = 10.4, H(7B)), 1.8−1.9 (m, 2H, H(5exo), H(6exo)), 2.08 (poorly resolved d, 1H, $J \approx 1.0$, H(4)), 2.28 (d, 1H, $^2J_{H,H}$ = 10.1, $PdCH^B$), 7.41 (m, 9H, *m*- and *p*-PPh), 7.65 (m, 6H, *o*-PPh), 9.70 (s, 1H, OH).

$^{13}C\{^1H\}$ NMR (δ, ppm): 21.0 and 22.1 (two CH_3), 25.1 (CH_2, C(5)), 32.8 (PdC)), 34.7 (CH_2, C(6)), 42.1 (CH_2, C(7)), 42.9 (C, C(3)), 53.2 (CH, C(4)), 64.9 (C, C(1)), 128.3 (d, $^3J_{C,P}$ = 10.8, *m*-PPh), 130.5 (d, $^4J_{C,P}$ = 1.7, *p*-PPh), 131.0 (d, $^1J_{C,P}$ = 49.6, *ipso*-PPh), 134.5 (d, $^2J_{C,P}$ = 12.2, *o*-PPh), 187.9 (C=N). $^{31}P\{^1H\}$ NMR (δ, ppm): 19.7. Anal. Calcd for $C_{28}H_{31}ClNOPPd$: C, 58.96; H, 5.48; N, 2.46. Found: C, 58.70; H, 5.68; N, 2.49%.

(*S,S*)-Chloro{[2-(methoxyimino)-3,3-dimethylbicyclo[2.2.1]heptyl]methyl-*C,N*} (triphenylphosphine-*P*)palladium(II) (199b). This compound was obtained as a white powder in 74% yield (0.0579 g, 0.0991 mmol) using complex **198b** (0.0430 g, 0.0667 mmol) and PPh_3 (0.0350 g, 0.134 mmol) and following the procedure described for compound **199a**. Mp: 179–181 °C; $[\alpha]^{24}_D$ -134, $[\alpha]^{24}_{546}$ -169, $[\alpha]^{24}_{435}$ -373 (*c* 0.348, EtOH); R_f 0.54 (2:1 hexane–ethyl acetate). ^1H NMR (δ, ppm): 0.84 (dd, 1H, $^2J_{H,H}$ = 10.7, $^2J_{H,P}$ = 9.0, $PdCH^A$), 1.18 (m, 1H, H(7)), 1.25, 1.27 (two s, 6H, 2CH_3), 1.50 (m, 1H, H(6endo)), 1.55 (m, 1H, H(5endo)), 1.72 (d, 1H, $^2J_{7A,7B}$ = 9.9, H(7A)), 1.82 (m, 1H, H(5exo)), 1.91 (m, 1H, H(6exo)), 2.00 (unresolved d, 1H, H(4)), 2.16 (d, 1H, $^2J_{H,H}$ = 10.7, $PdCH^B$), 4.10 (s, 3H, OCH_3), 7.39 (m, 9H, *m*- and *p*-PPh), 7.71 (m, 6H, *o*-PPh). $^{13}C\{^1H\}$ NMR (δ, ppm): 22.8 and 23.4 (two CH_3), 25.5 (CH_2, C(5)), 33.0 (PdC)), 34.8 (CH_2, C(6)), 43.4 (CH_2, C(7)), 44.2 (C, C(3)), 52.9 (CH, C(4)), 63.5 (OCH_3), 64.5 (C, C(1)), 128.5 (d, $^3J_{C,P}$ = 10.7, *m*-PPh), 130.7 (s, *p*-PPh), 131.8 (d, $^1J_{C,P}$ = 50.3, *ipso*-PPh), 135.1 (d, $^2J_{C,P}$ = 11.6, *o*-PPh), 196.6 (C=N). $^{31}P\{^1H\}$ NMR (δ, ppm): 20.3. Anal. Calcd for $C_{29}H_{33}ClNOPPd$: C, 59.60; H, 5.69; N, 2.40. Found: C, 59.90; H, 5.71; N, 2.40%.

VI.4. Preparation of CPCs and Their Reactions with $KPPh_2$

Complexes **177**, **178**, **212**, **217**, **219** and **222** were synthesized using published procedures.[17, 25, 31, 42, 103, 111, 353] The NMR spectra of the obtained compounds matched those reported in the literature.

VI.4.1. Synthesis and Characterization of New Compounds

(*R,R*)-1-{(Diphenylphosphino)methyl}-7,7-dimethylbicyclo[2.2.1]heptan-2-one *O*-Methyloxime (205). CPC **177** (0.0723g, 0.112 mmol) was added to a 25-mL Schlenk flask containing a magnetic stirring bar. The flask was evacuated and filled with Ar 5 times. Abs. THF (15 mL) was then added using a syringe followed by a 0.5 M solution of $KPPh_2$ (1 mL, 0.5 mmol). During the dropwise addition of $KPPh_2$ for 5 min, the yellow solution turned dark red. The mixture was stirred at rt for 18 h in Ar. The Schlenk flask was then placed on a rotavapor to remove THF. The dark-red solid residue was dissolved in CH_2Cl_2 (2 mL) and quickly separated into several fractions using preparative TLC (10:1 hexane–ethyl acetate). Fraction 3 corresponded to the pure product (0.0492 g, 0.135 mmol, 21%, colorless oil). $[\alpha]^{22}_{D}$ +154, $[\alpha]^{22}_{546}$ +173 (*c* 0.0460, EtOH). R_f 0.63 (10:1 hexane–ethyl acetate). ^{1}H NMR (δ, ppm): 0.83 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 1.20 (m, 1H, H(5endo)), 1.64 (m, 1H, H(6endo)), 1.77 (m, 2H, H(5exo), H(6exo)), 1.84 (m, 1H, H(4)), 1.95 (d, 1H, $^2J_{3endo,3exo}$ = 17.6, H(3endo)), 2.15 (dd, 1H, $^2J_{H,H}$ = 15.0, $^3J_{H,P}$ = 4.1, PCH^A), 2.48 (ddd, 1H, $^2J_{3exo,3endo}$ = 17.6, $^3J_{3exo,4} \approx {}^4J_{3exo,5exo} \approx$ 4.3, H(3exo)), 2.52 (dd, 1H, $^2J_{H,H}$ = 15.0, $^3J_{H,P}$ = 4.1, PCH^B), 3.76 (s, 3H, OCH_3), 7.32 (m, 6H, *m*- and *p*-PPh), 7.51 (m, 4H, *o*-PPh). $^{13}C\{^1H\}$ NMR (δ, ppm): 19.8 and 20.1 (two CH_3), 27.5 (d, $^1J_{C,P}$ = 18, PCH_2), 27.8 (CH_2, C(5)), 30.9 (CH_2, d, $^3J_{C,P}$ = 12, C(6)), 33.7 (CH_2, C(3)), 44.2 (CH, C(4)), 49.8 (quat. C, d, $^3J_{C,P}$ = 3.9, C(7)), 54.6 (quat. C, d, $^2J_{C,P}$ = 14, C(1)), 61.8 (OCH_3), 128.27, 128.47, 128.52, 128.76, 128.81 (all CH, *m*- and *p*-PPh; the signal at 128.81 ppm has a double intensity), 133.0 (CH, d, $^{2}J_{C,P}$ = 19, *o*-PPh^{A}), 133.7 (CH, d, $^{2}J_{C,P}$ = 20, *o*-PPh^{B}), 141.2 (quat. C, d, $^{1}J_{C,P}$ = 15, *ipso*-PPh^{A}), 141.3 (quat. C, d, $^{1}J_{C,P}$ = 17, *ipso*-PPh^{B}), 167.9 (quat. C, C=N). ^{31}P{^{1}H} NMR ($CDCl_3$, δ, ppm): -36.9. ^{31}P{^{1}H} NMR (C_6D_6, δ, ppm): -23.2. HRMS: [M + H]$^{+}$ calcd for $C_{23}H_{28}NOP$ 366.1981, found 366.1979.

(*R,R*)-*μ*-Chloro-μ-(diphenylphosphido)bis{[2-(methoxyimino)-7,7-dimethylbicyclo[2.2.1]heptyl]methyl-*C,N*}dipalladium(II) (206). The reaction was performed as described above for **205** except that 1 equiv. of $KPPh_2$ was used and the reaction time was 1 h. After solvent removal, the crude product was dissolved in ethyl acetate (2 mL) and separated into several fractions using preparative TLC (10:1 hexane–ethyl acetate). Fraction 2 corresponded to complex **206** (0.0198 g, 0.0249 mmol, 31%, orange solid). Mp: 194–196 °C; R_f 0.50 (10:1 hexane–ethyl acetate); $[\alpha]^{22}_{D}$ -189, $[\alpha]^{22}_{546}$ -190 (*c* 0.0650, EtOH). IR (Nujol mull, *v*, cm^{-1}): 1674 (C=N). ^{1}H NMR (δ, ppm): 0.62 (s, 3H, CH_3), 0.72 (s, 3H, CH_3), 0.74 (m, 1H, PdCH^{A}), 1.27 (ddd, 1H, $^{3}J_{5endo,6endo}$ = 13, $^{2}J_{5endo,5exo}$ = 9.6, $^{3}J_{5endo,6exo}$ = 4.3, H(5endo)), 1.39 (d, 1H, $^{2}J_{H,H}$ = 10, PdCH^{B}), 1.64 (td, 1H, $^{2}J_{6exo,6endo}$ = $^{3}J_{6endo,5endo}$ = 13, $^{3}J_{6endo,5exo}$ = 4.5, H(6endo)), 1.79 (m, 1H, H(5exo)), 1.91 (d, 1H, $^{2}J_{3endo,3exo}$ = 19, H(3endo)), 1.96 (ddd, 1H, $^{2}J_{6exo,6endo}$ = 13, $^{3}J_{6exo,5exo}$ = 9.6, $^{3}J_{6exo,5endo}$ = 4.3, H(6exo)), 1.99 (t, 1H, $^{3}J_{4,5exo}$ = $^{3}J_{4,3exo}$ = 4, H(4)), 2.37 (dt, 1H, $^{2}J_{3exo,3endo}$ = 19, $^{3}J_{3exo,4}$ = $^{4}J_{3exo,5exo}$ = 4, H(3exo)), 3.97 (s, 3H, OCH_3), 7.30 (m, 6H, *m*- and *p*-PPh), 7.84 (m, 4H, *o*-PPh). ^{13}C{^{1}H} NMR (δ, ppm): 18.5 and 20.2 (two CH_3), 19.4 (d, $^{1}J_{C,P}$ = 2.2, PCH_2), 27.3 (CH_2, C(5)), 33.4 (CH_2, C(3)), 33.8 (CH_2, C(6)), 46.8 (CH, C(4)), 48.2 (quat. C, C(7)), 62.7 (OCH_3), 65.9 (quat. C, C(1)), 127.9 (CH, d, $^{3}J_{C,P}$ = 10, *m*-PPh), 128.5 (CH, d, $^{4}J_{C,P}$ = 2.2, *p*-PPh), 134.4 (CH, d, $^{2}J_{C,P}$ = 12, *o*-PPh), 138.3 (quat. C, d, $^{1}J_{C,P}$ = 32, *ipso*-PPh), 186.1

(quat. C, C=N). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 4.9; $^{31}P\{^1H\}$ NMR (C_6D_6, δ, ppm): 18.0. Anal. Calcd for $C_{34}H_{46}ClN_2O_2PPd_2$: C, 51.43; H, 5.84; N, 3.53%. Found: C, 51.14; H, 5.85; N, 3.49%.

(*R,R*)-Di-*μ*-(diphenylphosphido)bis{[2-(methoxyimino)-7,7-dimethylbicyclo[2.2.1]heptyl]methyl-*C,N*}dipalladium(II) (207). The reaction was performed as described above for **205**. The purification by preparative TLC was performed using 5:1 hexane–ethyl acetate as an eluent. The use of halogenated solvents, such as CH_2Cl_2 and $CHCl_3$, was avoided during all steps of the product purification. The upper fraction on the TLC plate corresponded to the product (0.0163 g, 0.0173 mmol, ca. 26%, brown solid). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ, ppm): -76.9; $^{31}P\{^1H\}$ NMR (C_6D_6, δ, ppm): -64.3.

(*S,S*)-1-{(Diphenylphosphino)methyl}-3,3-dimethylbicyclo[2.2.1]heptan-2-one *O*-Methyloxime (210). The reaction was performed as described above for **205** using complex **198** (0.0794g, 0.123 mmol). The reaction mixture was separated into several fractions using preparative TLC (10:1 hexane–ethyl acetate). Fraction 3 corresponded to compound **210** (0.0461 g, 0.126 mmol, 51%, colorless oil). $[\alpha]^{24}_D$ +138, $[\alpha]^{24}_{546}$ +171, $[\alpha]^{24}_{435}$ +246 (*c* 0.150, EtOH). R_f 0.65 (10:1 hexane–ethyl acetate). ^1H NMR (δ, ppm): 1.19, 1.25 (two s, 6H, $2CH_3$), 1.31 (d, 1H, $^2J_{7A,7B}$ = 10.1, H(7A)), 1.42 (m, 1H, H(6endo)), 1.50 (m, 1H, H(5endo)), 1.58 (br. d, 1H, H(7B)), 1.75 (m, 2H, H(4), H(5exo)), 1.92 (tq, 1H, $^2J_{6exo,6endo} = {}^3J_{6exo,5endo}$ = 12.0, $^3J_{6exo,5exo} \approx {}^4J_{6exo,P} \approx$ 1.8, H(6exo)), 2.46 (dd, 1H, $^2J_{H,H}$ = 14.7, $^2J_{H,P}$ = 3.5, PCH^A), 2.59 (dd, 1H, $^2J_{H,H}$ = 14.7, $^2J_{H,P}$ = 4.1, PCH^B), 3.73 (s, 3H, OCH_3), 7.30 (m, 6H, *m*- and *p*-PPh), 7.47 (m, 4H, *o*-PPh). $^{13}C\{^1H\}$ NMR (δ, ppm): 22.5 and 23.1 (two CH_3), 25.0 (CH_2, C(5)), 30.7 (d, $^1J_{C,P}$ = 13.1, PCH_2), 33.3 (d, CH_2, $^3J_{C,P}$ = 9.2, C(6)), 41.2 (CH_2, C(7)), 44.3 (CH, C(4)), 48.3 (d, C, C(3)), 52.6 (d, C, $^2J_{C,P}$ = 16.7, C(1)), 61.2

(OCH_3), 128.22, 128.27, 128.32 (*m*- and *p*-PPh), 132.8 (d, $^2J_{C,P}$ = 19.2, *o*-PPh^A), 133.0 (d, $^2J_{C,P}$ = 19.3, *o*-PPh^B), 139.9 (d, $^1J_{C,P}$ = 12.6, *ipso*-PPh^A), 140.0 (d, $^1J_{C,P}$ = 10.8, *ipso*-PPh^B), 171.9 (C=N). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ, ppm): -37.1. HRMS: $[M + H]^+$ calcd for $C_{23}H_{28}NOP$ 366.1981, found 366.1964.

(*S,S*)-*μ*-Chloro-*μ*-(diphenylphosphido)bis{[2-(methoxyimino)-3,3-dimethylbicyclo[2.2.1]heptyl]methyl-*C,N*}dipalladium(II) (211). The reaction was performed as described above for the preparation of **206** using complex **198** (0.0817 g, 0.1268 mmol). The reaction mixture was separated into several fractions using preparative TLC (10:1 hexane–ethyl acetate). Fraction 2 corresponded to complex **211** (0.0180 g, 0.0227 mmol, 56%, orange solid). $[\alpha]^{23}_{D}$ -121, $[\alpha]^{23}_{546}$ -147, $[\alpha]^{23}_{435}$ -204 (*c* 0.222, EtOH). Mp: 209–211 °C; R_f 0.55 (10:1 hexane–ethyl acetate). ^{1}H NMR (δ, ppm): 1.05 (dd, 1H, $^2J_{H,H}$ = 9.6, $^3J_{H,P}$ = 4.8, PdCH^A), 1.14, 1.20 (two s, 6H, 2CH_3), 1.17 (m, 1H, H(7A)), 1.53 (m, 2H, H(6endo), 5endo)), 1.63 (m, 2H, H(7B), PdCH^B), 1.80 (m, 1H, H(5exo)), 1.91 (m, 2H, H(4), H(6exo)), 3.93 (s, 3H, OCH_3), 7.29 (m, 6H, *m*- and *p*-PPh), 7.82 (m, 4H, *o*-PPh). $^{13}C\{^1H\}$ NMR (δ, ppm): 22.5 and 23.0 (two CH_3), 25.6 (CH_2, C(5)), 25.7 (PCH_2), 35.1 (CH_2, C(6)), 43.4 (CH_2, C(7)), 44.0 (C, C(3)), 52.3 (CH, C(4)), 62.6 (OCH_3), 64.3 (C, C(1)), 127.9, (d, $^3J_{C,P}$ = 10.2, *m*-PPh), 128.4 (s, *p*-PPh), 134.4 (d, $^2J_{C,P}$ = 12.2, *o*-PPh), 138.6 (d, $^1J_{C,P}$ = 31.1, *ipso*-PPh), 190.6 (C=N). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 2.2. Anal. Calcd for $C_{34}H_{46}N_2O_2PClPd_2$: C, 51.43; H, 5.84; N, 3.53%. Found: C, 51.30; H, 5.84; N, 3.52%.

μ-Chloro-μ-(diphenylphosphido)bis(8-quinolinylmethyl-*C,N*)dipalladium (214). The reaction was performed as described above for preparation of **206** using CPC **212** (0.0498 g, 0.0693 mmol). The reaction mixture was separated into several fractions using preparative TLC (10:1 benzene–acetone). Fraction 1 corresponded to complex **214**

(0.0258 g, 0.0359 mmol, 56%, orange powder). Mp: 237–239 °C; R_f 0.65 (15:1 toluene–ethyl acetate). ^{1}H NMR (δ, ppm): 3.02 (s, 2H, CH_2), 7.35 (m, 6H, *m*- and *p*-PPh), 7.40 (t, 1H, $^3J_{H,H} = 7.5$, arom. CH), 7.45 (d, 1H, $^3J_{H,H} = 7.0$, arom. CH), 7.50 (dd, 1H, $^3J_{H,H} \approx 8.3$, $^4J_{H,H} \approx 4.7$, arom. CH), 7.56 (d, 1H, $^3J_{H,H} \approx 7.7$, arom. CH), 8.00 (m, 4H, *o*-PPh) 8.25 (dd, 1H, $^3J_{H,H} \approx 8.2$, $^4J_{H,H} \approx 1.3$, arom. CH), 9.11 (m, 1H, arom. CH). $^{13}C\{^1H\}$ NMR (δ, ppm): 25.7 (CH_2, CH_2), 120.9 (d, $^4J_{C,P} = 2.7$, CH), 123.4 (s, CH), 127.5 (s, CH), 127.9, (d, $^3J_{C,P} = 10.0$, *m*-PPh), 128.2 (d, $^4J_{C,P} = 2.5$, CH), 129.0 (s, C), 129.3 (s, *p*-PPh), 134.1 (d, $^2J_{C,P} = 11.9$, *o*-PPh), 137.7 (s, CH), 137.8 (d, $^1J_{C,P} = 32.1$, *ipso*-PPh), 146.8 (s, CH), 149.6 (s, C), 151.0 (d, $^4J_{C,P} = 1.9$, C). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 10.2. Anal. Calcd for $C_{32}H_{26}N_2PClPd_2$: C, 53.54; H, 3.65; N, 3.90%. Found: C, 53.27; H, 3.80; N, 3.85%.

8-[(Diphenyloxophosphino)methyl]quinoline (216). Complex **212** (0.1636 g, 0.2659 mmol) was added to an oven dried Ar-filled 50-mL Schlenk flask containing a magnetic stirring bar. The flask was evacuated and filled with Ar 5 times. Then abs. THF (17 mL) was added followed by a 0.5 M solution of $KPPh_2$ in THF (3.2 mL, 1.6 mmol). During the dropwise addition, the orange solution turned dark red, and then black. The mixture was stirred at rt for 48 h in Ar. The reaction mixture was then filtered through celite (h = 1 cm), and the flask with the filtrate was placed on a rotavapor to remove solvent. The crude product was dissolved in CH_2Cl_2 and separated into several fractions using preparative TLC (10:1 ethyl acetate–acetone). Fraction 1 corresponded to 8-methylquinoline **213** (0.0450 g, 0.314 mmol, 48%, colorless oil). Fraction 3 corresponded to compound **216** (0.0321 g, 0.0231 mmol, 21%, colorless oil). R_f 0.40 (10:1 ethyl acetate–acetone). ^{1}H NMR (δ, ppm): 4.56 (d, 2H, $^2J_{H,P} = 14.2$, PCH_2), 7.28 (t, 1H, $^3J_{H,H} = 4.2$, arom. H(3)), 7.31 (m, 4H, *o*-PPh), 7.38 (dt, 2H, $^3J_{H,H} = 7.4$, $^4J_{H,H} = 1.3$, *p*-PPh), 7.46 (t, 1H, $^2J_{H,P}$

= 15.4, arom. H(6)), 7.64 (d, 1H, $^3J_{H,P}$ = 8.2, arom. H(7)), 7.78 (m, 4H, *m*-PPh), 8.03 (dd, 1H, $^3J_{H,H}$ = 8.2, $^5J_{H,H}$ = 1.6, arom. H(5)), 8.05 (m, 1H, arom. H(4)), 8.76 (dd, 1H, $^3J_{H,H}$ = 4.1, $^5J_{H,H}$ = 1.6, arom. H(2)). $^{13}C\{^1H\}$ NMR (δ, ppm): 21.2 (d, $^1J_{C,P}$ = 67.9, PCH_2), 121.2 (s, arom. CH(3)), 126.8 (d, $^3J_{C,P}$ = 2.8, arom. CH(6)), 127.2 (d, $^4J_{C,P}$ = 1.0, arom. CH(7)), 128.5 (d, $^2J_{C,P}$ = 11.6, *o*-PPh), 131.2 (d, $^2J_{C,P}$ = 7.7, *ipso*-PPh), 131.55 (s, arom. CH(5)), 131.56 (d, $^2J_{C,P}$ = 9.2, *m*-PPh), 131.8 (d, $^2J_{C,P}$ = 2.3, *p*-PPh), 133.0 (s, arom. C(10)), 133.8 (two s, (s, arom. CH(8)), 136.6 (s, arom. CH(4)), 146.7 (d, $^2J_{C,P}$ = 5.5, arom. CH(9)), 149.4 (s, CH, arom. CH(2)). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 16.5. IR (Nujol mull, ν, cm^{-1}): 1199 s (P=O). HRMS: $[M + H]^+$ calcd for $C_{22}H_{19}NOP$ 343.1199, found 344.1108.

[2-(Di-*ortho*-tolylphosphino)benzyl]diphenylphosphine oxide (220). Complex **219** (0.0690 g, 0.0775 mmol) was added to an oven dried Ar-filled 25-mL Schlenk flask containing a magnetic stirring bar. The flask was evacuated and filled with Ar 5 times. Then abs. THF (10 mL) was added followed by a 0.5 M solution of $KPPh_2$ in THF (0.7 mL, 0.3 mmol). During the dropwise addition, the yellow solution turned dark red, and then brown. The mixture was stirred at rt for 48 h in Ar and then 48 h in air. The reaction mixture was then filtered through celite (h = 1 cm), and the flask with the filtrate was placed on a rotavapor to remove solvent. The mixture was separated into several fractions using preparative TLC (10:1 ethyl acetate–acetone). Fraction 1 corresponded to tri(*O*-tolyl)phosphine **221** (0.001 g, 0.003 mmol, 2%, white powder). Fraction 2 corresponded to product **220** (0.00147 g, 0.0303 mmol, 20%, pale yellow oil). R_f 0.59 (10:1 ethyl acetate–acetone). ^1H NMR (δ, ppm): 2.26 (s, 6H, CH_3), 4.00 (d, 2H, $^2J_{H,P}$ = 9.6, PCH_2), 6.61 (dd, 2H, $^3J_{H,P}$ = 7.4, $^3J_{H,H}$ = 4.6, arom. CH of C_6H_4-CH_2P), 7.00 (dd, 1H, $^3J_{H,H}$ = 7.6, $^4J_{H,P}$ = 3.9, arom. CH of C_6H_4-CH_2P), 7.05 (m, 3H, arom. CH(3), CH(5) of tolyl), 7.20 (t, 2H, $^3J_{H,H}$ =

6.0, arom. CH(4) of tolyl), 7.23−7.30 (m, 3H, arom. CH(3), CH(6) of tolyl), 7.35 (td, 4H, $^{3}J_{H,P}$ = 7.5, $^{3}J_{H,H}$ = 2.8, *o*-PPh), 7.42 (t, 2H, $^{3}J_{H,H}$ = 6.9, *p*-PPh), 7.74 (dd, 4H, $^{3}J_{H,P}$ = 11.4, $^{3}J_{H,H}$ = 7.4, *m*-PPh), 7.95 (t, 1H, $^{3}J_{H,H}$ = 6.3, arom. CH of C_6H_4-CH_2P). $^{13}C\{^{1}H\}$ NMR (δ, ppm): 21.6, 21.8 (two s, CH_3), 35.0 (dd, $^{1}J_{C,P}$ = 67.2, $^{3}J_{C,P}$ = 25.9, PCH_2), 126.7(s, arom. CH(5) of tolyl), 127.8 (s, arom. CH(3) of tolyl), 128.8 (d, $^{3}J_{C,P}$ = 11.7, *o*-PPh), 129.3 (s, arom. CH(6) of tolyl), 129.6 (s, arom. CH(3) of tolyl), 130.5 (d, $^{4}J_{C,P}$ = 4.7, arom. CH(4) of tolyl), 131.2 (t, $^{4}J_{C,P}$ = 4.3, arom. CH of C_6H_4-CH_2P), 131.5 (d, $^{3}J_{C,P}$ = 9.4, *m*-PPh), 132.0 (s, *p*-PPh), 133.3 (d, $^{1}J_{C,P}$ = 99.3, arom. C(1) of tolyl), 133.5 (s, arom. CH of C_6H_4-CH_2P), 134.3 (s, arom. CH of C_6H_4-CH_2P), 134.5 (d, $^{2}J_{C,P}$ = 9.3, PPh), 135.0 (t, $^{3}J_{C,P}$ = 8.4, arom. CH of C_6H_4-CH_2P), 137.7 (dd, $^{1}J_{C,P}$ = 26.4, $^{3}J_{C,P}$ = 6.3, arom. C of C_6H_4-CH_2P), 142.8 (d, $^{1}J_{C,P}$ = 25.9, C(2) of tolyl). $^{31}P\{^{1}H\}$ NMR ($CDCl_3$, δ, ppm): -45.08 and 15.35 (two d, $^{4}J_{P,P}$ = 9.2). IR (Nujol mull, ν, cm^{-1}): 1198 s (P=O). HRMS: $[M + Na + H]^{+}$ calcd for $C_{33}H_{30}O_2P_2Na$ 543.1691, found 543.1440.

[6-Methyl-1-(methylthio)benzyl]diphenylphosphine oxide (224). The compound was obtained using the procedure described above for oxide **220** using complex **222** (0.1309 g, 0.2233 mmol). The reaction mixture was separated into two fractions using preparative TLC (10:1 ethyl acetate–acetone). Fraction 1 corresponded to 2,6-dimethylthioanisole **225** (0.0483 g, 0.317 mmol, 71%, colorless oil). Fraction 2 corresponded to compound **224** (0.0351 g, 0.0996 mmol, 22%, purple oil). R_f 0.50 (10:1 ethyl acetate–acetone). ^{1}H NMR (δ, ppm): 2.04 (s, 3H, CH_3), 2.48 (s, 3H, SCH_3), 4.24 (d, 2H, $^{2}J_{H,P}$ = 14.1, PCH_2), 7.10 (m, 2H, arom. H(4), H(5)), 7.33 (m, 1H, arom. H(3)),7.42 (dt, 4H, $^{3}J_{H,P}$ = $^{3}J_{H,H}$ = 7.7, $^{4}J_{H,H}$ = 2.7, *o*-PPh), 7.49 (dt, 2H, $^{3}J_{H,H}$ = 7.4, $^{4}J_{H,H}$ = 1.3, *p*-PPh), 7.72 (dd, 4H, $^{3}J_{H,H}$ = 7.2, $^{3}J_{H,H}$ = 7.2, *m*-PPh). $^{13}C\{^{1}H\}$ NMR (δ, ppm): 19.1 (s, CH_3), 22.2

(s, SCH_3), 36.6 (d, $^1J_{C,P}$ = 67.0, PCH_2), 128.6 (d, $^5J_{C,P}$ = 1.7, arom. CH(5)), 128.8 (d, $^2J_{C,P}$ = 11.8, *o*-PPh), 129.0 (d, $^3J_{C,P}$ = 4.8, CH(3)), 129.7 (d, $^4J_{C,P}$ = 2.7, arom. CH(4)), 131.7 (d, $^3J_{C,P}$ = 9.1, *m*-PPh)), 132.1 (d, $^4J_{C,P}$ = 2.8, *p*-PPh), 132.7 (s, C(6)), 133.5 (s, C(2)), 136.36 (t, $^1J_{C,P}$ = 9.2, *ipso*-PPh), 143.5 (s, C(1)). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 15.03. IR (Nujol mull, v, cm^{-1}): 1187 s (P=O). HRMS: $[M + H]^+$ calcd for $C_{21}H_{22}OPS$ 353.1123, found 353.1005.

(*R,R*)-1-{(Diphenyloxophosphino)methyl}-7,7-dimethylbicyclo[2.2.1]heptan-2-one *O*-Methyloxime (226). Phosphine **205** was exposed to the air to give the corresponding oxide as an orange-yellow oil in a quantitative yield. $[\alpha]^{23}_D$ -18, $[\alpha]^{23}_{546}$ -13 (*c* 0.099, EtOH). R_f 0.57 (5:3 hexane–acetone). IR (CH_2Cl_2, v, cm^{-1}): 1671 (C=N), 1184 (P=O). ^1H NMR (δ, ppm): 0.81 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.12 (m, 1H, H(5endo)), 1.30 (m, 1H, H(6endo)), 1.82 (m, 2H, H(5exo), H(4)), 1.88 (d, 1H, $^2J_{3endo,3exo}$ = 18, H(3endo)), 2.15 (t, 1H, $^2J_{H,H}$ = $^3J_{H,P}$ = 16, PCH^A), 2.40 (m, 2H, H(6exo), H(3exo)), 3.06 (dd, 1H, $^2J_{H,H}$ = $^3J_{H,P}$ = 16, PCH^B), 3.72 (s, 3H, OCH_3), 7.45 (m, 6H, *o*- and *p*-PPh), 7.77 (m, 2H, *m*-PPh^A), 7.95 (m, 2H, *m*-PPh^B). $^{13}C\{^1H\}$ NMR (δ, ppm): 19.6 and 19.9 (two CH_3), 27.3 (d, $^1J_{C,P}$ = 73, PCH_2), 28.0 (CH_2, C(5)), 29.4 (CH_2, d, $^3J_{C,P}$ = 5.1, C(6)), 33.8 (CH_2, C(3)), 43.2 (CH, C(4)), 50.3 (quat. C, d, $^3J_{C,P}$ = 4.6, C(7)), 53.2 (quat. C, d, $^2J_{C,P}$ = 4.9, C(1)), 61.7 (OCH_3), 128.6 (CH, d, $^2J_{C,P}$ = 12, *o*-PPh^A), 128.8 (CH, d, $^2J_{C,P}$ = 12, *o*-PPh^B), 130.8 (CH, d, $^3J_{C,P}$ = 8.9, *m*-PPh^A), 131.6 (CH, br. s, *p*-PPh), 131.7 (CH, d, $^3J_{C,P}$ = 9.4, *m*-PPh^B), 134.9 (quat. C, d, $^1J_{C,P}$ = 98, *ipso*-PPh^A), 136.6 (quat. C, d, $^1J_{C,P}$ = 99, *ipso*-PPh^B), 167.5 (quat. C, d, $^4J_{C,P}$ = 5.3, C=N). $^{31}P\{^1H\}$ NMR ($CDCl_3$, δ, ppm): 15.1. $^{31}P\{^1H\}$ NMR (C_6D_6, δ, ppm): 25.0. HRMS: $[M + H]^+$ calcd for $C_{23}H_{28}NO_2P$ 382.1894, found 382.1894.

APPENDICES

APPENDIX A

X-RAY DATA TABLES OF COMPLEX **177**

Table 2. Crystal data, data collection, structure solution and structure refinement for **177**.

Empirical formula	$C_{11} H_{18} Cl NO Pd$	
Formula weight	322.11	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	*a* = 6.8825(3) Å	α = 90°
	b = 18.1917(7) Å	β = 90°
	c = 19.6478(7) Å	γ = 90°
Volume	2459.99(17) $Å^3$	
Z	8	
Density (calculated)	1.739 Mg/m^3	
Absorption coefficient	1.700 mm^{-1}	
F(000)	1296	
Crystal size	0.29 x 0.12 x 0.08 mm^3	
Theta range for data collection	1.53 to 30.19°	
Index ranges	$-8 \leq h \leq 9$, $-24 \leq k \leq 25$, $-27 \leq l \leq 27$	
Reflections collected	35022	
Independent reflections	6869 [*R*(int) = 0.0267]	
Completeness to theta = 30.19°	98.3%	
Absorption correction	None	
Max. and min. transmission	0.8831 and 0.6384	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6869 / 0 / 277	
Goodness-of-fit on F^2	1.199	
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0193, *wR*2 = 0.0462	
R indices (all data)	*R*1 = 0.0228, *wR*2 = 0.0626	
Absolute structure parameter	-0.03(2)	
Largest diff. peak and hole	0.601 and -0.486 e.$Å^{-3}$	

Table 3. Selected bond lengths for **177**.

Bond	*d*/ Å	Bond	*d*/ Å
Pd(1)-C(10)	2.024(2)	C(2)-C(3)	1.496(4)
Pd(1)-N(1)	2.027(2)	C(3)-C(4)	1.554(4)
Pd(1)-Cl(2)	2.3311(7)	C(4)-C(5)	1.528(4)
Pd(1)-Cl(1)	2.4793(6)	C(4)-C(7)	1.557(4)
Pd(2)-C(30)	2.013(3)	C(5)-C(6)	1.557(4)
Pd(2)-N(2)	2.046(2)	C(7)-C(9)	1.522(4)
Pd(2)-Cl(1)	2.3292(7)	C(7)-C(8)	1.530(4)
Pd(2)-Cl(2)	2.5199(6)	C(21)-C(22)	1.485(4)
O(1)-N(1)	1.411(3)	C(21)-C(30)	1.508(4)
O(1)-C(11)	1.433(3)	C(21)-C(26)	1.551(4)
O(2)-N(2)	1.415(3)	C(21)-C(27)	1.567 (4)
O(2)-C(31)	1.417(3)	C(22)-C(23)	1.499(4)
N(1)-C(2)	1.284(3)	C(23)-C(24)	1.545(4)
N(2)-N(22)	1.274(3)	C(24)-C(25)	1.541(5)
C(1)-C(2)	1.491(4)	C(24)-C(27)	1.556 (4)
C(1)-C(10)	1.523(4)	C(25)-C(26)	1.542(5)
C(1)-C(7)	1.571(4)	C(27)-C(29)	1.524(4)
C(1)-C(6)	1.550(4)	C(27)-C(28)	1.528(4)

Table 4. Selected angles for **177**.

Bond	angle/°	Bond	angle/°
C(10)-Pd(1)-N(1)	82.14(10)	Cl(1)-Pd(2)-Cl(2)	103.62(6)
C(10)-Pd(1)-Cl(2)	90.50(8)	Pd(2)-Cl(1)-Pd(1)	93.37(2)
N(1)-Pd(1)-Cl(2)	172.62(6)	Pd(1)-Cl(2)-Pd(2)	92.28(2)
C(10)-Pd(1)-Cl(1)	176.00(8)	N(1)-O(1)-C(11)	109.93(19)
N(1)-Pd(1)-Cl(1)	100.25(6)	N(2)-O(2)-C(31)	110.6(2)
Cl(2)-Pd(1)-Cl(1)	87.13(2)	C(2)-N(1)-O(1)	113.9(2)
C(30)-Pd(2)-N(2)	82.39(10)	C(2)-N(1)-Pd(1)	116.47(18)
C(30)-Pd(2)-Cl(1)	87.76(9)	O(1)-N(1)-Pd(1)	129.58(15)
N(2)-Pd(2)-Cl(1)	170.14(6)	C(22)-N(2)-O(2)	113.1(2)
C(30)-Pd(2)-Cl(2)	173.98(9)	C(22)-N(2)-Pd(2)	115.73(18)
N(2)-Pd(2)-Cl(2)	103.62(6)	O(2)-N(2)-Pd(2)	129.79(17)

C(2)-C(1)-C(10)	111.0(2)	C(22)-C(21)-C(30)	112.0(2)
C(2)-C(1)-C(6)	104.3(2)	C(22)-C(21)-C(26)	105.0(2)
C(10)-C(1)-C(6)	117.1(2)	C(30)-C(21)-C(26)	115.8(3)
C(2)-C(1)-C(7)	99.1(2)	C(22)-C(21)-C(27)	98.9(2)
C(10)-C(1)-C(7)	120.6(2)	C(30)-C(21)-C(27)	120.7(2)
C(6)-C(1)-C(7)	102.1(2)	C(26)-C(21)-C(27)	102.1(2)
N(1)-C(2)-C(1)	117.0(2)	N(2)-C(22)-C(21)	118.0(3)
N(1)-C(2)-C(3)	132.7(2)	N(2)-C(22)-C(23)	132.0(3)
C(1)-C(2)-C(3)	110.3(2)	C(21)-C(22)-C(23)	109.8(2)
C(2)-C(3)-C(4)	99.4(2)	C(22)-C(23)-C(24)	99.8(2)
C(5)-C(4)-C(3)	106.7(3)	C(25)-C(24)-C(23)	106.9(3)
C(5)-C(4)-C(7)	102.9(2)	C(25)-C(24)-C(27)	102.2(2)
C(3)-C(4)-C(7)	102.8(2)	C(23)-C(24)-C(27)	103.0(2)
C(4)-C(5)-C(6)	103.4(2)	C(24)-C(25)-C(26)	103.1(2)
C(1)-C(6)-C(5)	103.4(2)	C(25)-C(26)-C(21)	104.0(2)
C(9)-C(7)-C(8)	107.9(3)	C(29)-C(27)-C(28)	107.8(3)
C(9)-C(7)-C(4)	114.1(2)	C(29)-C(27)-C(24)	114.5(2)
C(8)-C(7)-C(4)	114.1(2)	C(28)-C(27)-C(24)	114.7(2)
C(9)-C(7)-C(1)	113.8(2)	C(29)-C(27)-C(21)	113.5(2)
C(8)-C(7)-C(1)	113.4(2)	C(28)-C(27)-C(21)	112.9(2)
C(4)-C(7)-C(1)	93.1(2)	C(24)-C(27)-C(21)	93.1(2)
C(1)-C(10)-Pd(1)	109.25(17)	C(21)-C(30)-Pd(2)	110.95(18)

APPENDIX B

X-RAY DATA TABLES OF COMPLEX **186**

Table 5. Crystal data, data collection, structure solution and structure refinement for 156.

Empirical formula	$C_{24} H_{42} Cl_2 N_4 Pd_2$	
Formula weight	670.31	
Temperature	123(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	*a* = 12.1816(17) Å	α = 90°
	b = 7.1564(10) Å	β = 109.964(2)°
	c = 16.823(2) Å	γ = 90°
Volume	1378.4(3) $Å^3$	
Z	2	
Density (calculated)	1.615 Mg/m^3	
Absorption coefficient	1.517 mm^{-1}	
F(000)	680	
Crystal color, morphology	Yellow, Block	
Crystal size	0.220 x 0.200 x 0.180 mm^3	
Theta range for data collection	1.779 to 27.617°	
Index ranges	$-15 \leq h \leq 15$, $-9 \leq k \leq 9$, $-21 \leq l \leq 21$	
Reflections collected	16179	
Independent reflections	6351 [*R*(int) = 0.0329]	
Observed reflections	5902	
Completeness to theta = 25.242°	100.0%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.4915 and 0.4383	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6351 / 1 / 299	
Goodness-of-fit on F^2	1.040	
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0298, *wR*2 = 0.0570	
R indices (all data)	*R*1 = 0.0336, *wR*2 = 0.0596	
Absolute structure parameter	-0.04(2)	
Largest diff. peak and hole	0.680 and -0.503 e.$Å^{-3}$	

Table 6. Selected bond lengths for **186**.

Bond	*d*/ Å	Bond	*d*/ Å
Pd(1)-C(3)	1.982(5)	C(4)-C(7)	1.545(7)
Pd(1)-N(2)	2.076(5)	C(5)-C(6)	1.551(8)
Pd(1)-Cl(1A)	2.3331(14)	C(7)-C(9)	1.533(8)
Pd(1)-Cl(1)	2.5012(13)	C(7)-C(10)	1.536(8)
Pd(1A)-C(3A)	2.007(5)	N(1A)-C(2A)	1.267(7)
Pd(1A)-N(2A)	2.079(5)	N(1A)-N(2A)	1.489(6)
Pd(1A)-Cl(1)	2.3416(14)	N(2A)-C(11A)	1.468(8)
Pd(1A)-Cl(1A)	2.4799(14)	N(2A)-C(12A)	1.492(7)
N(1)-C(2)	1.271(7)	C(1A)-C(2A)	1.501(7)
N(1)-N(2)	1.495(6)	C(1A)-C(8A)	1.507(8)
N(2)-C(11)	1.474(7)	C(1A)-C(6A)	1.550(9)
N(2)-C(12)	1.475(8)	C(1A)-C(7A)	1.576(7)
C(1)-C(8)	1.507(7)	C(2A)-C(3A)	1.491(8)
C(1)-C(2)	1.521(7)	C(3A)-C(4A)	1.535(7)
C(1)-C(7)	1.557(8)	C(4A)-C(5A)	1.542(8)
C(1)-C(6)	1.569(7)	C(4A)-C(7A)	1.565(8)
C(2)-C(3)	1.501(8)	C(5A)-C(6A)	1.539(8)
C(3)-C(4)	1.548(7)	C(7A)-C(9A)	1.511(7)
C(4)-C(5)	1.513(8)	C(7A)-C(10A)	1.534(8)

Table 7. Selected angles for **186**.

Bond	angle/°	Bond	angle/°
C(3)-Pd(1)-N(2)	80.8(2)	C(3A)-Pd(1A)-Cl(1A)	175.46(16)
C(3)-Pd(1)-Cl(1A)	93.87(18)	N(2A)-Pd(1A)-Cl(1A)	96.00(13)
N(2)-Pd(1)-Cl(1A)	174.12(12)	Cl(1)-Pd(1A)-Cl(1A)	88.40(4)
C(3)-Pd(1)-Cl(1)	174.36(17)	Pd(1A)-Cl(1)-Pd(1)	91.34(5)
N(2)-Pd(1)-Cl(1)	97.45(13)	Pd(1)-Cl(1A)-Pd(1A)	92.08(5)
Cl(1A)-Pd(1)-Cl(1)	88.08(4)	C(2)-N(1)-N(2)	108.5(4)
C(3A)-Pd(1A)-N(2A)	80.8(2)	C(11)-N(2)-C(12)	110.1(5)
C(3A)-Pd(1A)-Cl(1)	94.68(18)	C(11)-N(2)-N(1)	106.4(4)
N(2A)-Pd(1A)-Cl(1)	175.21(14)	C(12)-N(2)-N(1)	104.0(4)

C(11)-N(2)-Pd(1)	113.7(4)
C(12)-N(2)-Pd(1)	110.1(4)
N(1)-N(2)-Pd(1)	112.1(3)
C(8)-C(1)-C(2)	116.6(5)
C(8)-C(1)-C(7)	120.0(5)
C(2)-C(1)-C(7)	101.0(5)
C(8)-C(1)-C(6)	115.6(5)
C(2)-C(1)-C(6)	99.7(4)
C(7)-C(1)-C(6)	100.6(5)
N(1)-C(2)-C(3)	125.6(5)
N(1)-C(2)-C(1)	125.5(5)
C(3)-C(2)-C(1)	108.6(5)
C(2)-C(3)-C(4)	100.2(4)
C(2)-C(3)-Pd(1)	105.9(4)
C(4)-C(3)-Pd(1)	129.4(4)
C(5)-C(4)-C(7)	103.9(5)
C(5)-C(4)-C(3)	108.0(5)
C(7)-C(4)-C(3)	100.5(4)
C(4)-C(5)-C(6)	103.7(4)
C(5)-C(6)-C(1)	103.7(5)
C(9)-C(7)-C(10)	106.8(5)
C(9)-C(7)-C(4)	112.6(5)
C(10)-C(7)-C(4)	116.2(5)
C(9)-C(7)-C(1)	114.0(5)
C(10)-C(7)-C(1)	112.6(5)
C(4)-C(7)-C(1)	94.7(4)
C(2A)-N(1A)-N(2A)	108.9(4)
C(11A)-N(2A)-N(1A)	104.8(4)
C(11A)-N(2A)-C(12A)	109.7(5)
N(1A)-N(2A)-C(12A)	107.6(4)
C(11A)-N(2A)-Pd(1A)	109.5(4)
N(1A)-N(2A)-Pd(1A)	112.9(3)
C(12A)-N(2A)-Pd(1A)	112.1(4)
C(2A)-C(1A)-C(8A)	116.4(5)
C(2A)-C(1A)-C(6A)	107.5(5)
C(8A)-C(1A)-C(6A)	114.9(4)
C(2A)-C(1A)-C(7A)	96.5(4)
C(8A)-C(1A)-C(7A)	117.9(5)
C(6A)-C(1A)-C(7A)	101.2(5)
N(1A)-C(2A)-C(3A)	126.5(5)
N(1A)-C(2A)-C(1A)	124.7(5)
C(3A)-C(2A)-C(1A)	108.0(5)
C(2A)-C(3A)-C(4A)	101.5(4)
C(2A)-C(3A)-Pd(1A)	106.3(4)
C(4A)-C(3A)-Pd(1A)	129.2(4)
C(3A)-C(4A)-C(5A)	105.5(5)
C(3A)-C(4A)-C(7A)	103.5(5)
C(5A)-C(4A)-C(7A)	101.3(4)
C(6A)-C(5A)-C(4A)	102.1(5)
C(5A)-C(6A)-C(1A)	105.6(5)
C(9A)-C(7A)-C(10A)	107.3(5)
C(9A)-C(7A)-C(4A)	115.9(5)
C(10A)-C(7A)-C(4A)	112.6(4)
C(9A)-C(7A)-C(1A)	113.5(4)
C(10A)-C(7A)-C(1A)	113.9(5)
C(4A)-C(7A)-C(1A)	93.4(4)

APPENDIX C

X-RAY DATA TABLES OF COMPLEX **199a**

Table 8. Crystal data, data collection, structure solution and structure refinement for **199a**.

Empirical formula	$C_{28}H_{31}ClNOPPd$	
Formula weight	570.36	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	*a* = 27.051(2) Å	α = 90°
	b = 11.8212(11) Å	β = 121.429(1)°
	c = 19.0231(17) Å	γ = 90°
Volume	5190.7(8) $Å^3$	
Z	8	
Density (calculated)	1.460 Mg/m^3	
Absorption coefficient	0.900 mm^{-1}	
F(000)	2336	
Crystal color, morphology	colourless, needle	
Crystal size	0.40 x 0.13 x 0.10 mm^3	
Theta range for data collection	1.764 to 27.508°	
Index ranges	$-34 \le h \le 32$, $-15 \le k \le 15$, $-24 \le l \le 24$	
Reflections collected	23130	
Independent reflections	5932 [*R*(int) = 0.0502]	
Observed reflections	4451	
Completeness to theta = 25.242°	99.9%	
Absorption correction	Multi-scan	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5932 / 0 / 301	
Goodness-of-fit on F^2	1.005	
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0432, *wR*2 = 0.0918	
R indices (all data)	*R*1 = 0.0659, *wR*2 = 0.1021	
Largest diff. peak and hole	1.815 and -1.026 e.$Å^{-3}$	

Table 9. Selected bond lengths for **199a**.

Bond	*d*/ Å	Bond	*d*/ Å
Pd1-C1	2.051(4)	P1-C23	1.822(4)
Pd1-N1	2.064(3)	C11-C12	1.381(5)
Pd1-P1	2.2218(10)	C11-C16	1.395(5)
Pd1-Cl1	2.4019(9)	C12-C13	1.385(6)
C1-C2	1.526(5)	C13-C14	1.378(6)
C2-C3	1.502(5)	C14-C15	1.371(6)
C2-C7	1.539(6)	C15-C16	1.373(6)
C2-C8	1.550(6)	C17-C22	1.391(6)
C3-N1	1.273(5)	C17-C18	1.391(6)
C3-C4	1.507(5)	C18-C19	1.391(7)
N1-O1	1.391(4)	C19-C20	1.379(9)
C4-C9	1.521(6)	C20-C21	1.371(9)
C4-C10	1.545(7)	C21-C22	1.369(6)
C4-C5	1.556(7)	C23-C24	1.378(5)
C5-C6	1.522(8)	C23-C28	1.390(5)
C5-C8	1.548(7)	C24-C25	1.395(5)
C6-C7	1.540(7)	C25-C26	1.366(7)
P1-C17	1.814(4)	C26-C27	1.352(7)
P1-C11	1.820(3)	C27-C28	1.388(6)

Table 10. Selected angles for **199a**.

Bond	angle/°	Bond	angle/°
C1-Pd1-N1	81.43(14)	C3-C2-C8	99.5(3)
C1-Pd1-P1	89.70(11)	C1-C2-C8	119.9(3)
N1-Pd1-P1	171.11(9)	C7-C2-C8	101.2(4)
C1-Pd1-Cl1	167.92(12)	N1-C3-C2	115.3(3)
N1-Pd1-Cl1	87.18(9)	N1-C3-C4	133.6(4)
P1-Pd1-Cl1	101.61(4)	C2-C3-C4	111.1(3)
C2-C1-Pd1	106.2(3)	C3-N1-O1	117.9(3)
C3-C2-C1	112.0(3)	C3-N1-Pd1	116.4(3)
C3-C2-C7	104.8(3)	O1-N1-Pd1	125.6(2)
C1-C2-C7	116.9(4)	C3-C4-C9	113.2(3)

C3-C4-C10	109.8(4)	C14-C13-C12	119.8(4)
C9-C4-C10	108.4(4)	C15-C14-C13	120.0(4)
C3-C4-C5	97.7(3)	C14-C15-C16	120.5(4)
C9-C4-C5	114.9(4)	C15-C16-C11	120.1(4)
C10-C4-C5	112.6(4)	C22-C17-C18	119.8(4)
C6-C5-C8	99.6(5)	C22-C17-P1	119.3(3)
C6-C5-C4	111.0(4)	C18-C17-P1	120.9(3)
C8-C5-C4	103.1(4)	C19-C18-C17	119.7(5)
C5-C6-C7	104.8(4)	C20-C19-C18	119.2(5)
C6-C7-C2	102.5(5)	C21-C20-C19	121.1(5)
C5-C8-C2	93.8(3)	C20-C21-C22	120.1(6)
C17-P1-C11	103.65(16)	C21-C22-C17	120.0(5)
C17-P1-C23	106.15(17)	C24-C23-C28	118.0(3)
C11-P1-C23	107.01(16)	C24-C23-P1	124.2(3)
C17-P1-Pd1	115.83(13)	C28-C23-P1	117.7(3)
C11-P1-Pd1	113.28(12)	C23-C24-C25	120.7(4)
C23-P1-Pd1	110.25(12)	C26-C25-C24	120.4(5)
C12-C11-C16	119.0(3)	C27-C26-C25	119.4(4)
C12-C11-P1	123.0(3)	C26-C27-C28	121.3(4)
C16-C11-P1	117.5(3)	C27-C28-C23	120.2(4)
C11-C12-C13	120.4(4)		

APPENDIX D

X-RAY DATA TABLES OF COMPLEX **199b**

Table 11. Crystal data, data collection, structure solution and structure refinement for **199b**.

Empirical formula	$C_{29} H_{33} Cl N O P Pd$	
Formula weight	584.38	
Temperature	123(2) K	
Wavelength	1.54178 Å	
Crystal system	monoclinic	
Space group	$P2_1$	
Unit cell dimensions	*a* = 10.9541(7) Å	α = 90°
	b = 9.1372(7) Å	β = 108.297(4)°
	c = 13.8615(9) Å	γ = 90°
Volume	1317.25(16) $Å^3$	
Z	2	
Density (calculated)	1.473 Mg/m^3	
Absorption coefficient	7.353 mm^{-1}	
F(000)	600	
Crystal color, morphology	colorless, Needle	
Crystal size	0.186 x 0.117 x 0.042 mm^3	
Theta range for data collection	3.358 to 74.506°	
Index ranges	$-13 \leq h \leq 13, -11 \leq k \leq 9, -17 \leq l \leq 17$	
Reflections collected	34115	
Independent reflections	5246 [*R*(int) = 0.0417]	
Observed reflections	5083	
Completeness to theta = 67.679°	100.0%	
Absorption correction	Multi-scan	
Max. and min. transmission	0.4709 and 0.3395	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5246 / 1 / 310	
Goodness-of-fit on F^2	1.042	
Final *R* indices [*I*>2sigma(*I*)]	*R*1 = 0.0289, *wR*2 = 0.0696	
R indices (all data)	*R*1 = 0.0305, *wR*2 = 0.0707	
Absolute structure parameter	-0.020(9)	

Largest diff. peak and hole	0.578 and -0.594 e.Å^{-3}

Table 12. Selected bond lengths for **199b**.

Bond	*d*/ Å	Bond	*d*/ Å
Pd1-C1	2.063(5)	P1-C24	1.843(5)
Pd1-N1	2.115(4)	C12-C13	1.379(6)
Pd1-P1	2.2250(12)	C12-C17	1.398(6)
Pd1-Cl1	2.3822(11)	C13-C14	1.388(7)
N1-C3	1.273(6)	C14-C15	1.380(7)
N1-O1	1.414(5)	C15-C16	1.388(7)
O1-C11	1.430(7)	C16-C17	1.383(7)
C1-C2	1.517(6)	C18-C19	1.392(7)
C2-C3	1.500(6)	C18-C23	1.408(7)
C2-C7	1.547(7)	C19-C20	1.397(8)
C2-C8	1.561(6)	C20-C21	1.384(8)
C3-C4	1.519(6)	C21-C22	1.383(8)
C4-C9	1.534(7)	C22-C23	1.385(8)
C4-C10	1.541(7)	C24-C25	1.379(8)
C4-C5	1.562(7)	C24-C29	1.383(7)
C5-C6	1.537(7)	C25-C26	1.389(7)
C5-C8	1.538(7)	C26-C27	1.383(9)
C6-C7	1.557(7)	C27-C28	1.372(10)
P1-C12	1.825(5)	C28-C29	1.392(8)
P1-C18	1.825(5)		

Table 13. Selected angles for **199b**.

Bond	angle/°	Bond	angle/°
C1-Pd1-N1	79.25(17)	O1-N1-Pd1	130.9(3)
C1-Pd1-P1	90.25(13)	N1-O1-C11	108.9(4)
N1-Pd1-P1	167.59(11)	C2-C1-Pd1	105.5(3)
C1-Pd1-Cl1	174.23(13)	C3-C2-C1	110.7(4)
N1-Pd1-Cl1	95.05(11)	C3-C2-C7	106.3(4)
P1-Pd1-Cl1	95.31(4)	C1-C2-C7	117.6(4)
C3-N1-O1	114.9(4)	C3-C2-C8	98.5(4)
C3-N1-Pd1	112.9(3)	C1-C2-C8	121.0(4)

C7-C2-C8	100.3(4)	C13-C12-P1	119.7(3)
N1-C3-C2	117.3(4)	C17-C12-P1	121.0(3)
N1-C3-C4	132.1(4)	C12-C13-C14	120.4(4)
C2-C3-C4	110.6(4)	C15-C14-C13	120.2(5)
C3-C4-C9	112.1(4)	C14-C15-C16	119.8(5)
C3-C4-C10	111.3(4)	C17-C16-C15	120.1(4)
C9-C4-C10	109.3(4)	C16-C17-C12	120.2(4)
C3-C4-C5	98.3(4)	C19-C18-C23	119.2(5)
C9-C4-C5	114.3(4)	C19-C18-P1	123.5(4)
C10-C4-C5	111.2(4)	C23-C18-P1	117.3(4)
C6-C5-C8	100.8(4)	C18-C19-C20	120.0(5)
C6-C5-C4	110.6(4)	C21-C20-C19	120.2(5)
C8-C5-C4	102.8(4)	C22-C21-C20	120.1(5)
C5-C6-C7	102.9(4)	C21-C22-C23	120.3(5)
C2-C7-C6	104.0(4)	C22-C23-C18	120.1(5)
C5-C8-C2	94.5(4)	C25-C24-C29	119.3(5)
C12-P1-C18	105.7(2)	C25-C24-P1	118.7(4)
C12-P1-C24	102.1(2)	C29-C24-P1	121.9(4)
C18-P1-C24	105.6(2)	C24-C25-C26	120.6(5)
C12-P1-Pd1	116.17(15)	C27-C26-C25	119.8(5)
C18-P1-Pd1	110.21(16)	C28-C27-C26	119.7(4)
C24-P1-Pd1	116.07(16)	C27-C28-C29	120.5(5)
C13-C12-C17	119.3(4)	C24-C29-C28	120.0(5)

APPENDIX E

SELECTED SPECTRA

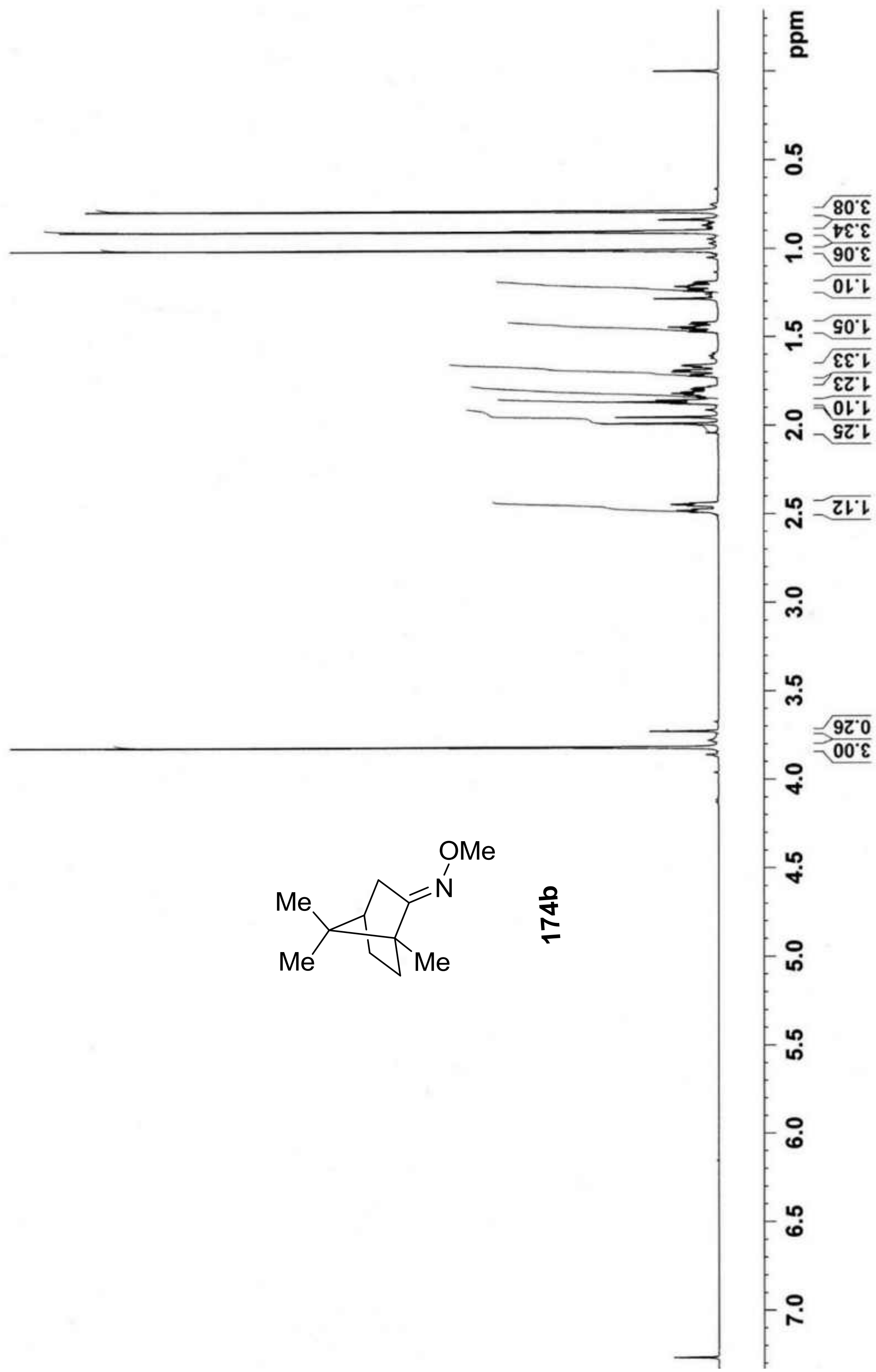

Figure 10. ^{1}H NMR spectrum of **174b**.

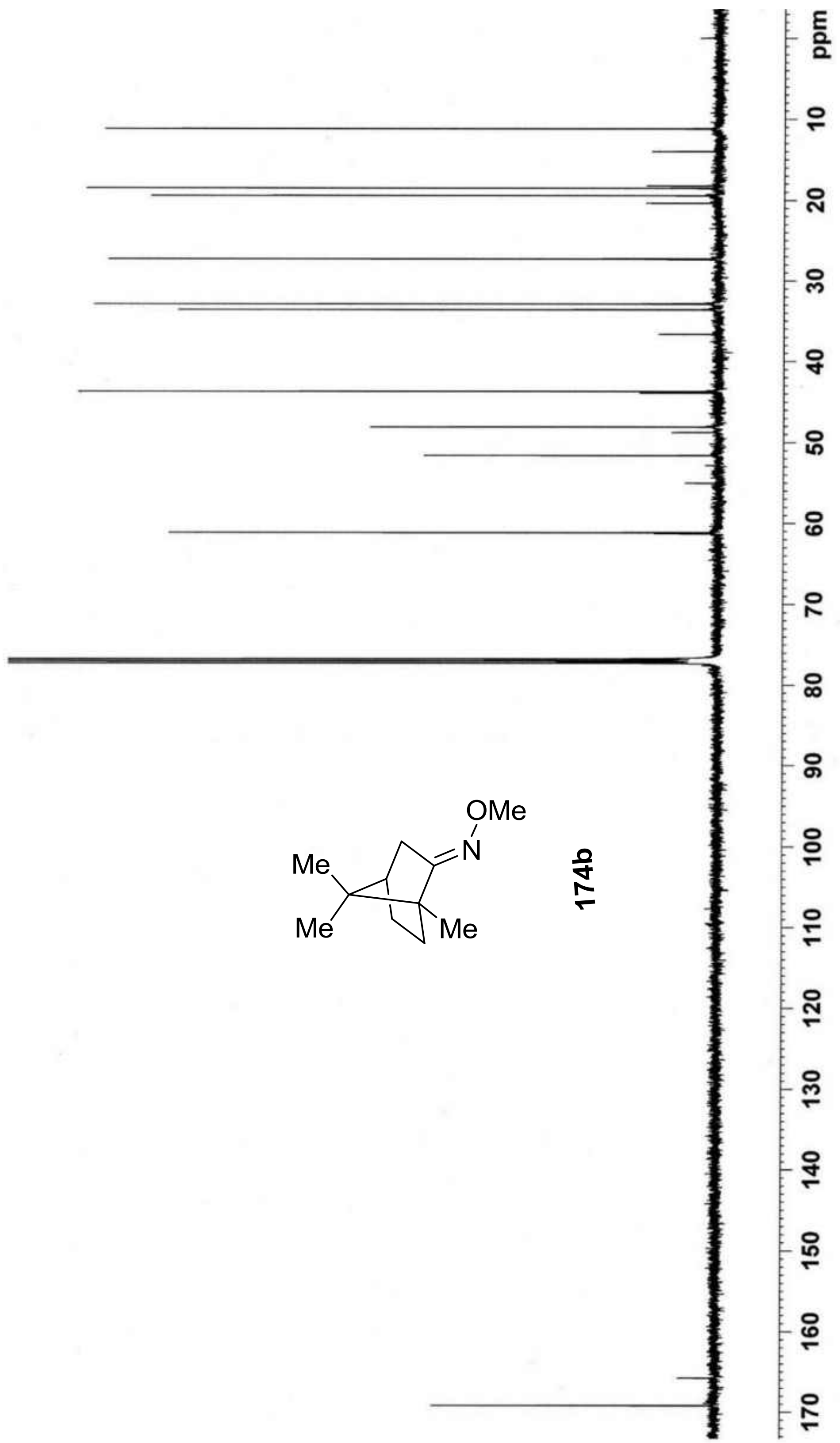

Figure 11. $^{13}C\{^{1}H\}$ NMR spectrum of **174b**.

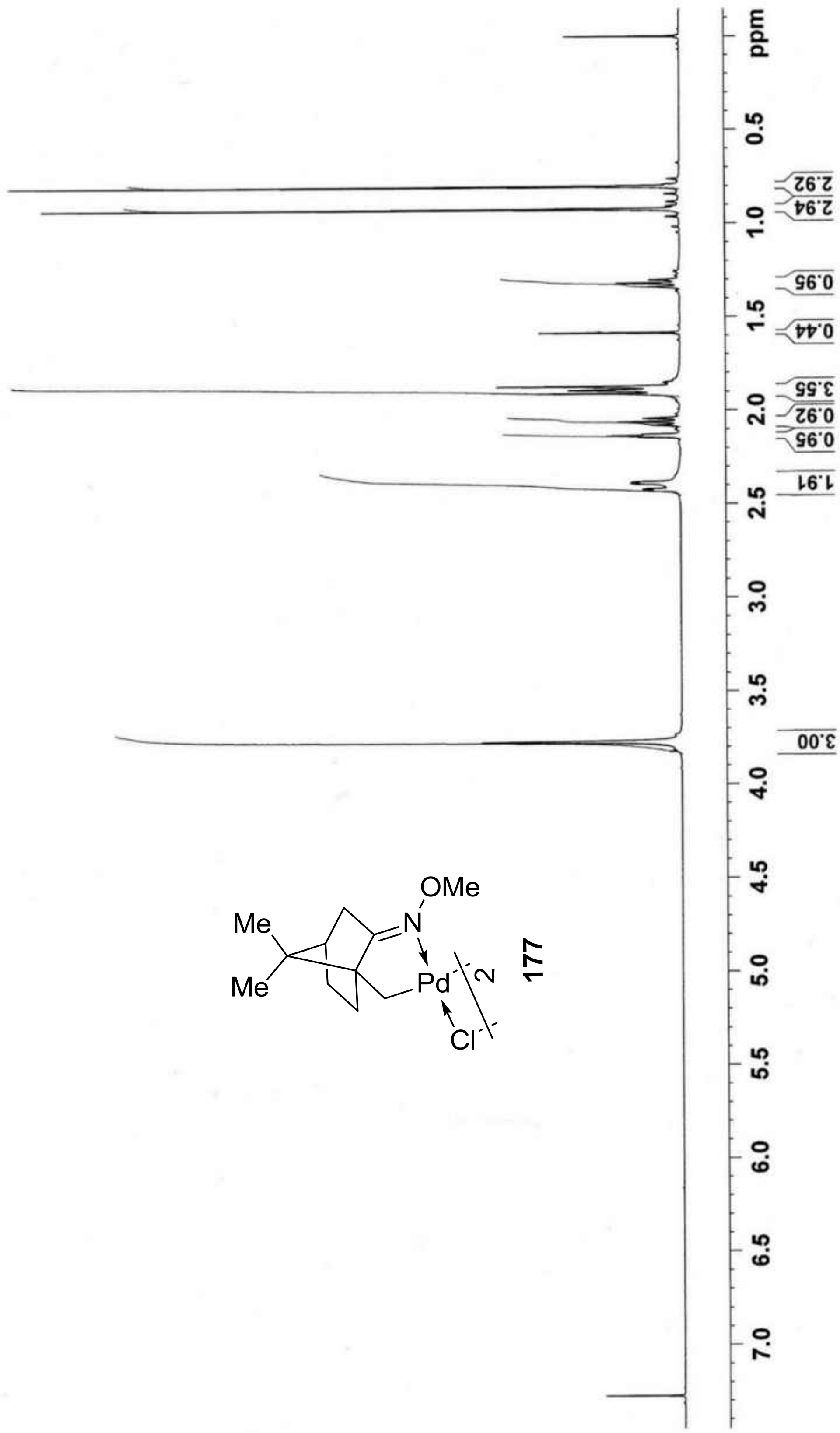

Figure 12. ^{1}H NMR spectrum of **177**.

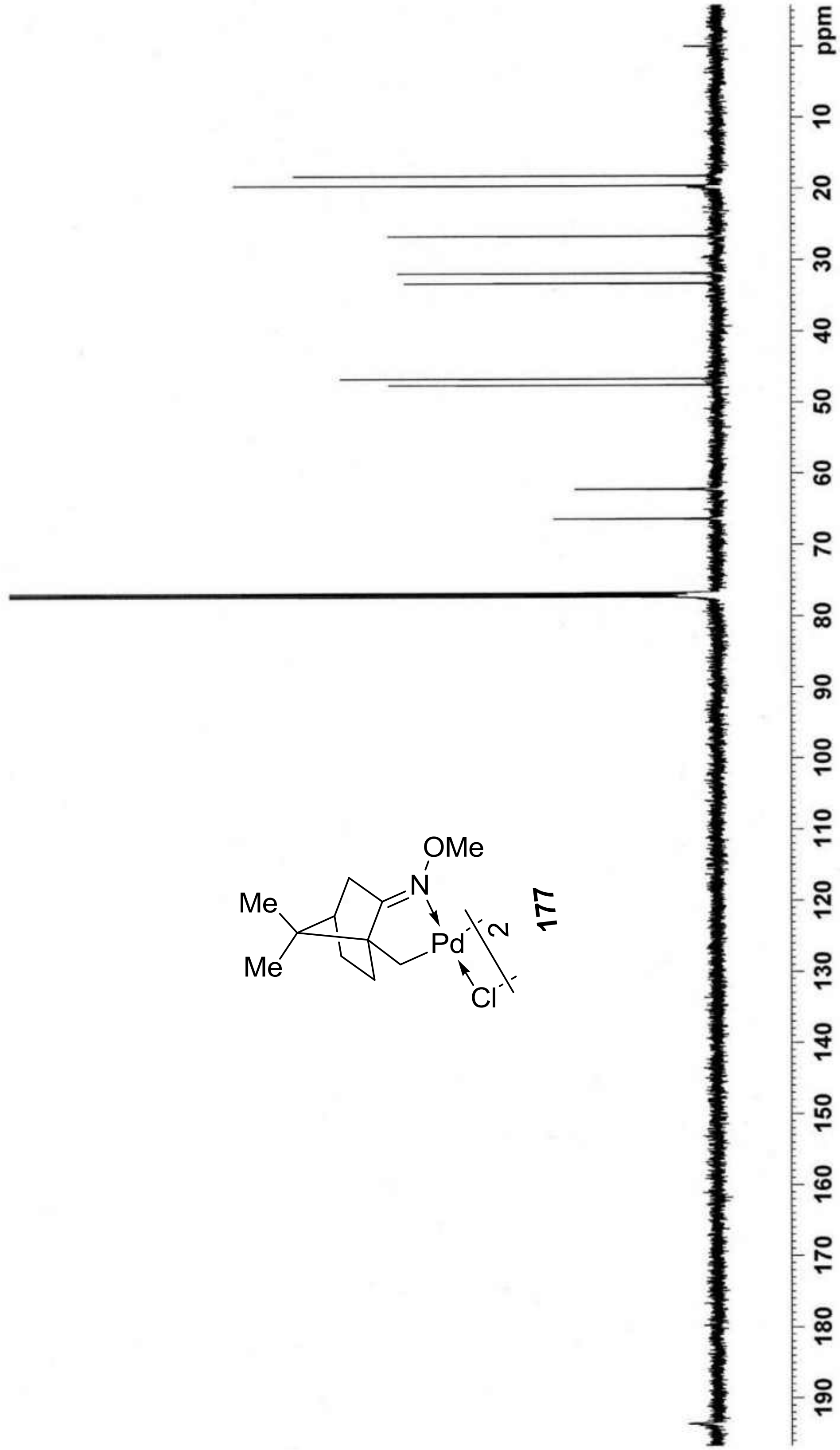

Figure 13. $^{13}C\{^{1}H\}$ NMR spectrum of **177**.

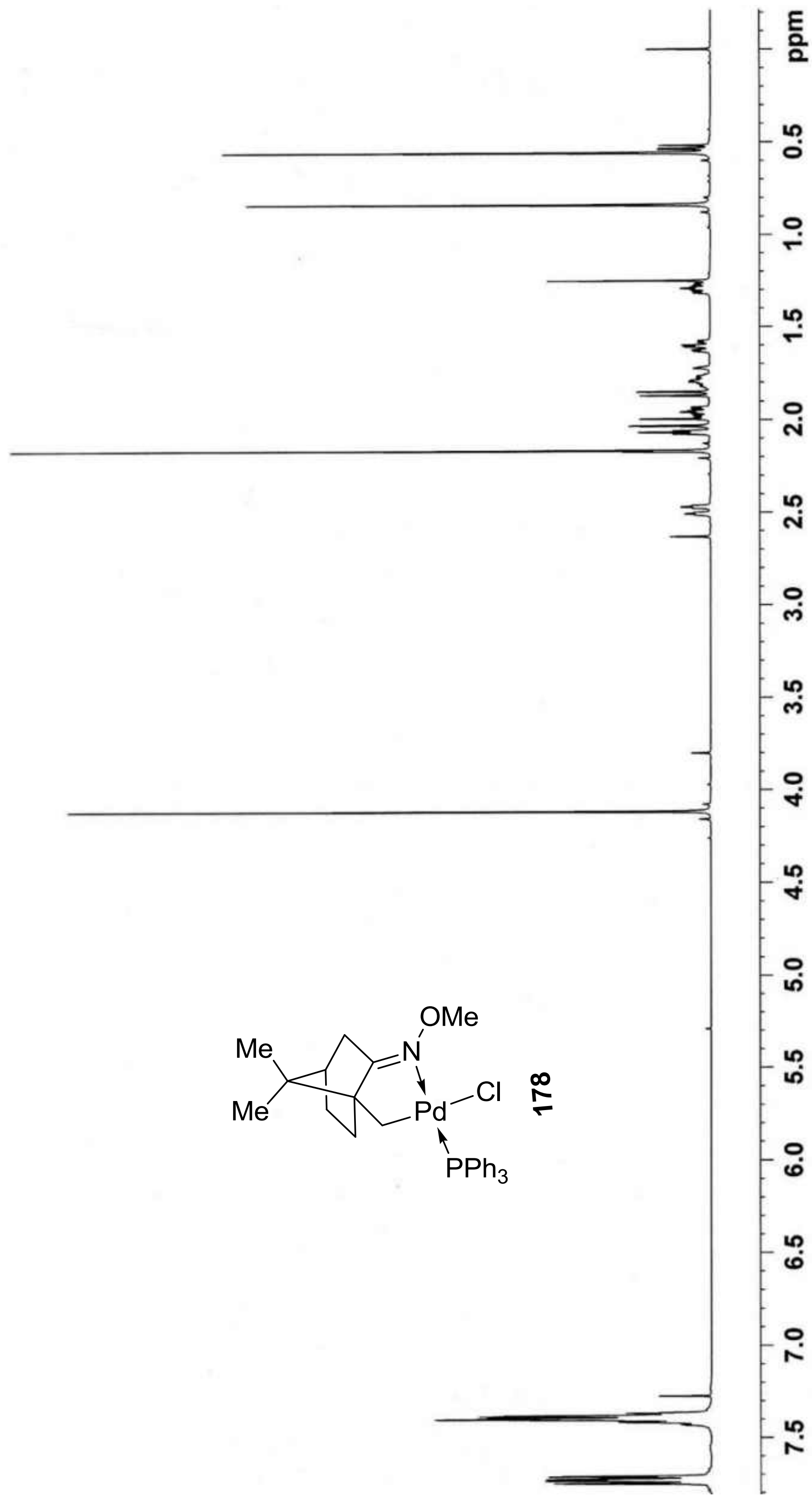

Figure 14. ^{1}H NMR spectrum of **178**.

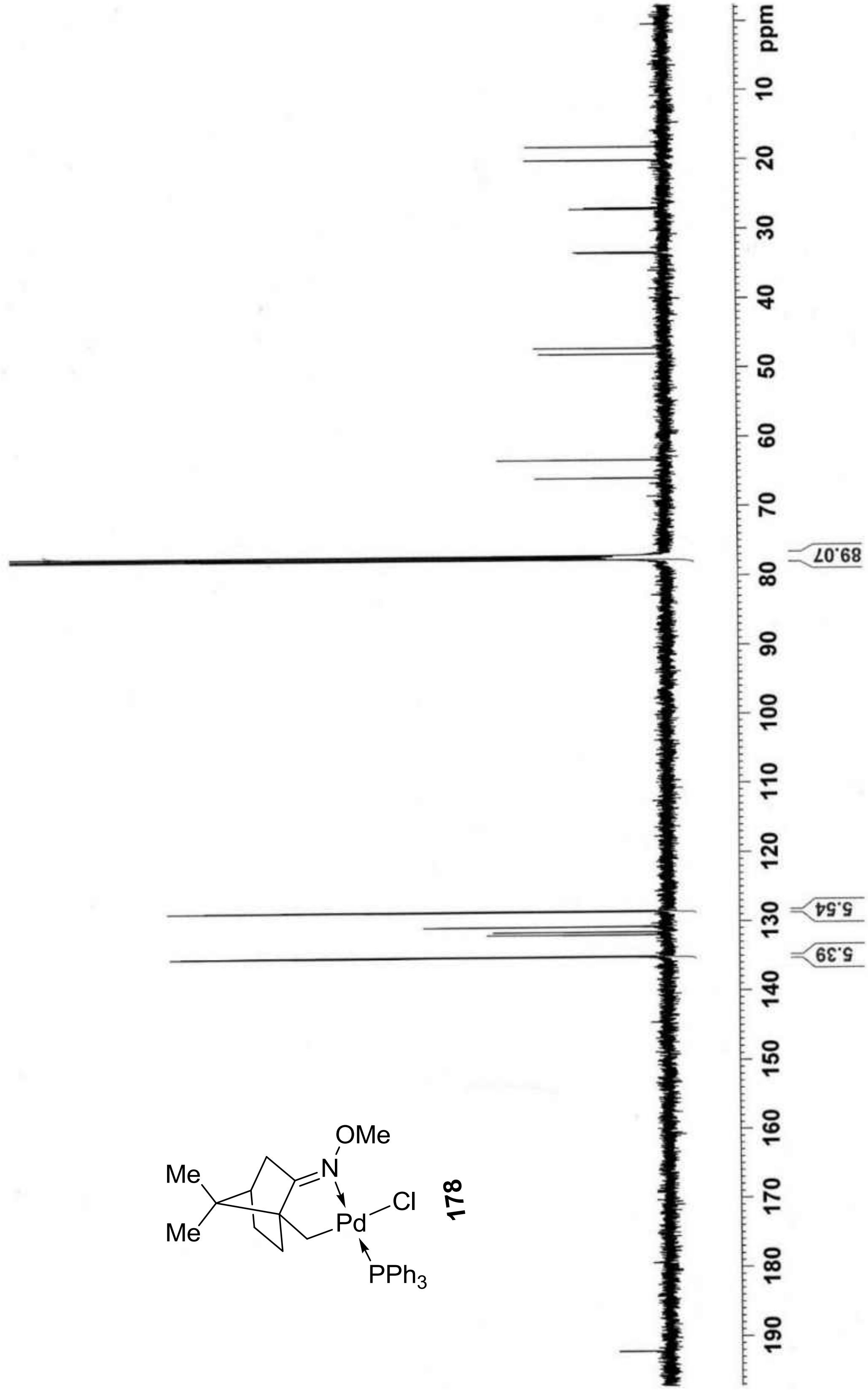

Figure 15. $^{13}C\{^1H\}$ NMR spectrum of **178**.

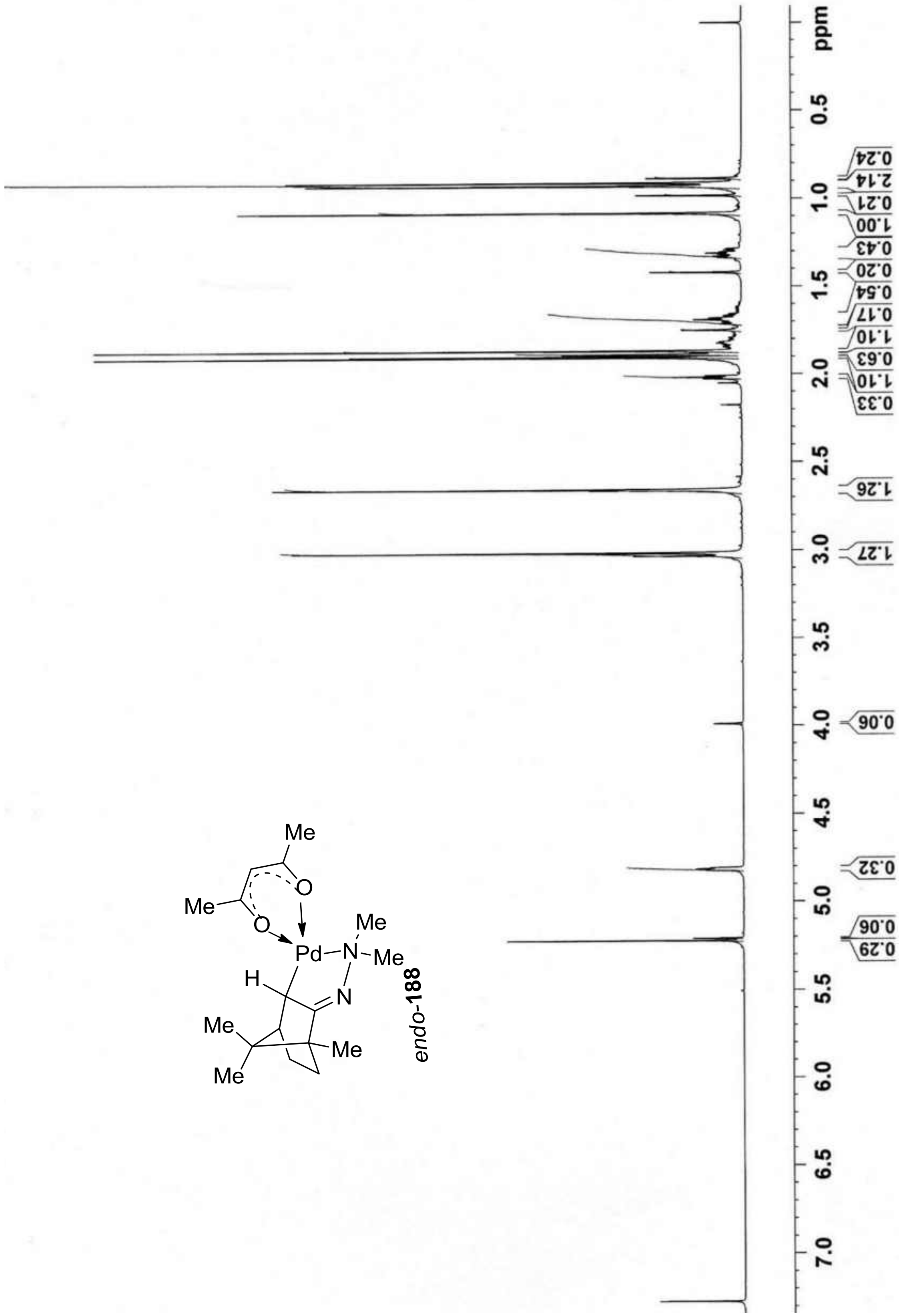

Figure 16. [1]H NMR spectrum of *endo*-**188**.

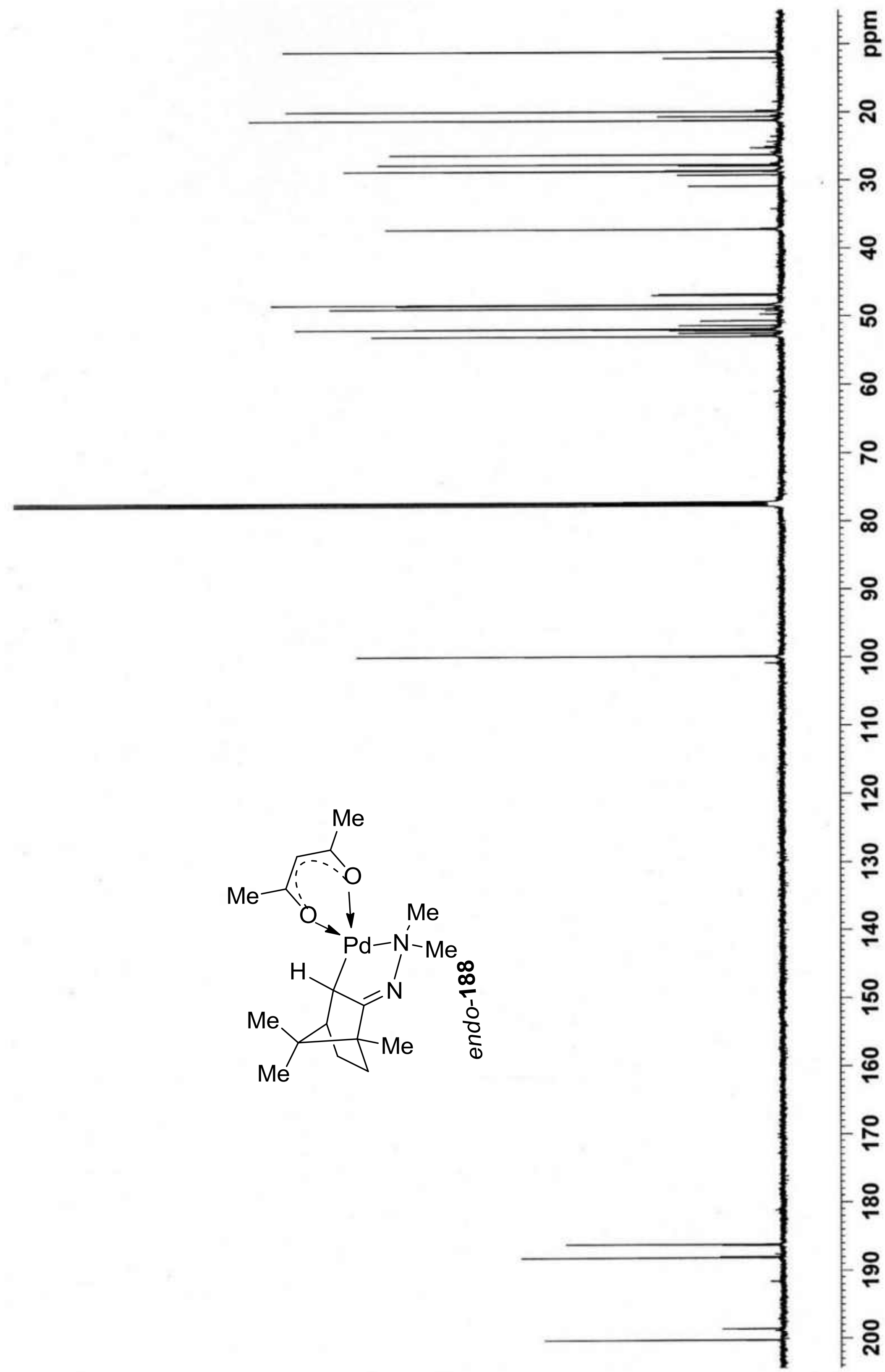

Figure 17. $^{13}C\{^{1}H\}$ NMR spectrum of *endo*-**188**.

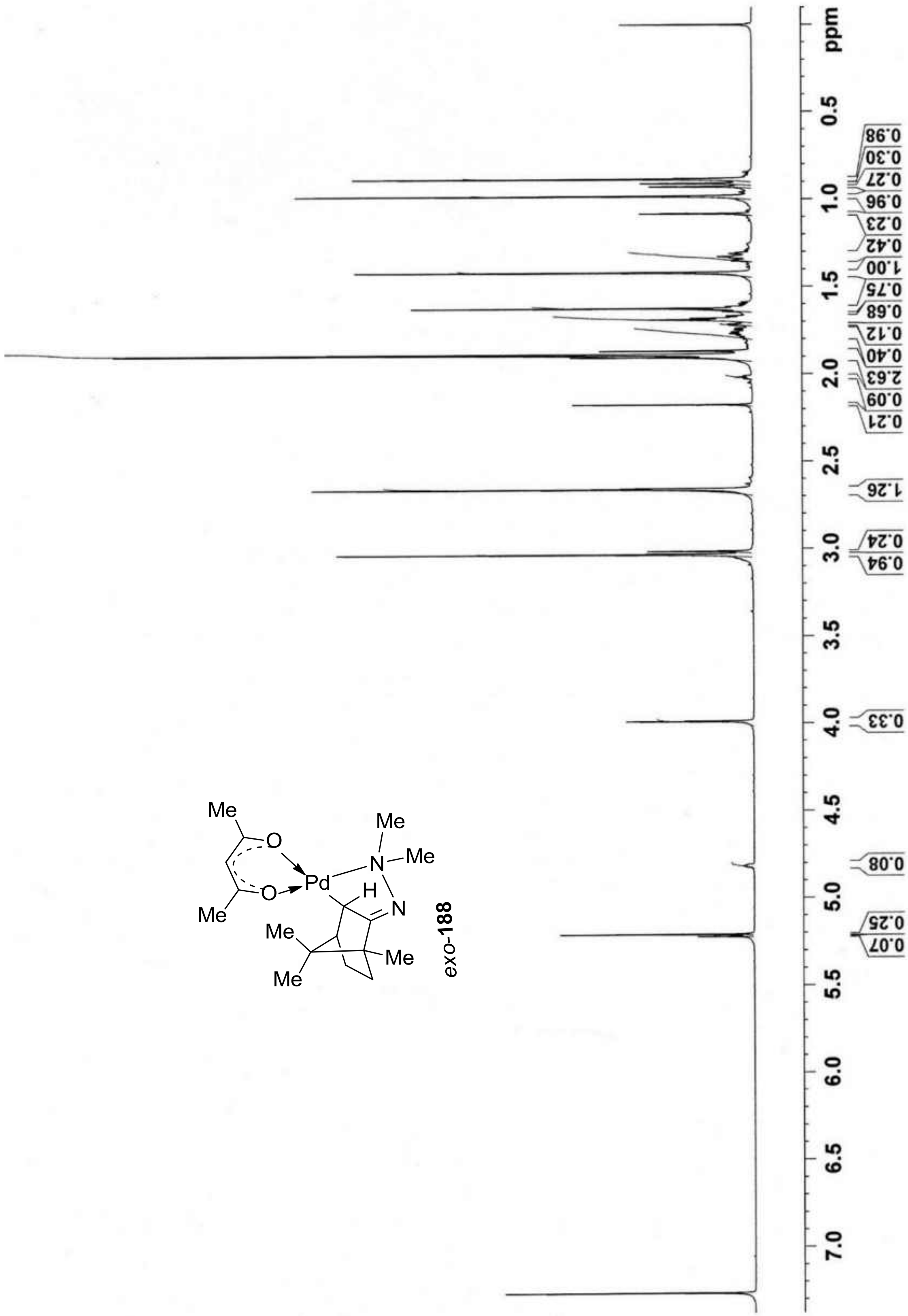

Figure 18. ^{1}H NMR spectrum of *exo*-**188**.

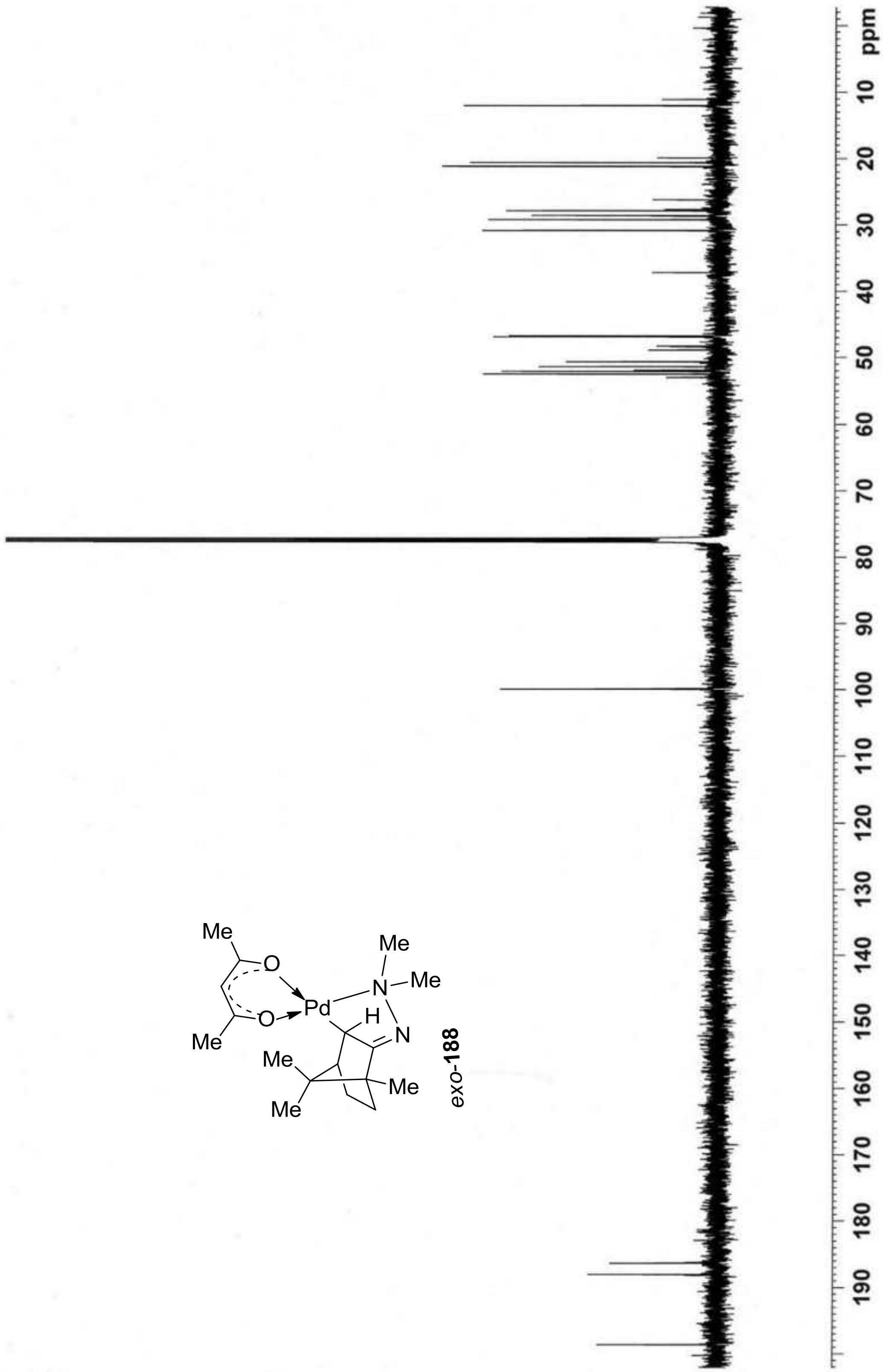

Figure 19. $^{13}C\{^{1}H\}$ NMR spectrum of *exo*-**188**.

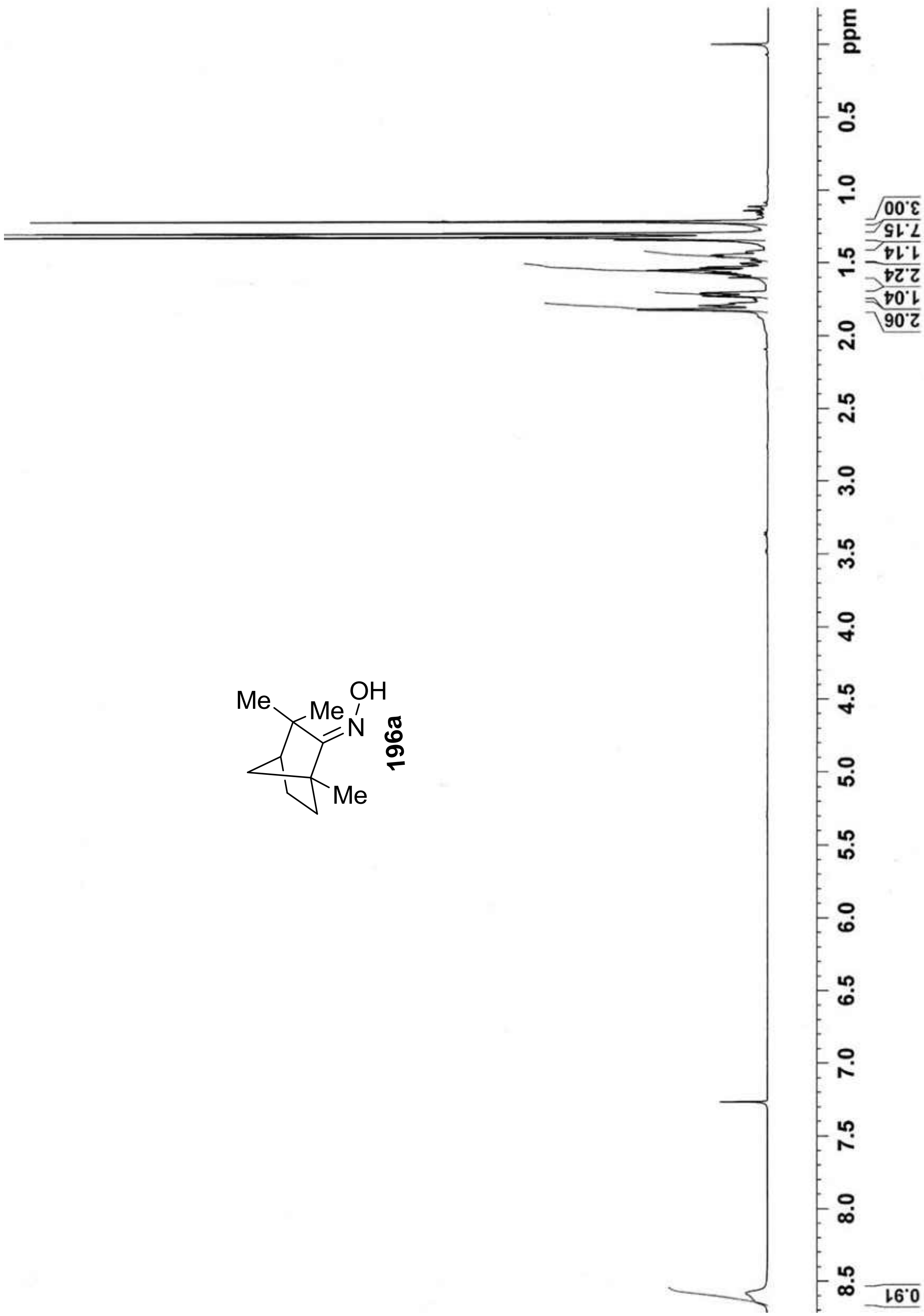

Figure 20. ^{1}H NMR spectrum of **196a**.

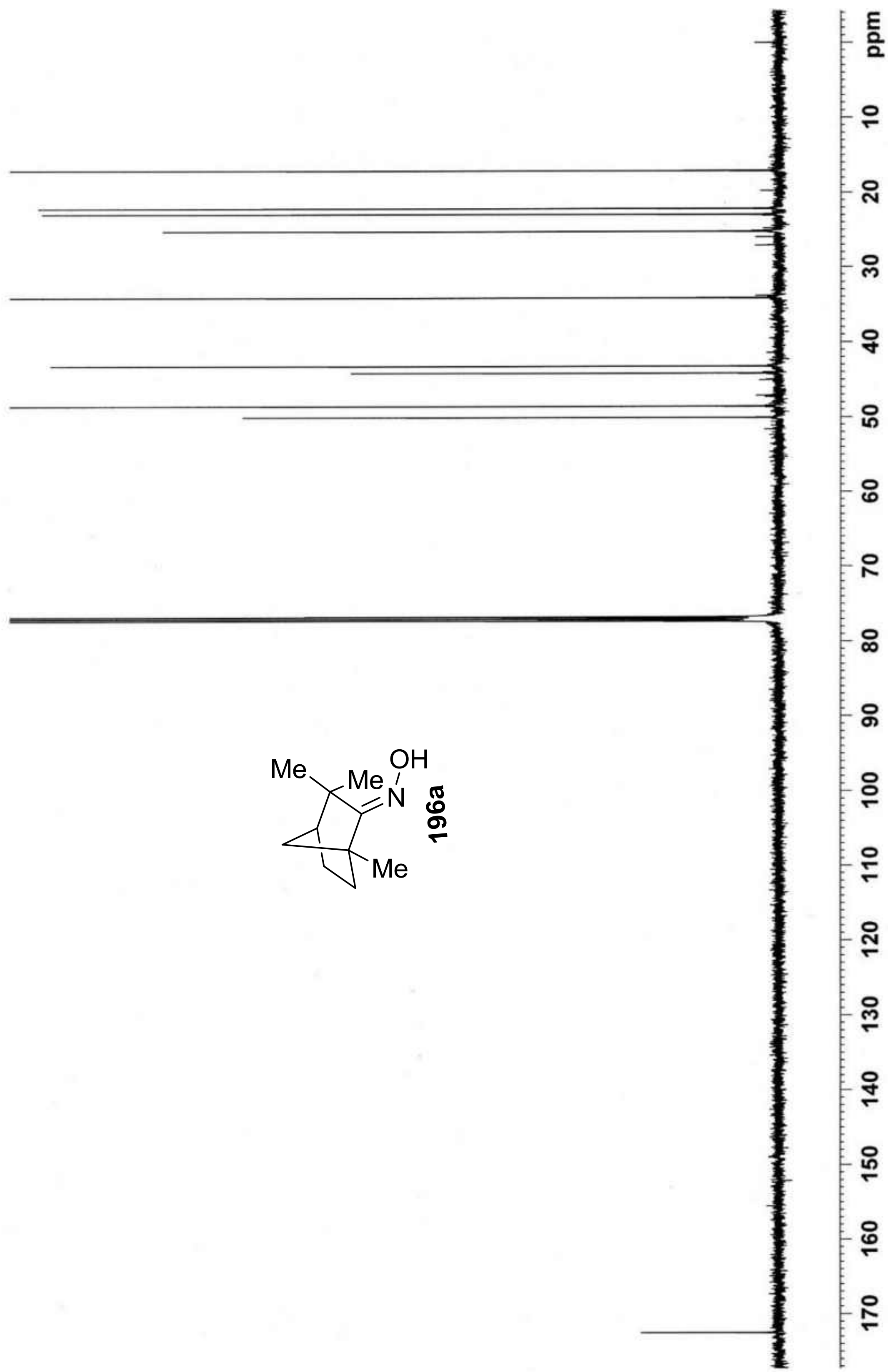

Figure 21. $^{13}C\{^{1}H\}$ NMR spectrum of **196a**.

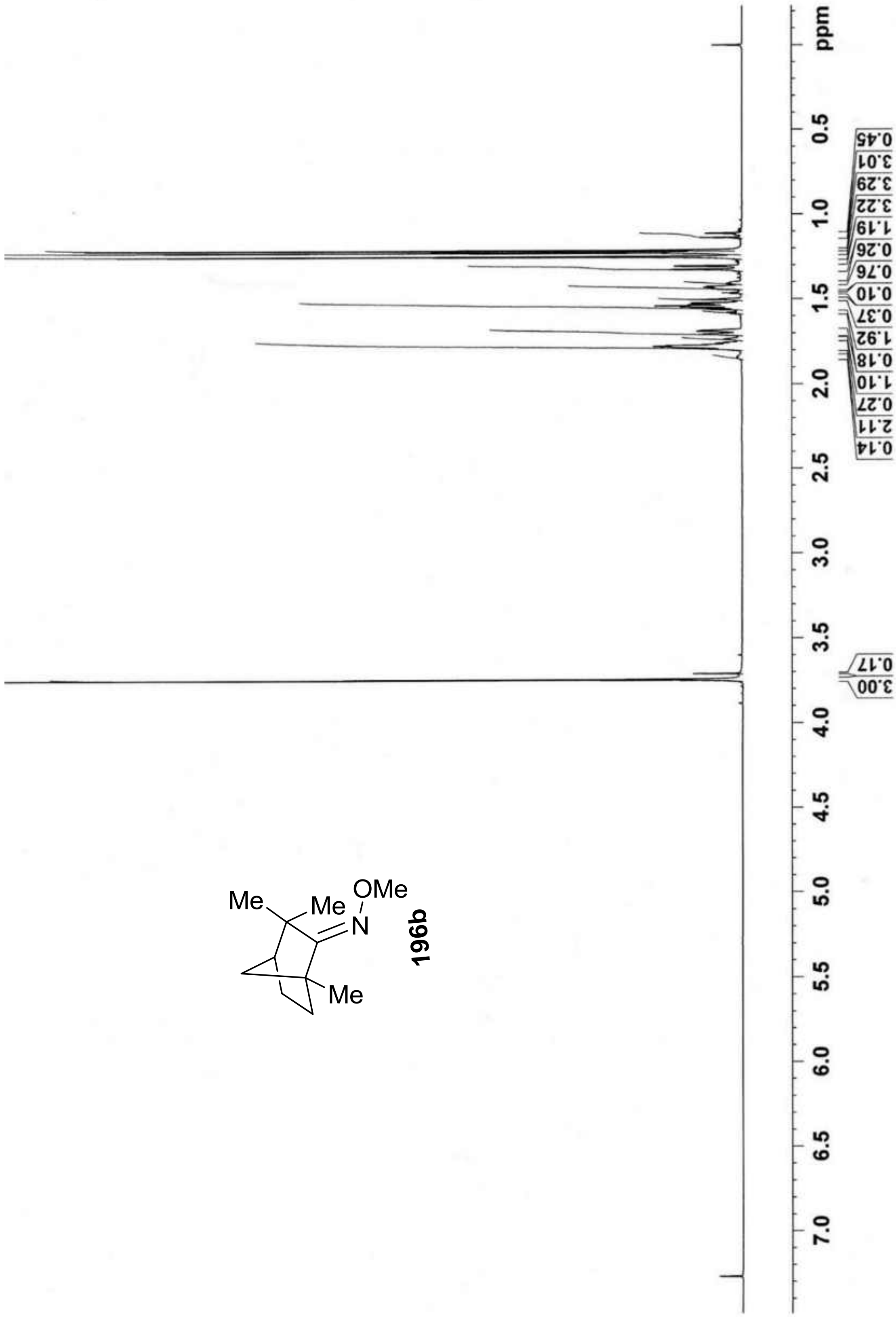

Figure 22. ^{1}H NMR spectrum of **196b**.

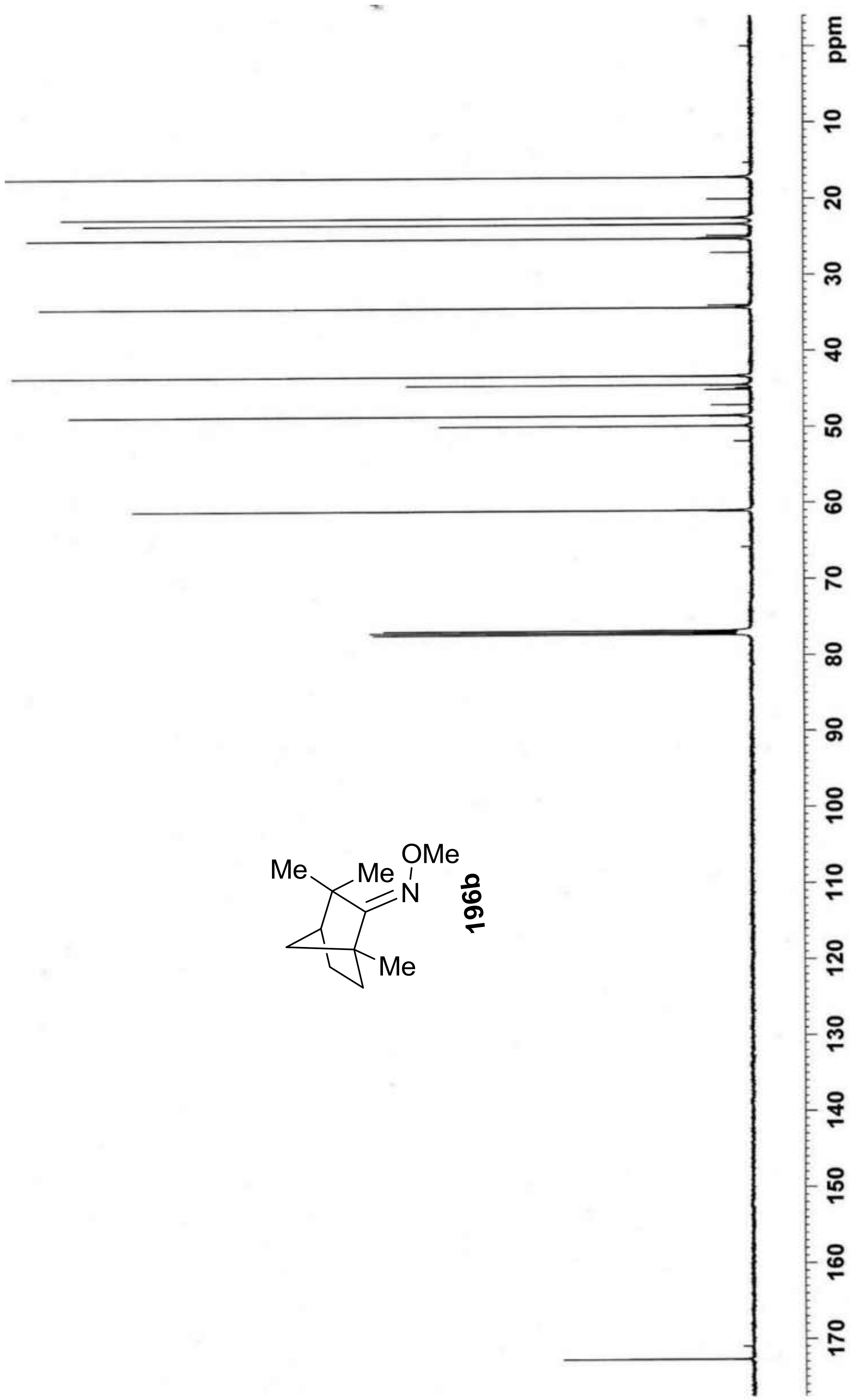

Figure 23. $^{13}C\{^{1}H\}$ NMR spectrum of **196b**.

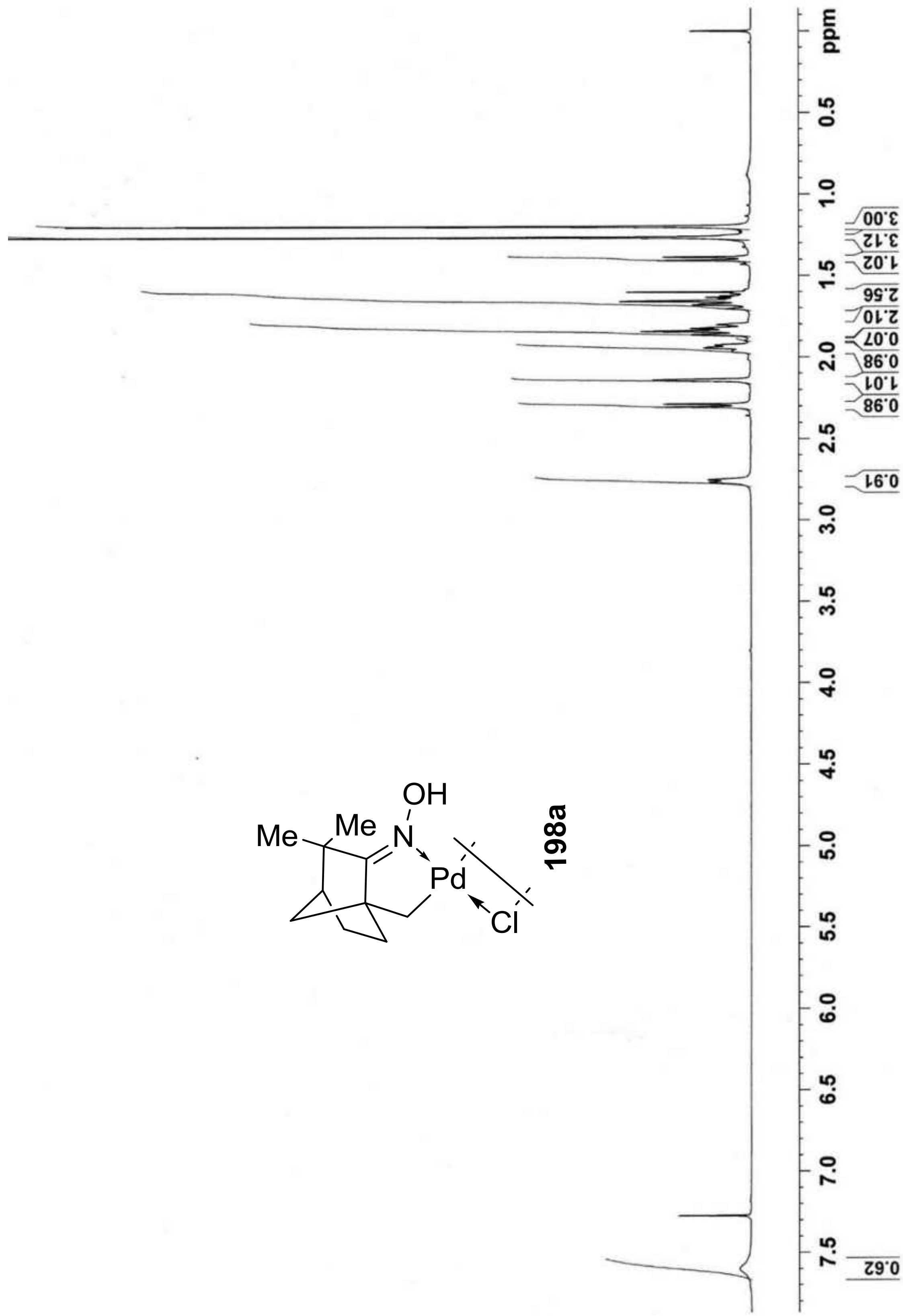

Figure 24. ^{1}H NMR spectrum of **198a**.

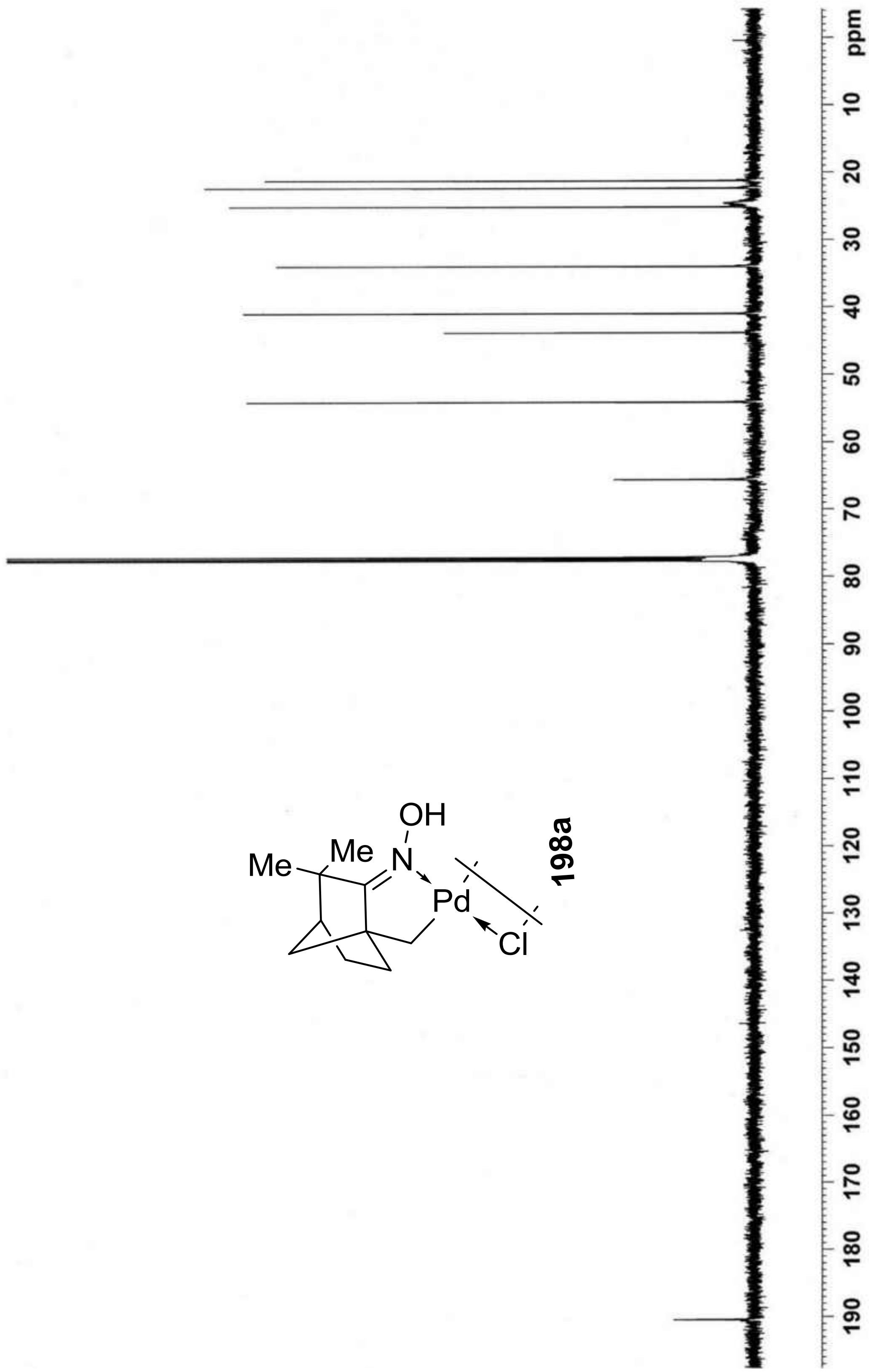

Figure 25. $^{13}C\{^{1}H\}$ NMR spectrum of **198a**.

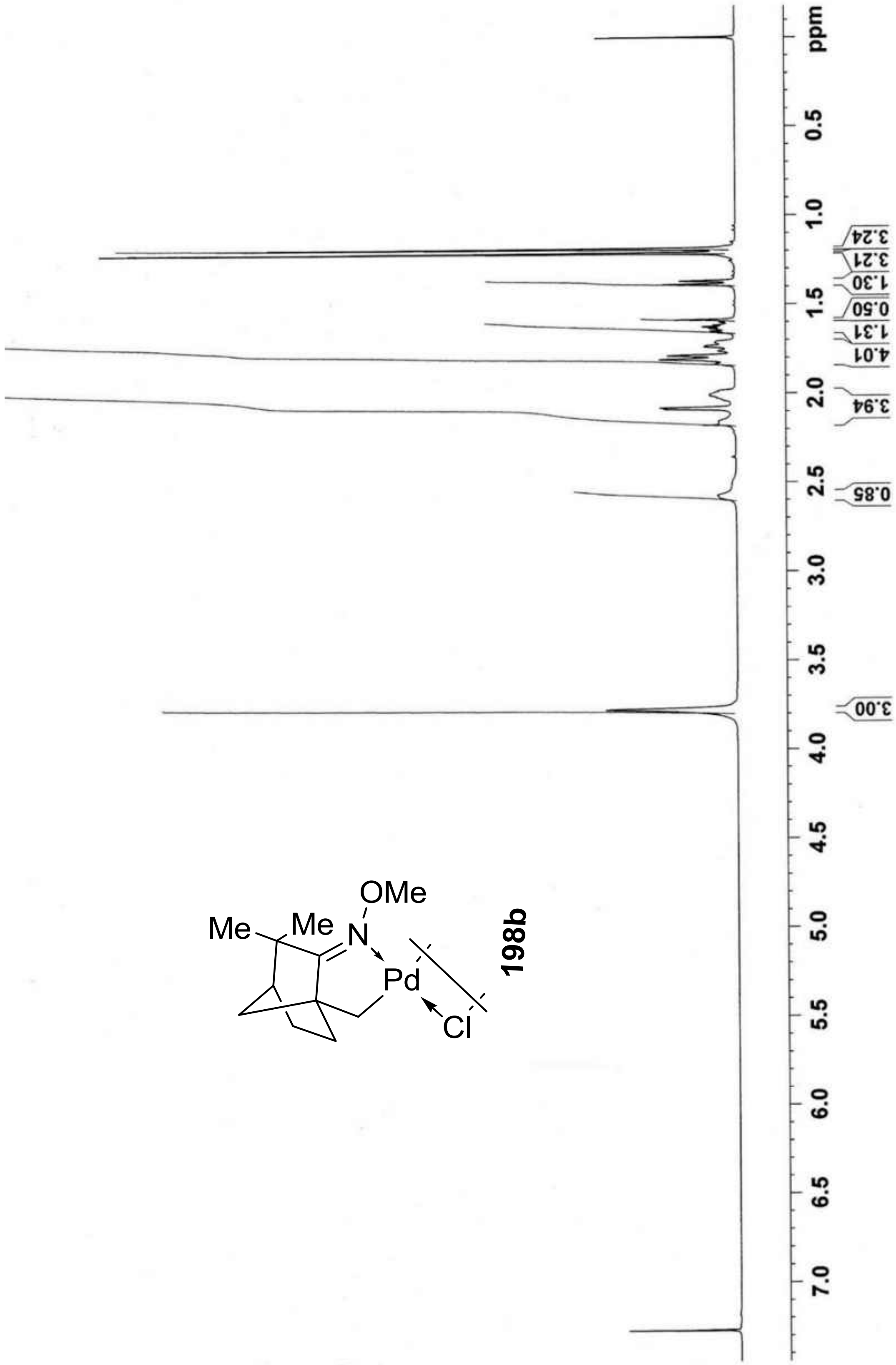

Figure 26. [1]H NMR spectrum of **198b**.

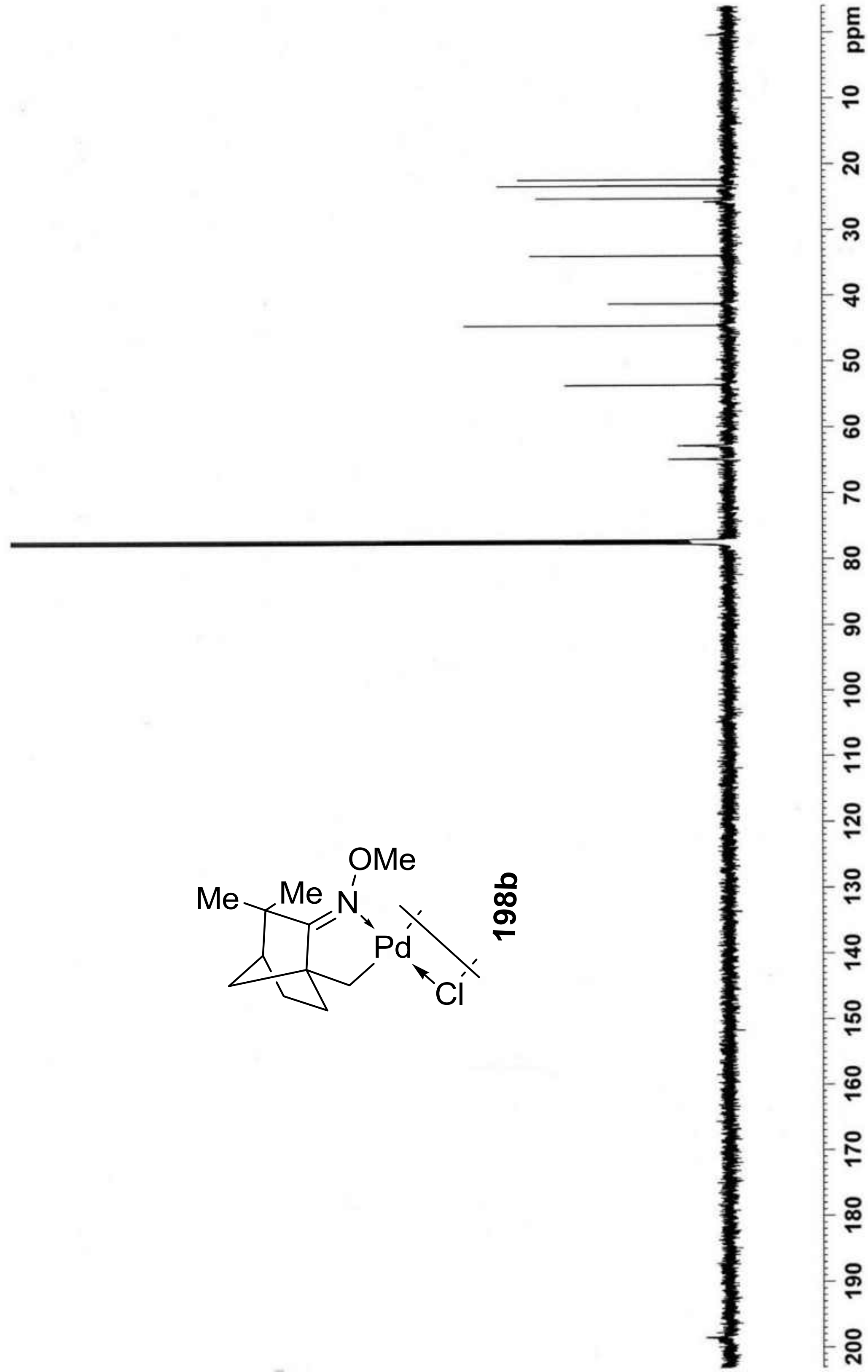

Figure 27. $^{13}C\{^{1}H\}$ NMR spectrum of **198b**.

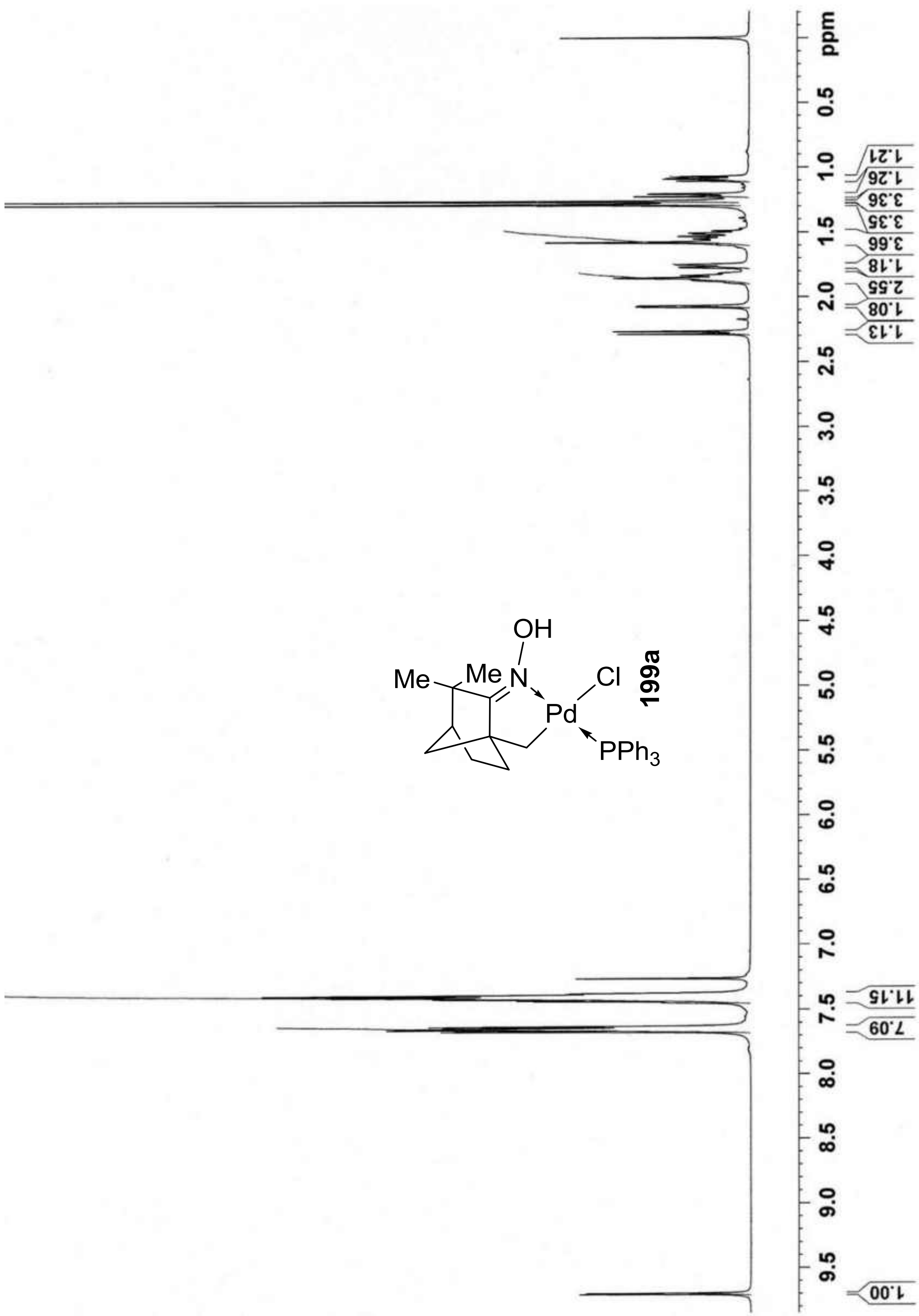

Figure 28. ^{1}H NMR spectrum of **199a**.

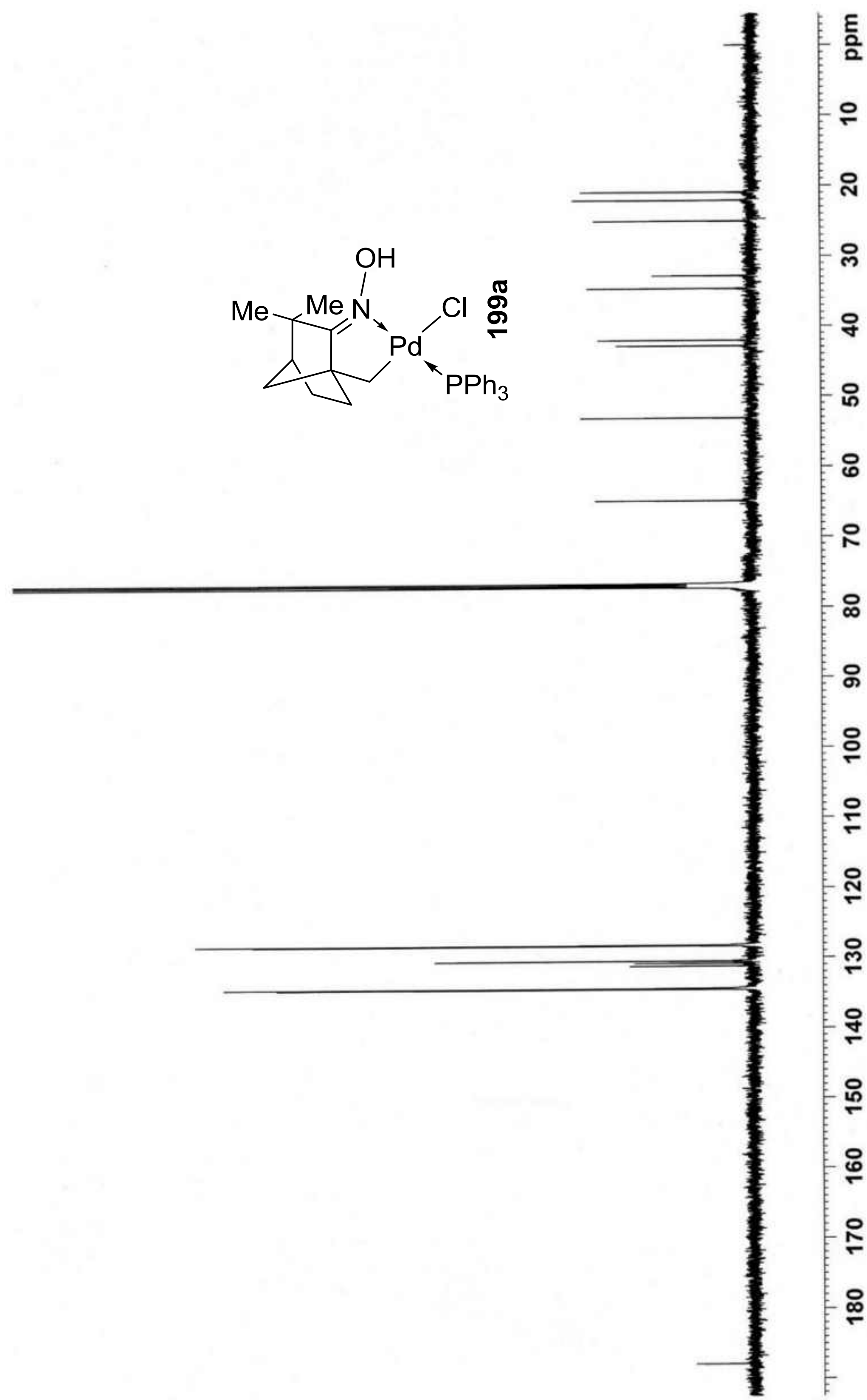

Figure 29. $^{13}C\{^{1}H\}$ NMR spectrum of **199a**.

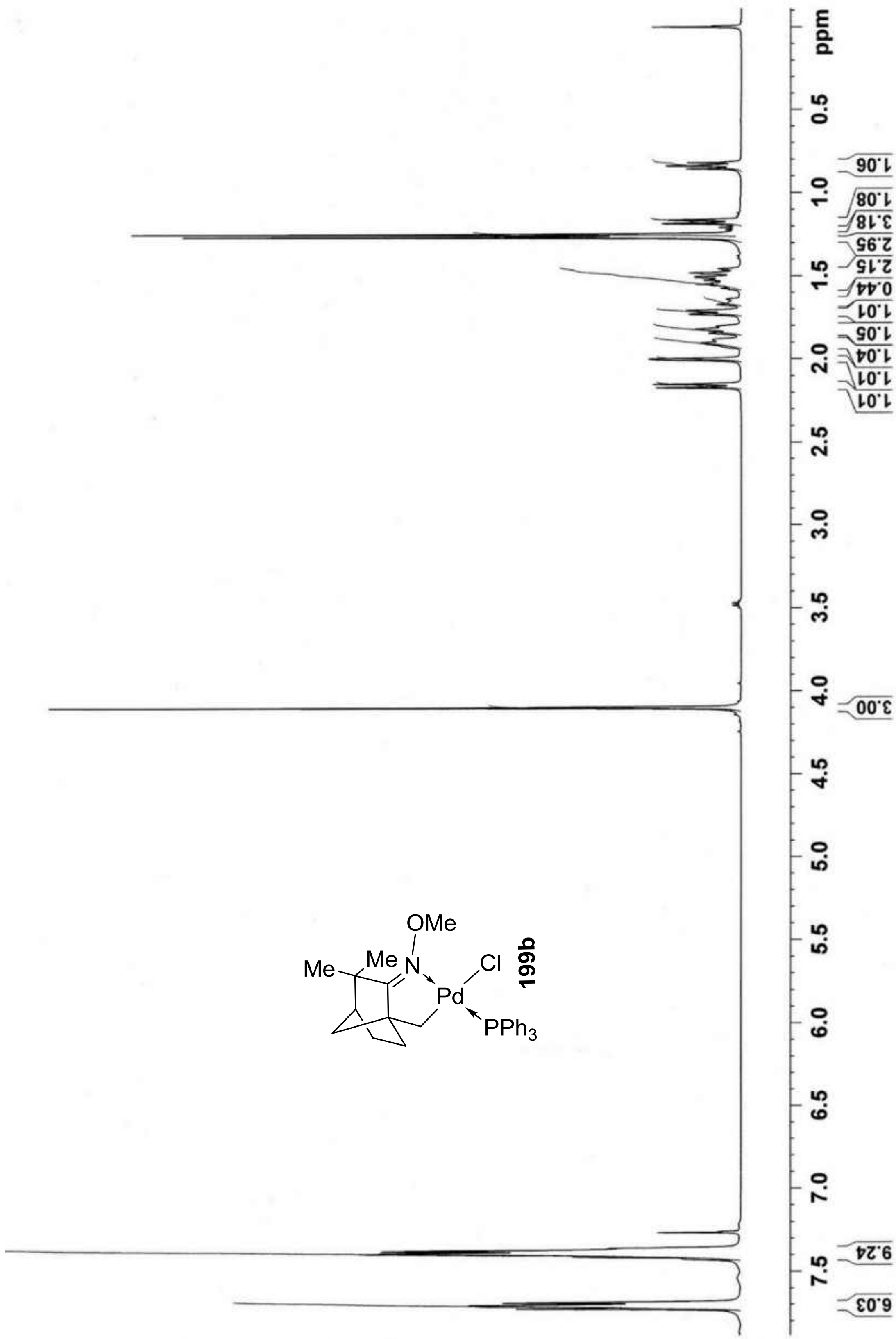

Figure 30. ^{1}H NMR spectrum of **199b**.

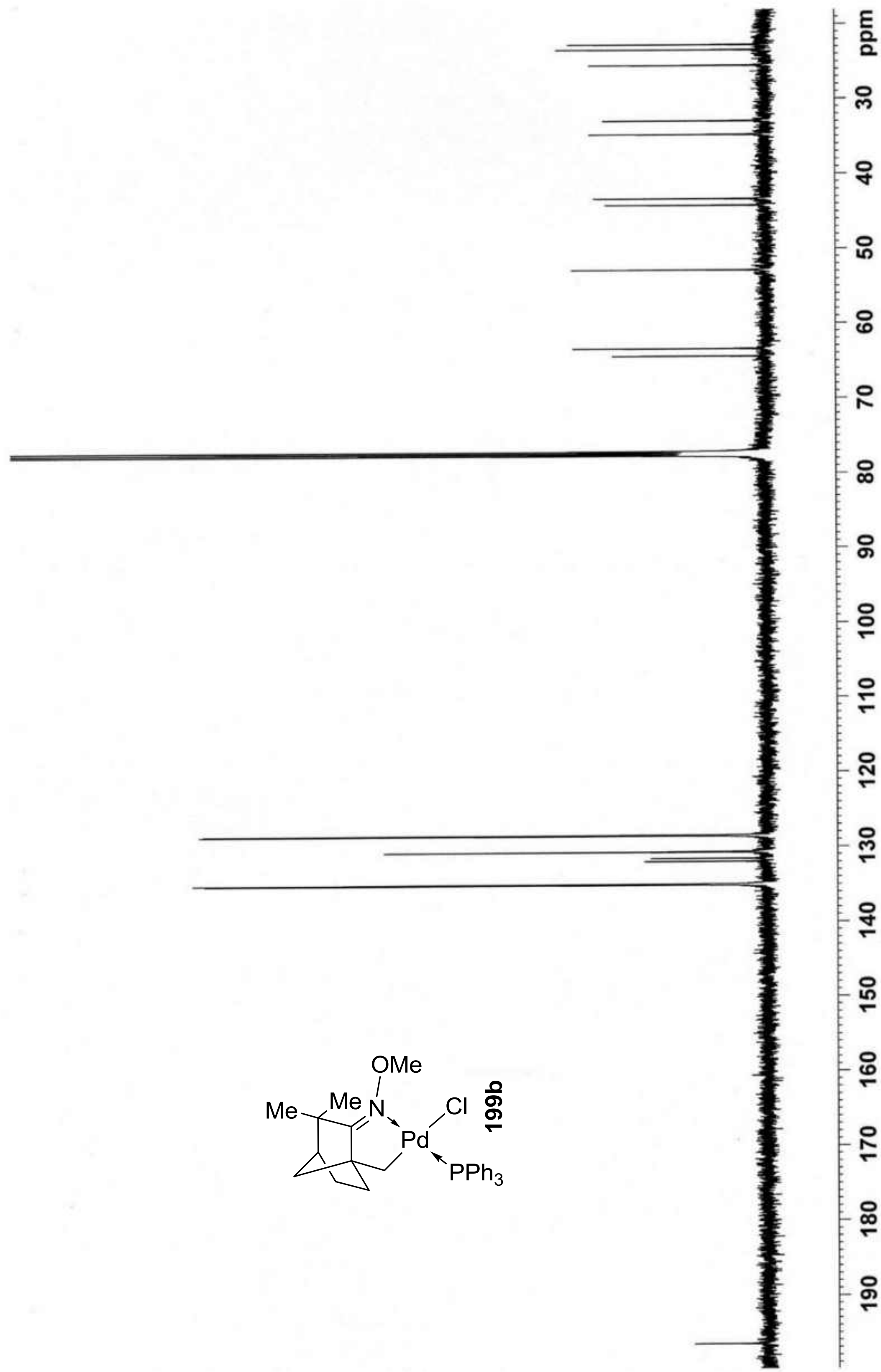

Figure 31. $^{13}C\{^{1}H\}$ NMR spectrum of **199b**.

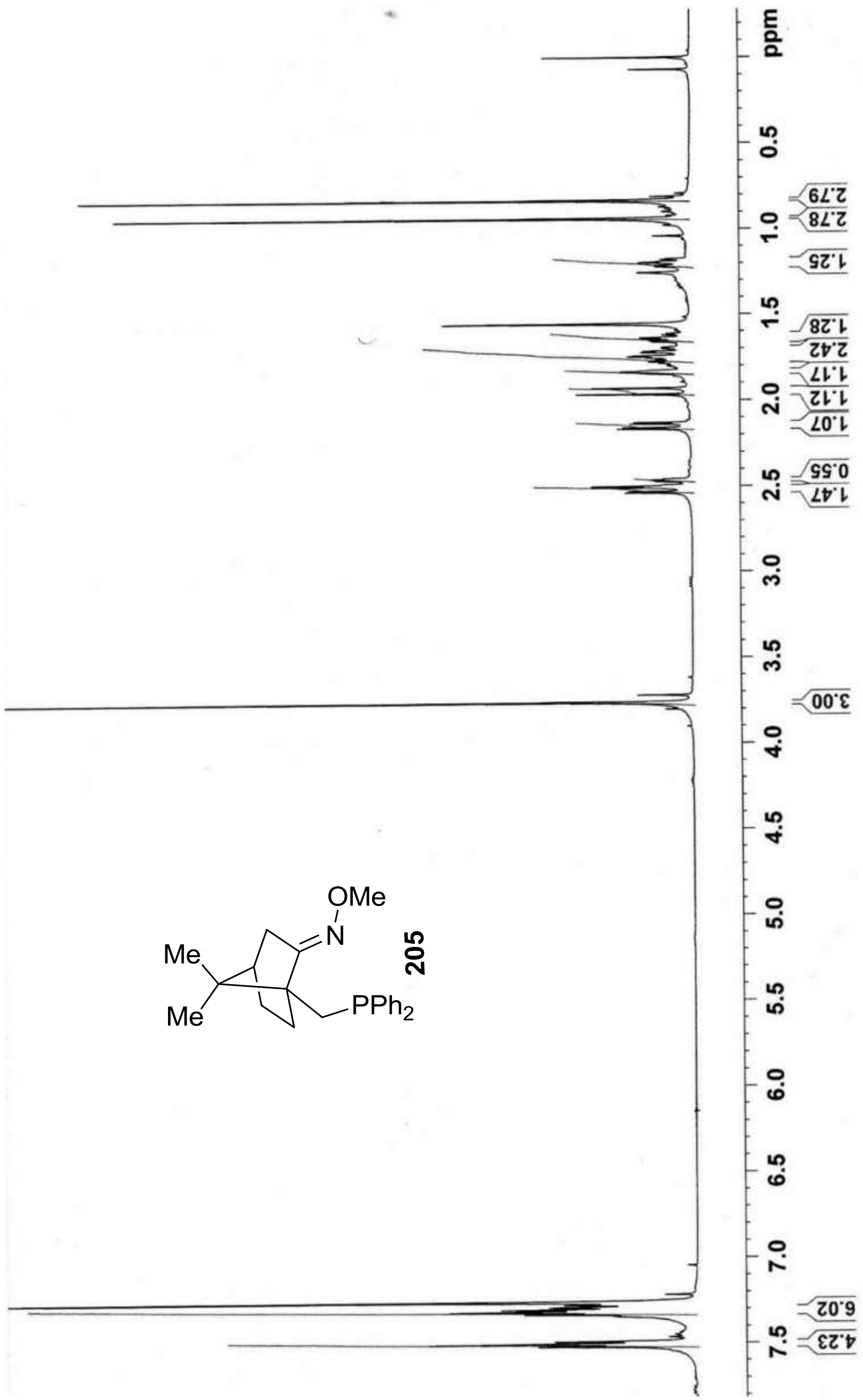

Figure 32. [1]H NMR spectrum of **205**.

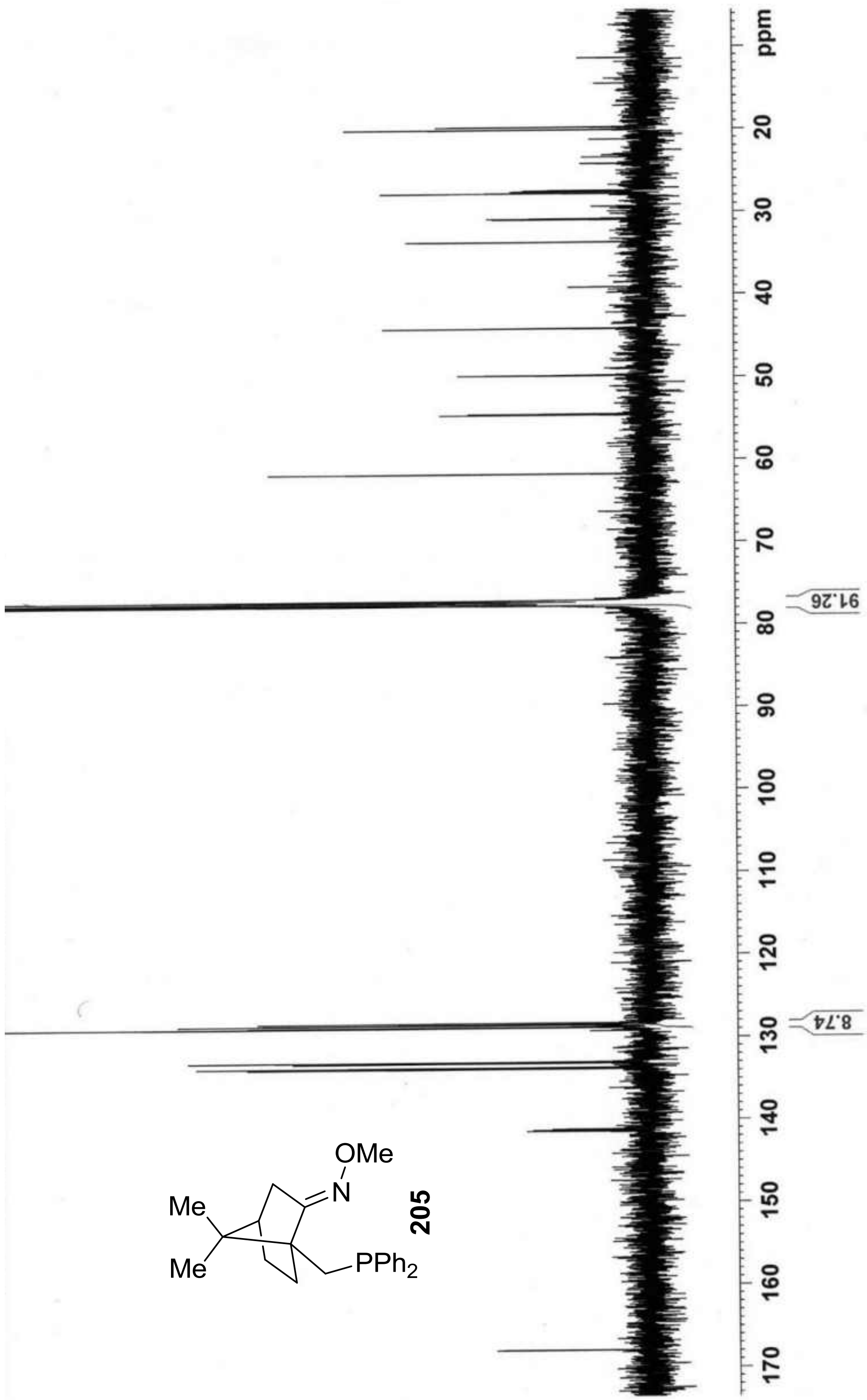

Figure 33. $^{13}C\{^{1}H\}$ NMR spectrum of **205**.

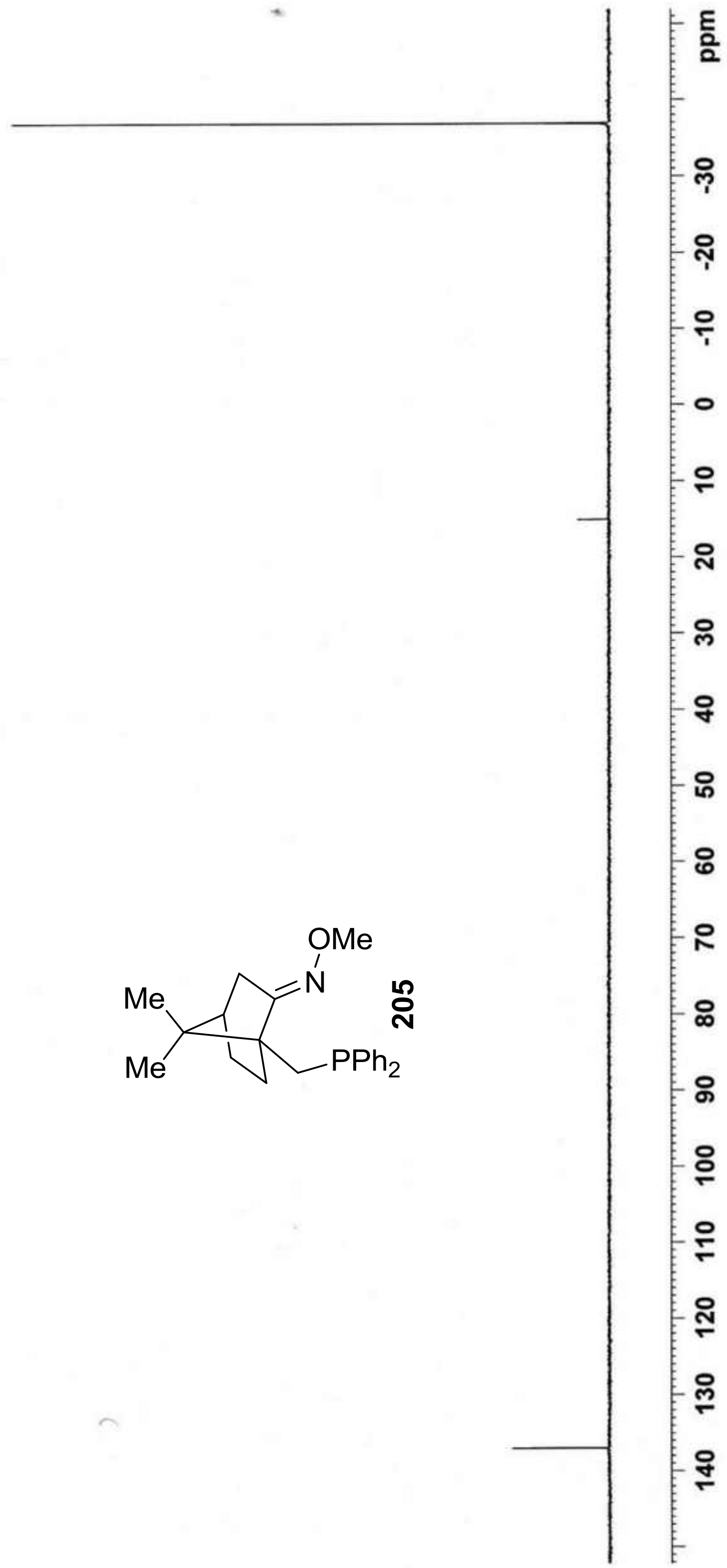

Figure 34. $^{31}P\{^{1}H\}$ NMR spectrum of **205**.

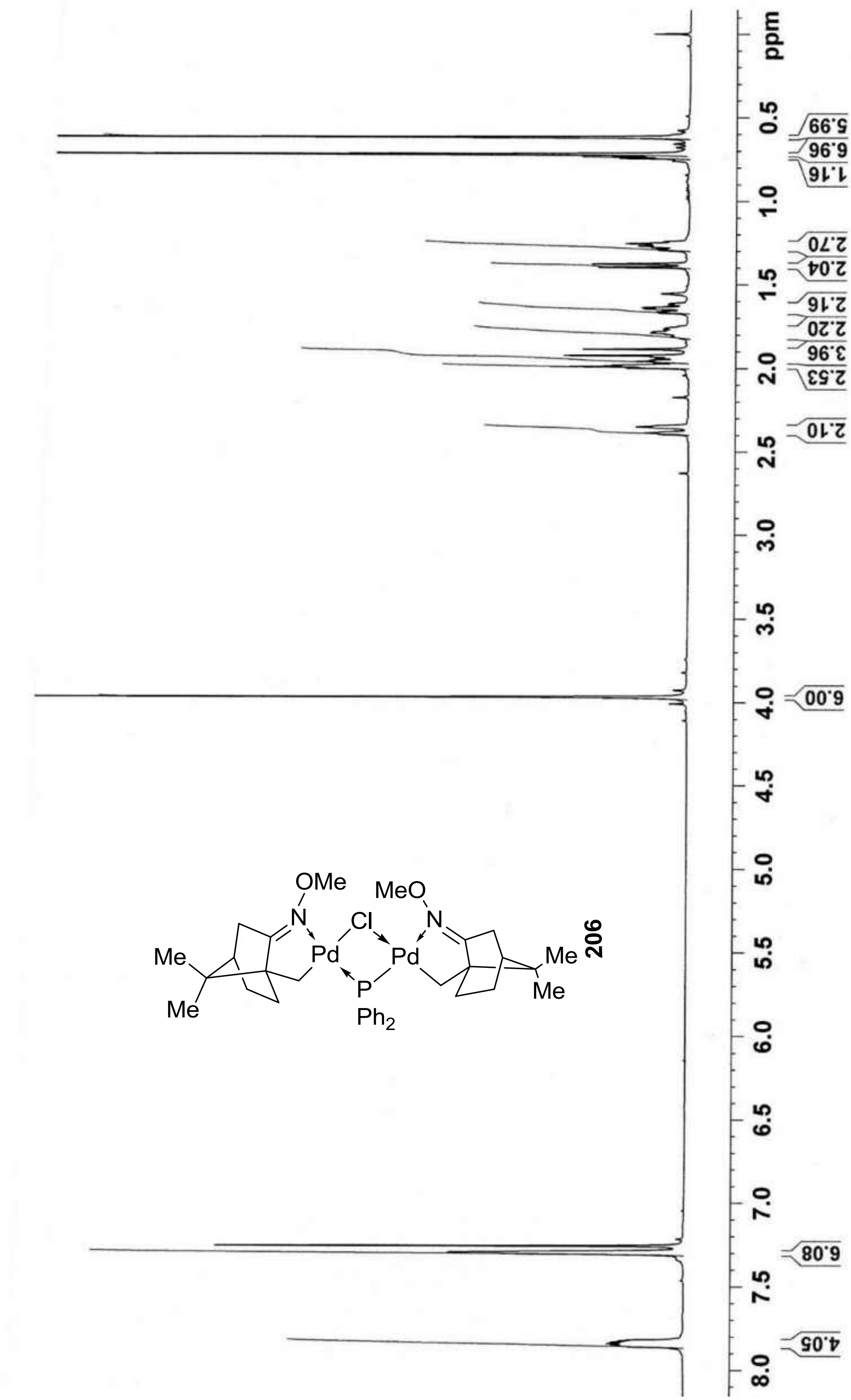

Figure 35. [1]H NMR spectrum of **206**.

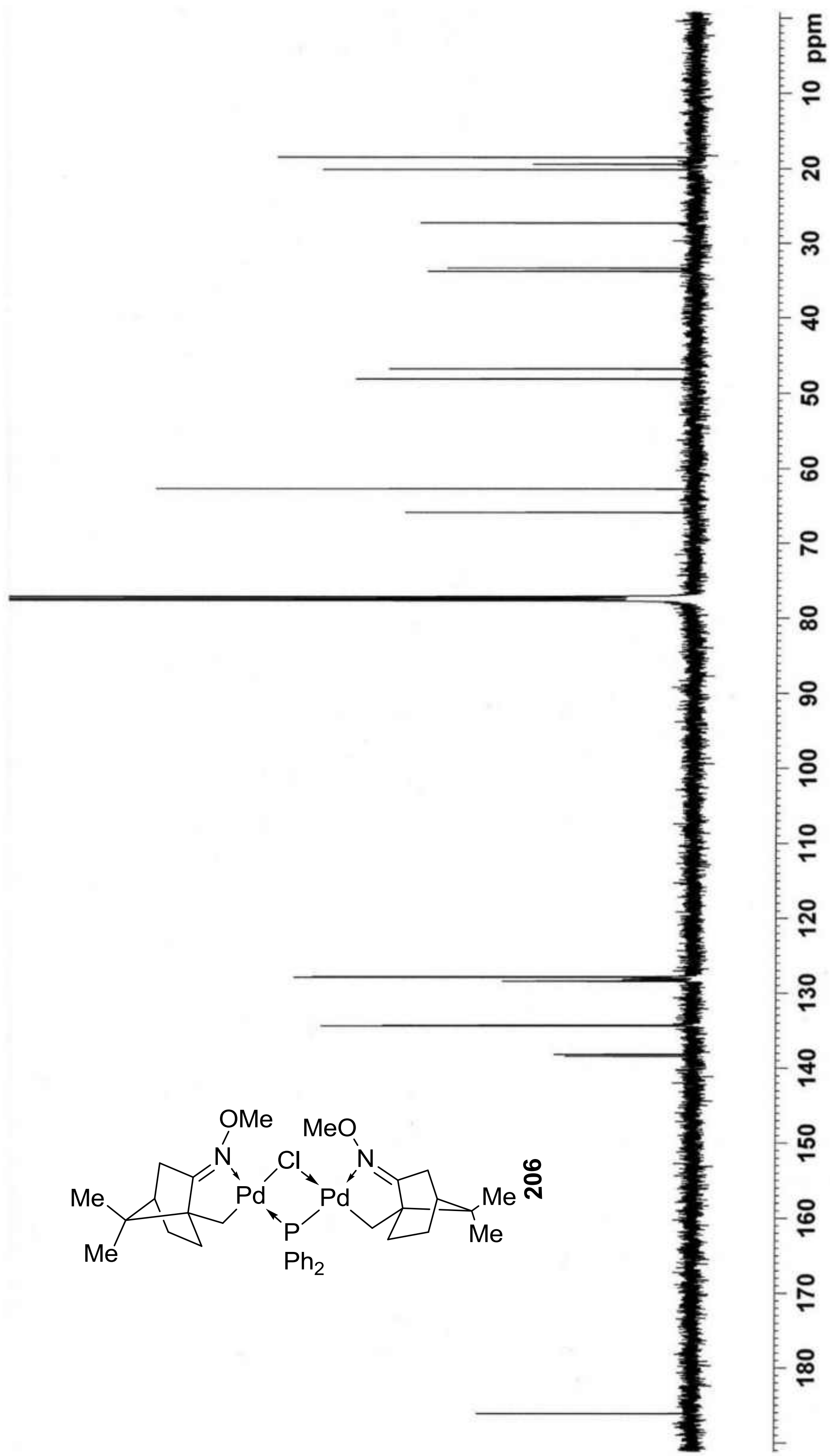

Figure 36. $^{13}C\{^{1}H\}$ NMR spectrum of **206**.

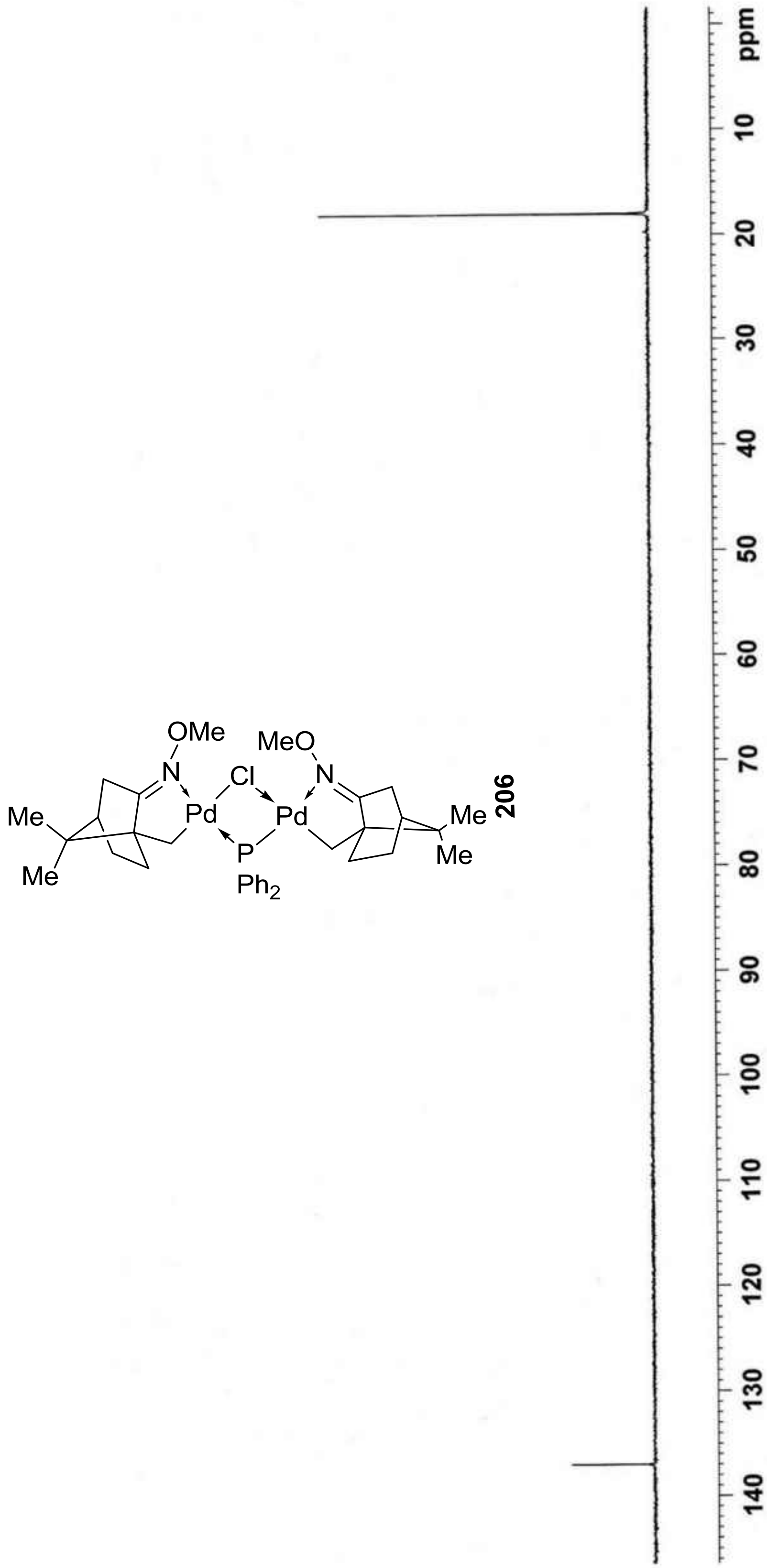

Figure 37. $^{31}P\{^1H\}$ NMR spectrum of **206**.

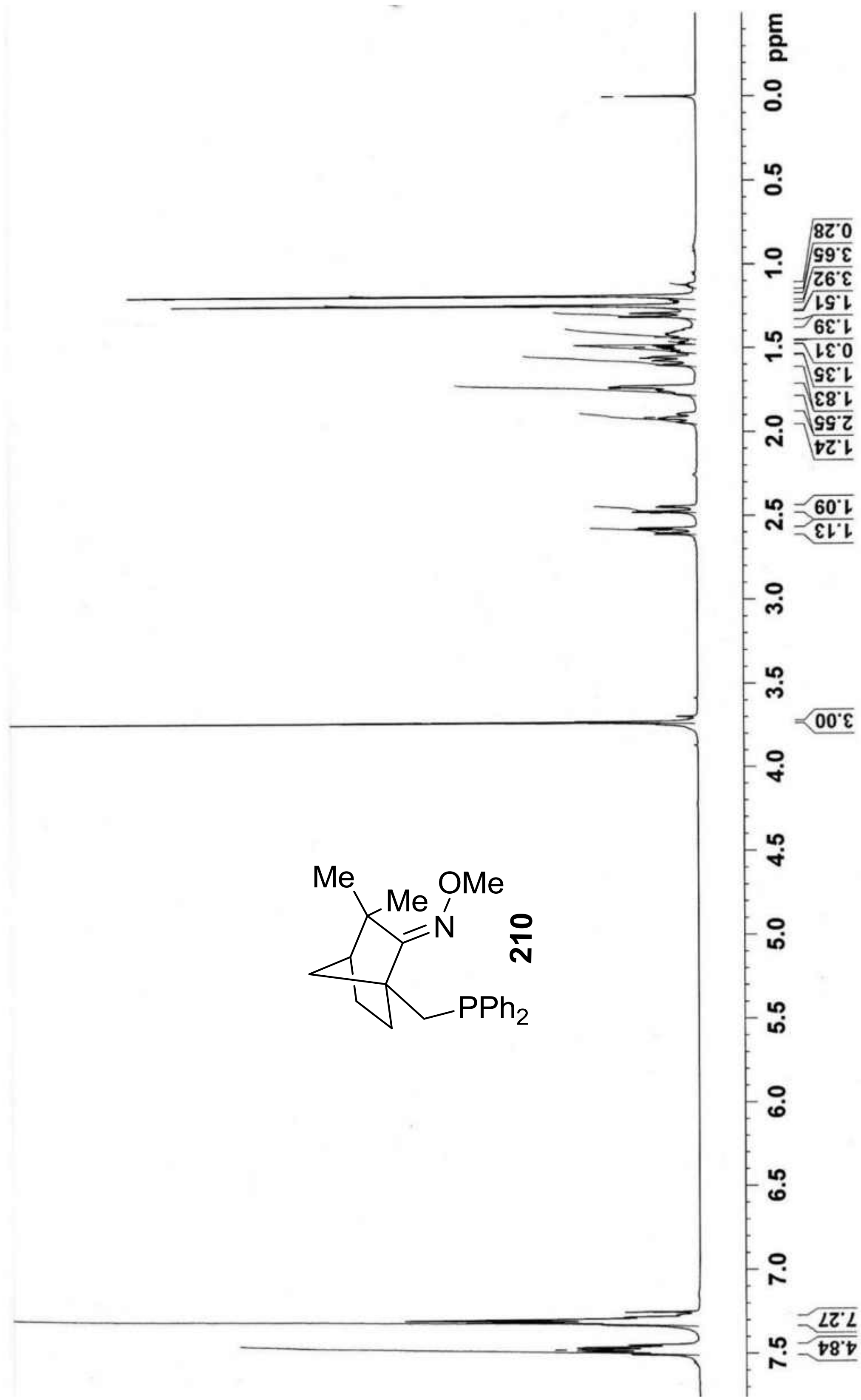

Figure 38. ^{1}H NMR spectrum of **210**.

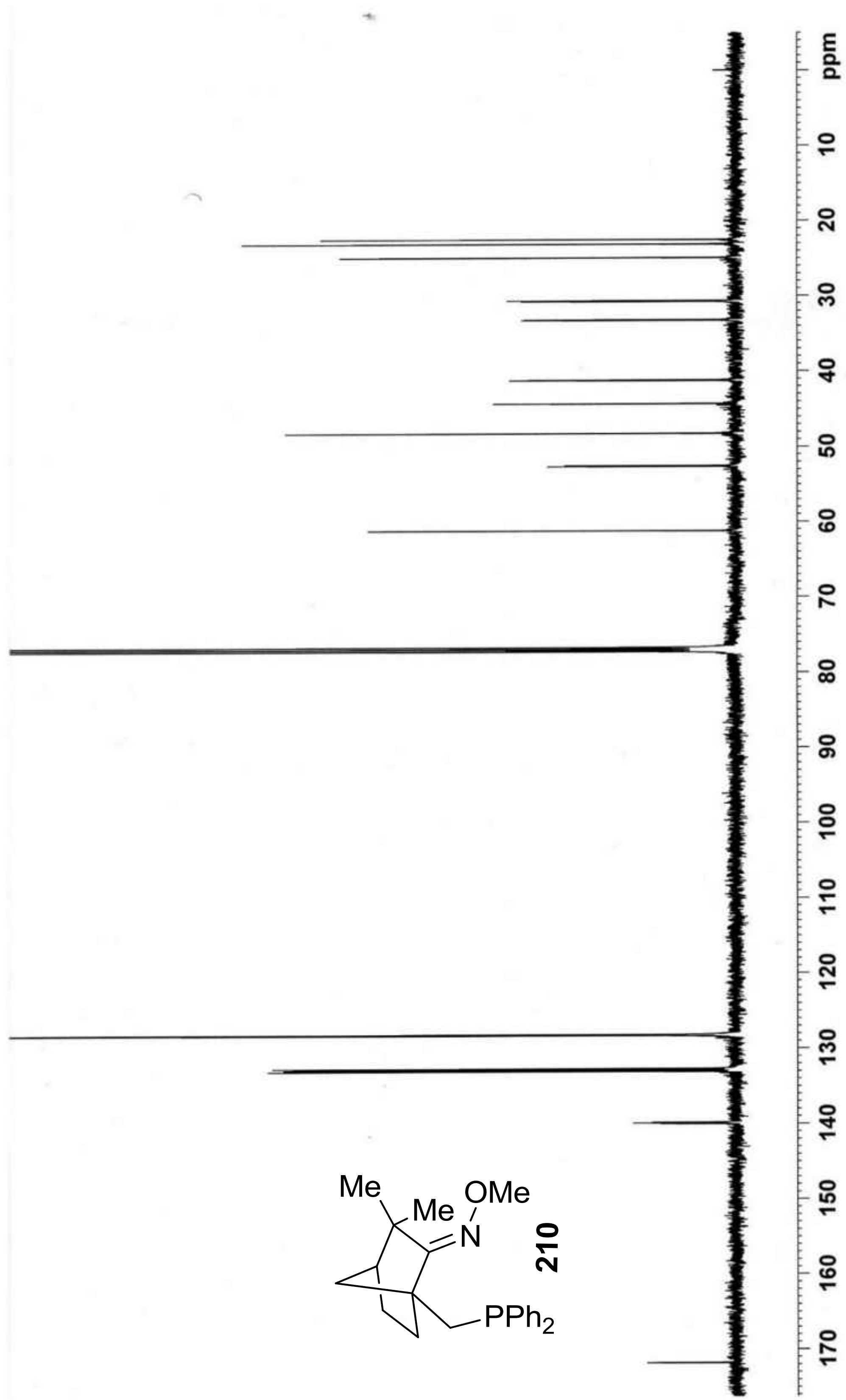

Figure 39. $^{13}C\{^{1}H\}$ NMR spectrum of **210**.

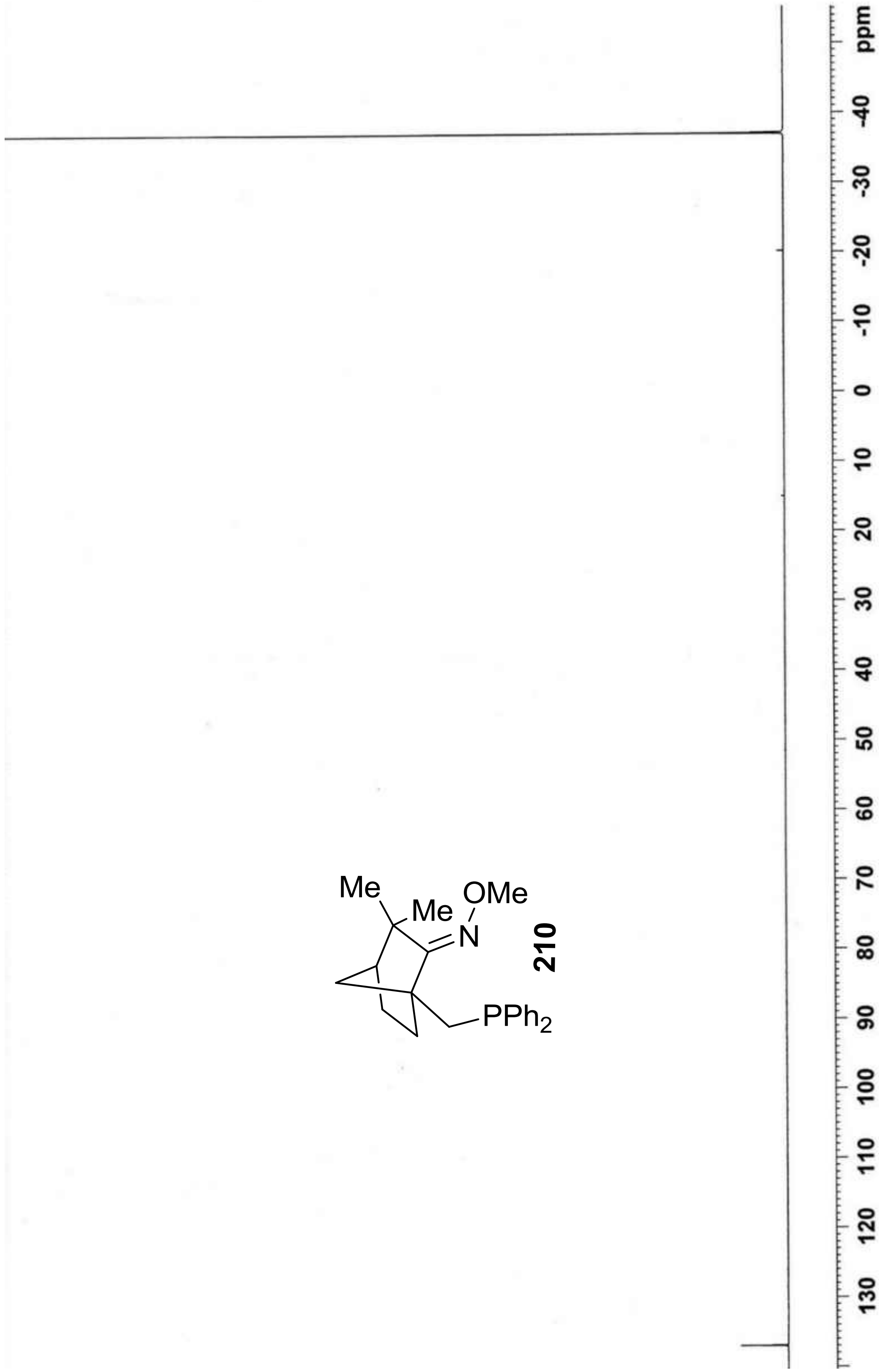

Figure 40. ${}^{31}P\{{}^{1}H\}$ NMR spectrum of **210**.

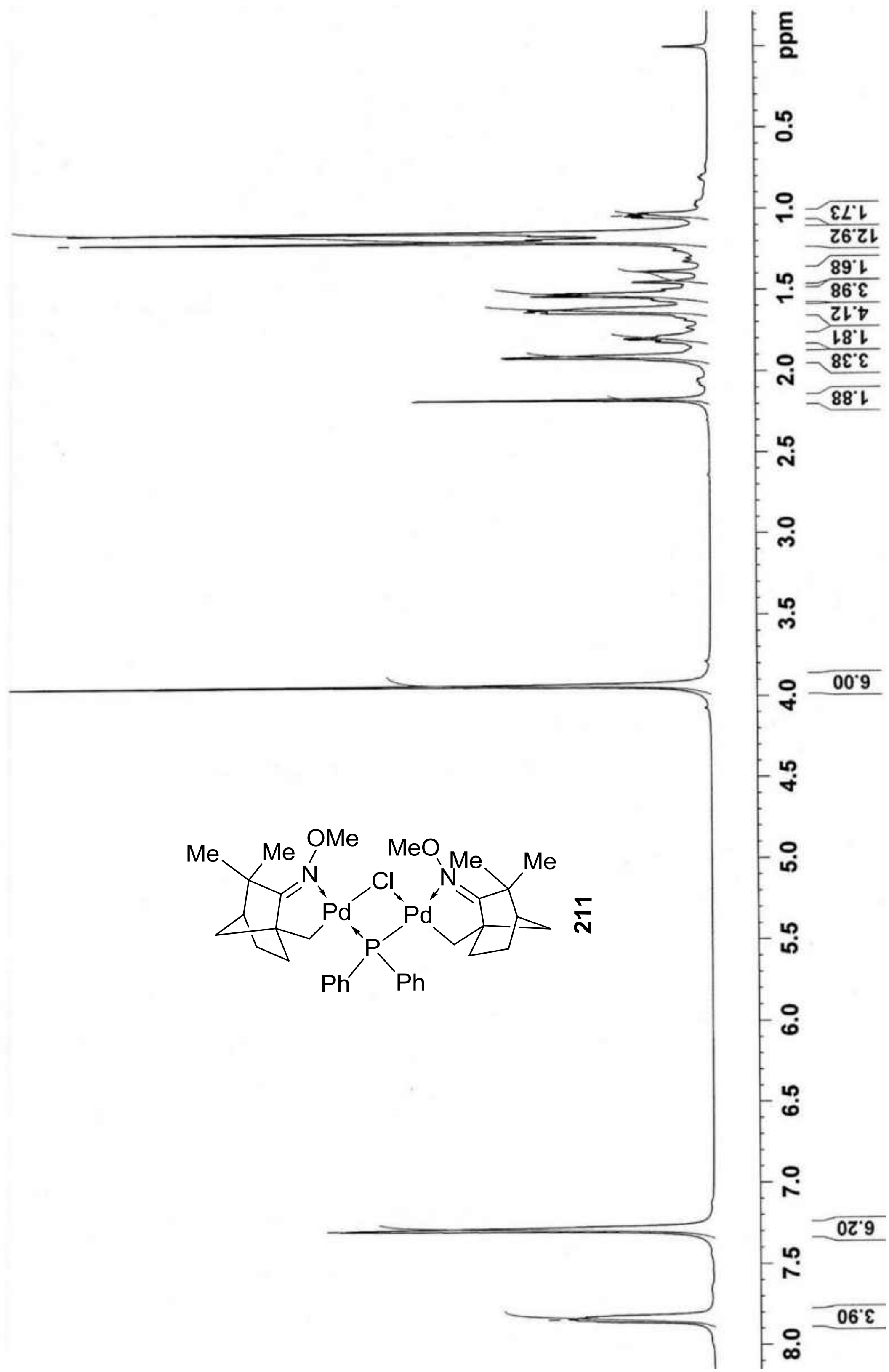

Figure 41. ^{1}H NMR spectrum of **211**.

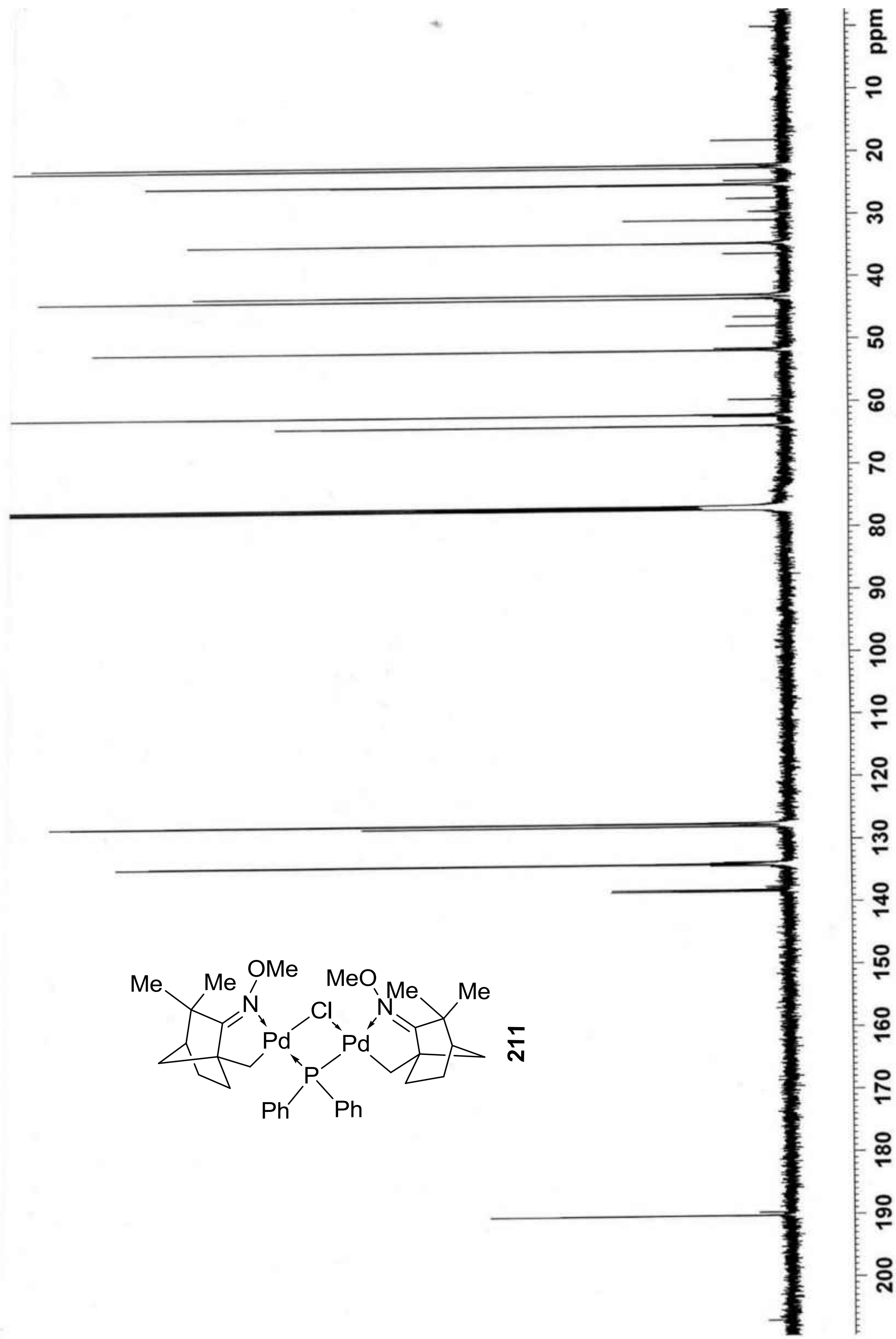

Figure 42. $^{13}C\{^1H\}$ NMR spectrum of **211**.

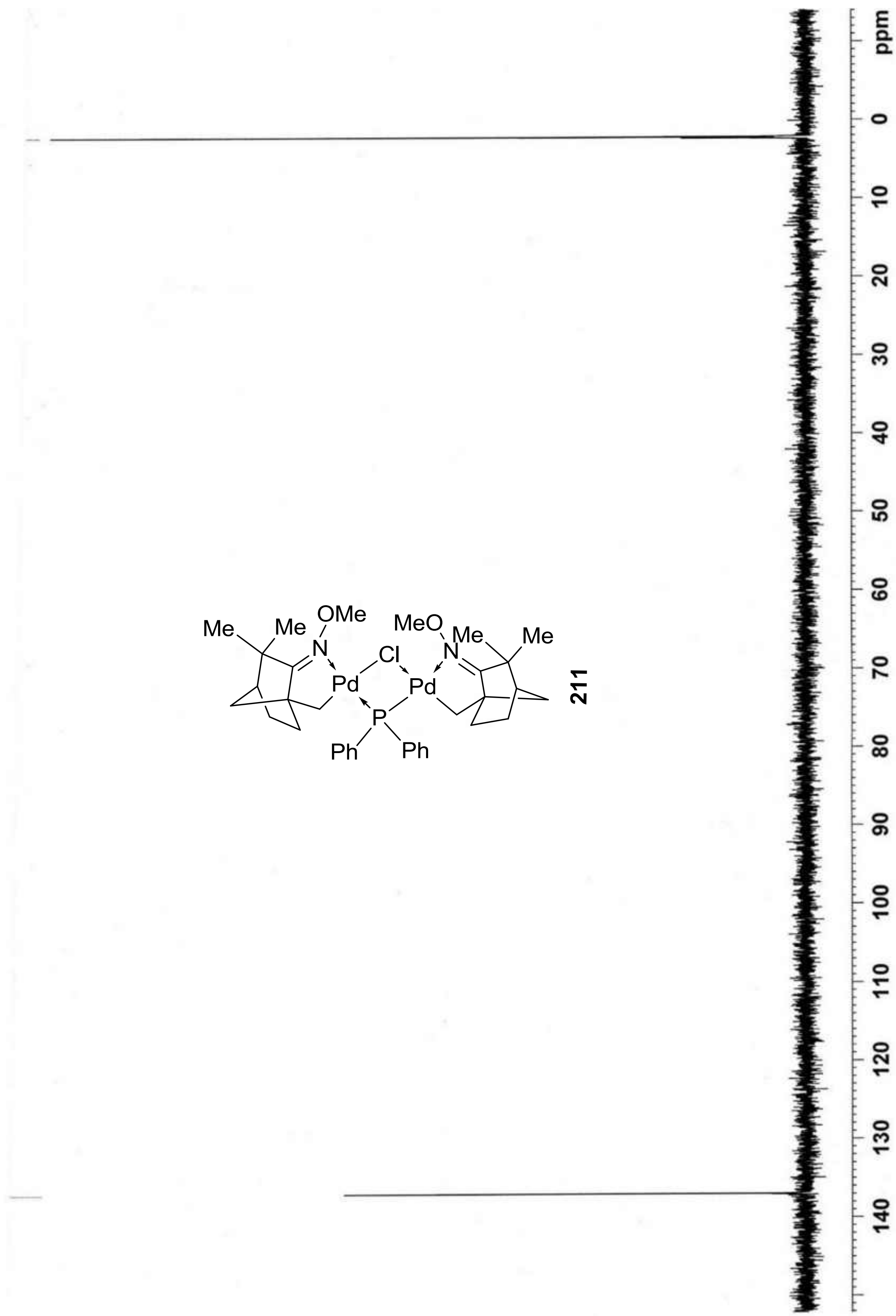

Figure 43. $^{31}P\{^{1}H\}$ NMR spectrum of **211**.

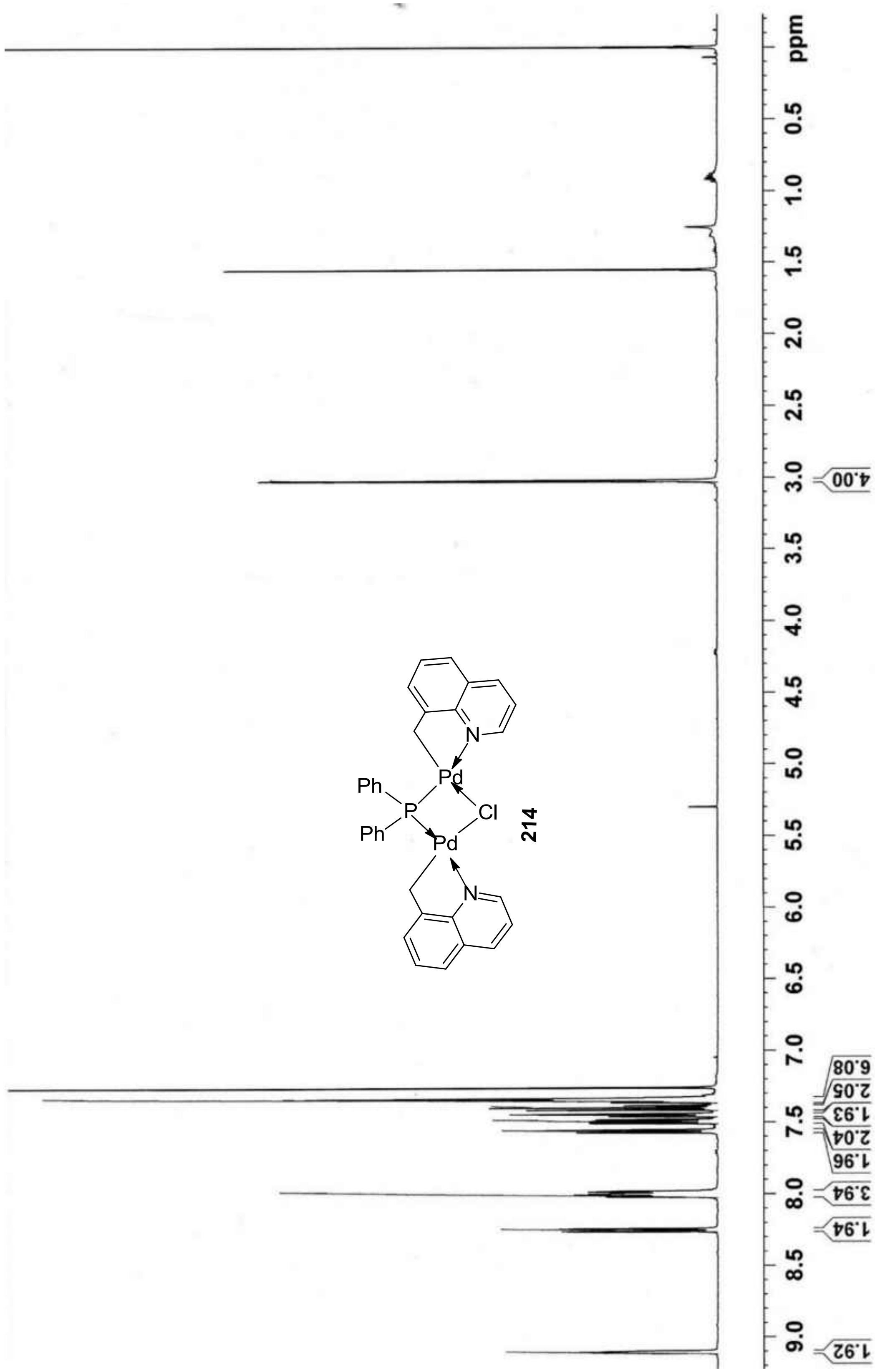

Figure 44. ^{1}H NMR spectrum of **214**.

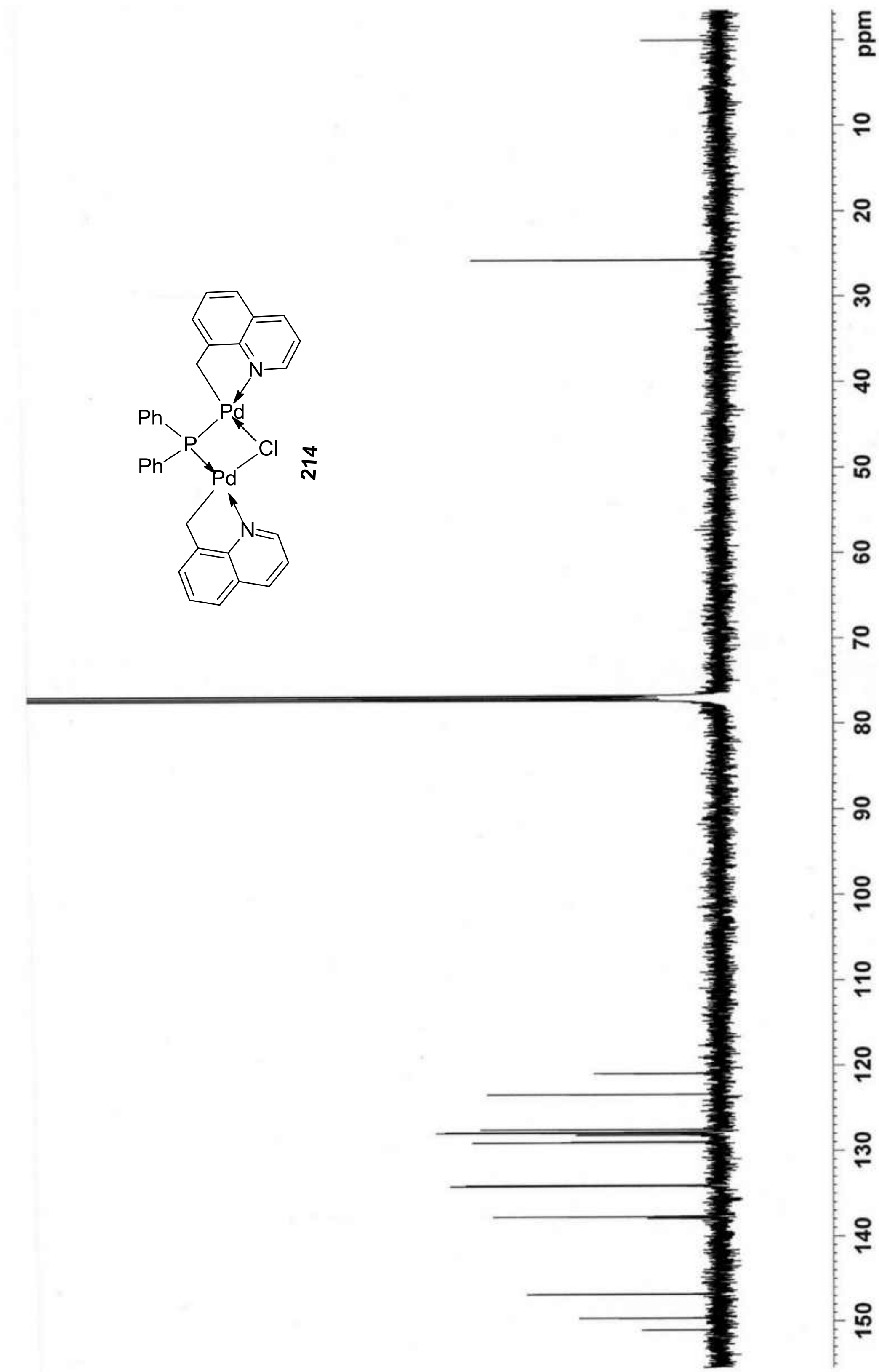

Figure 45. $^{13}C\{^{1}H\}$ NMR spectrum of **214**.

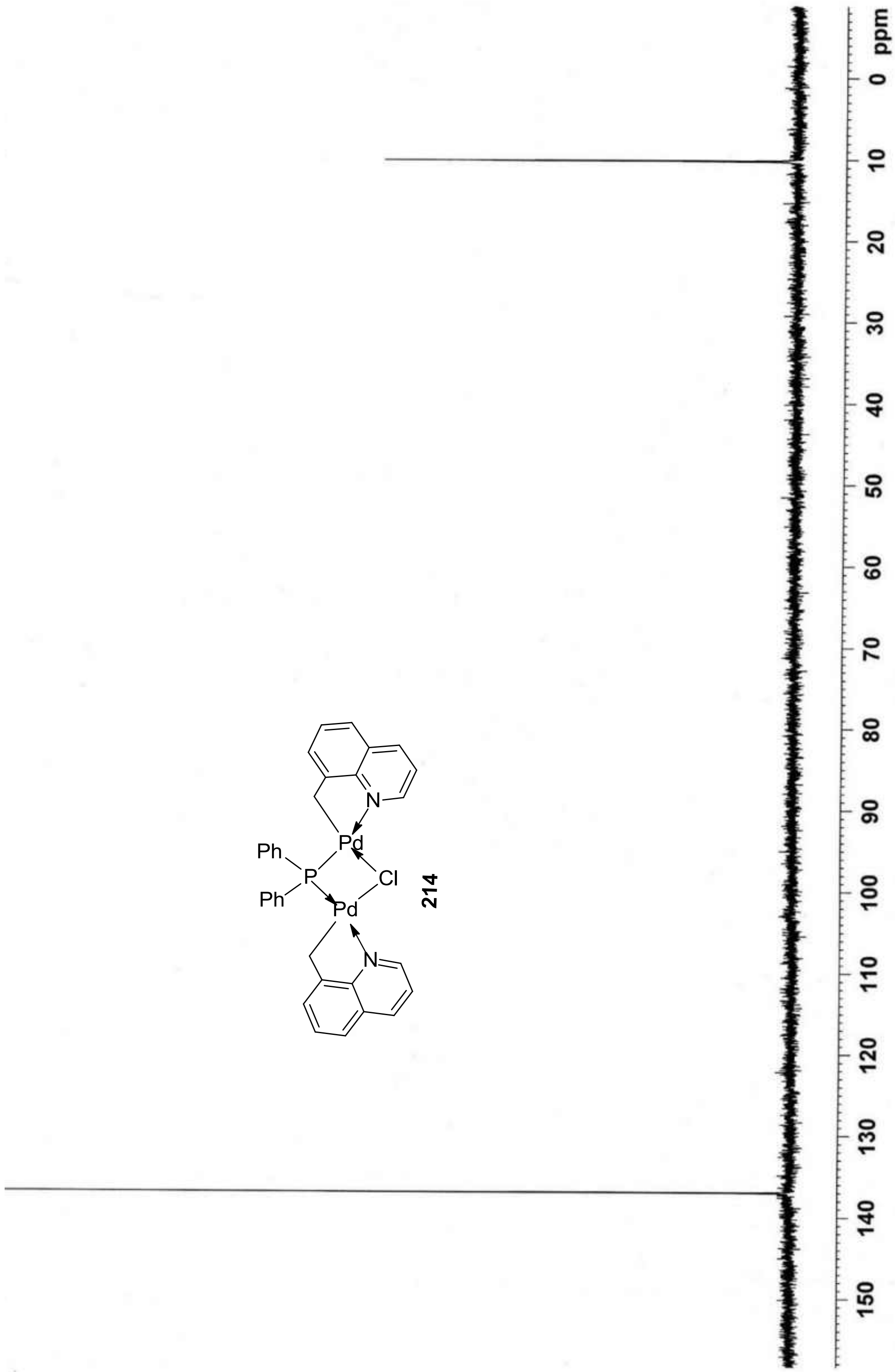

Figure 46. $^{31}P\{^{1}H\}$ NMR spectrum of **214**.

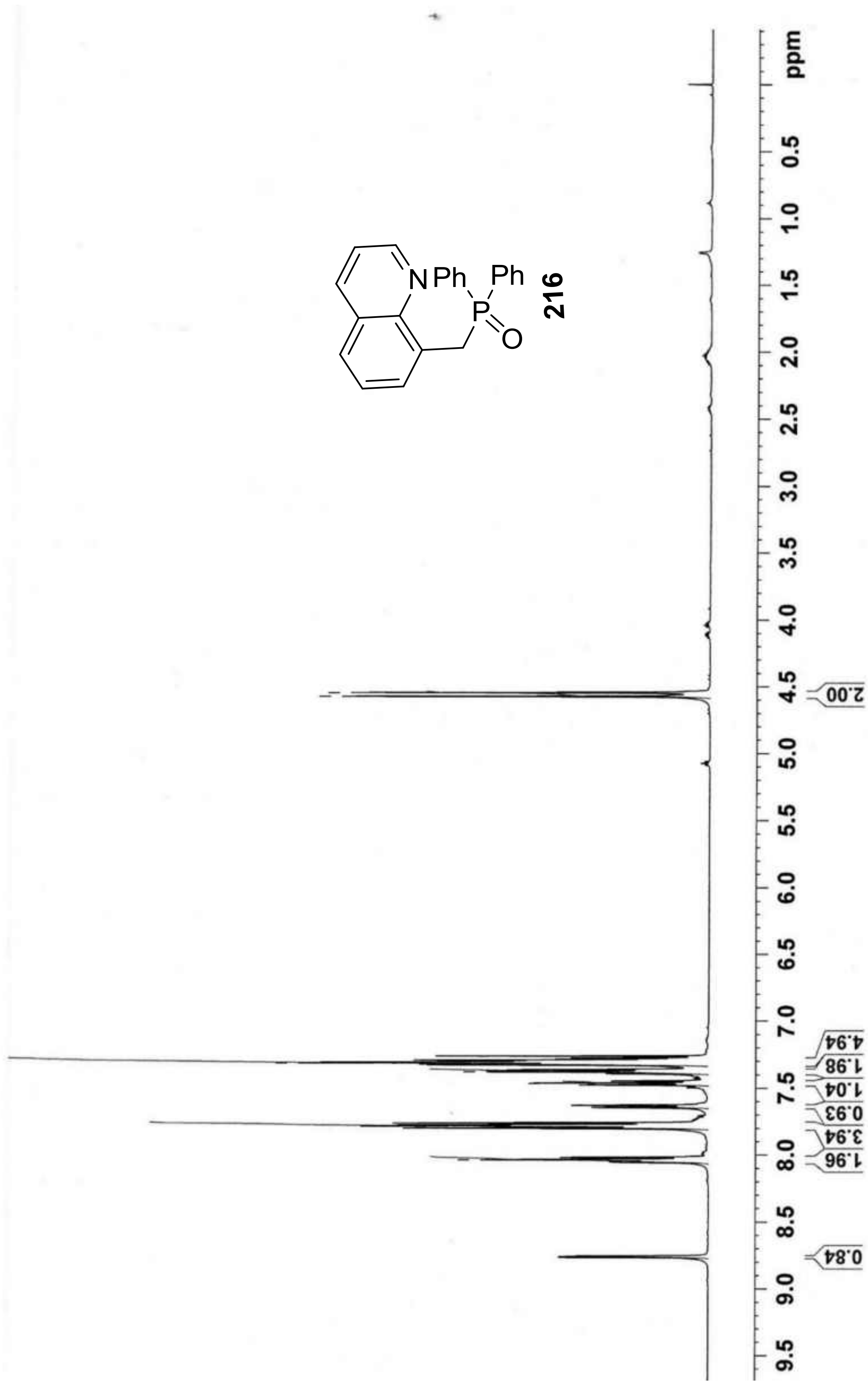

Figure 47. ^{1}H NMR spectrum of **216**.

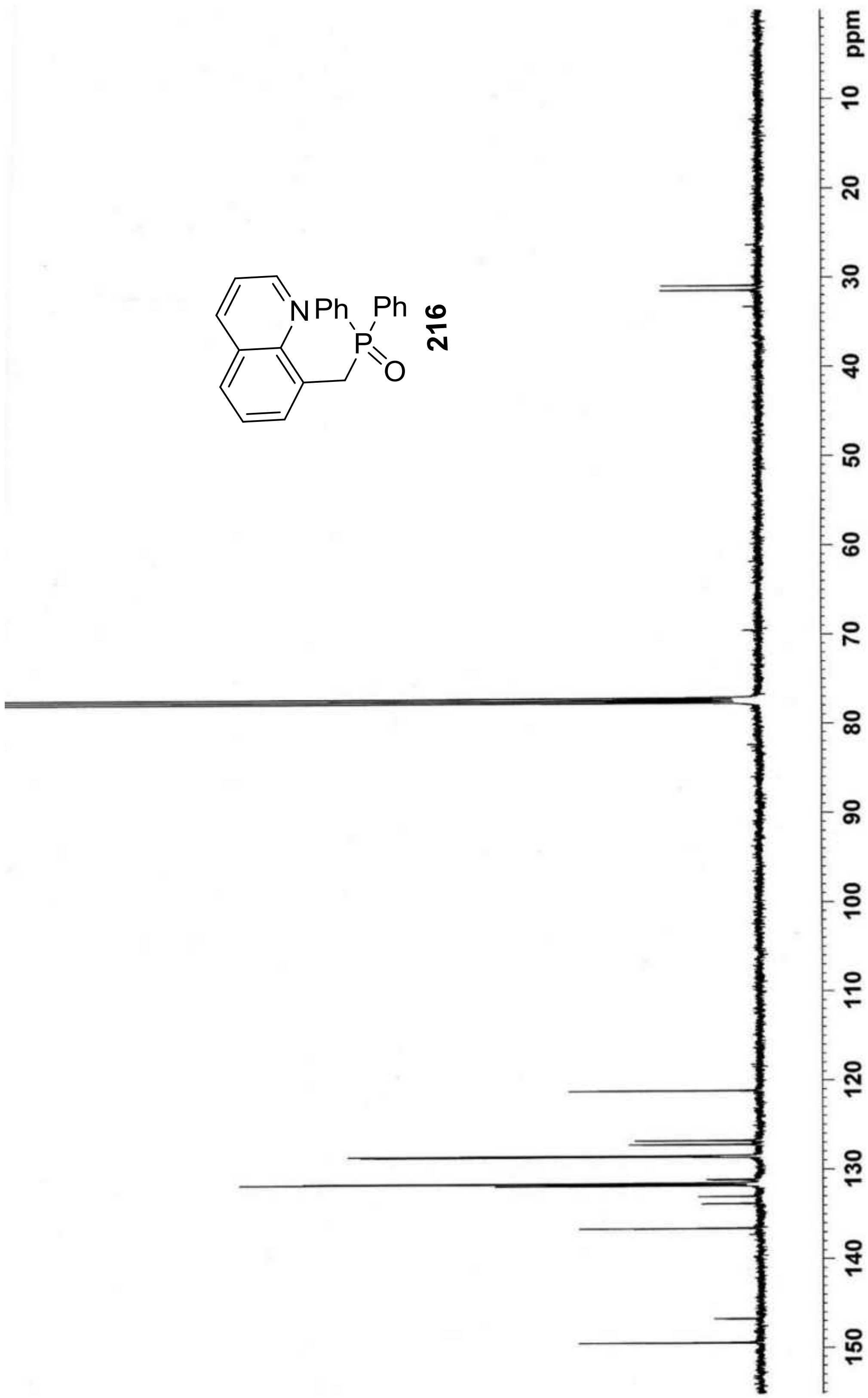

Figure 48. $^{13}C\{^{1}H\}$ NMR spectrum of **216**.

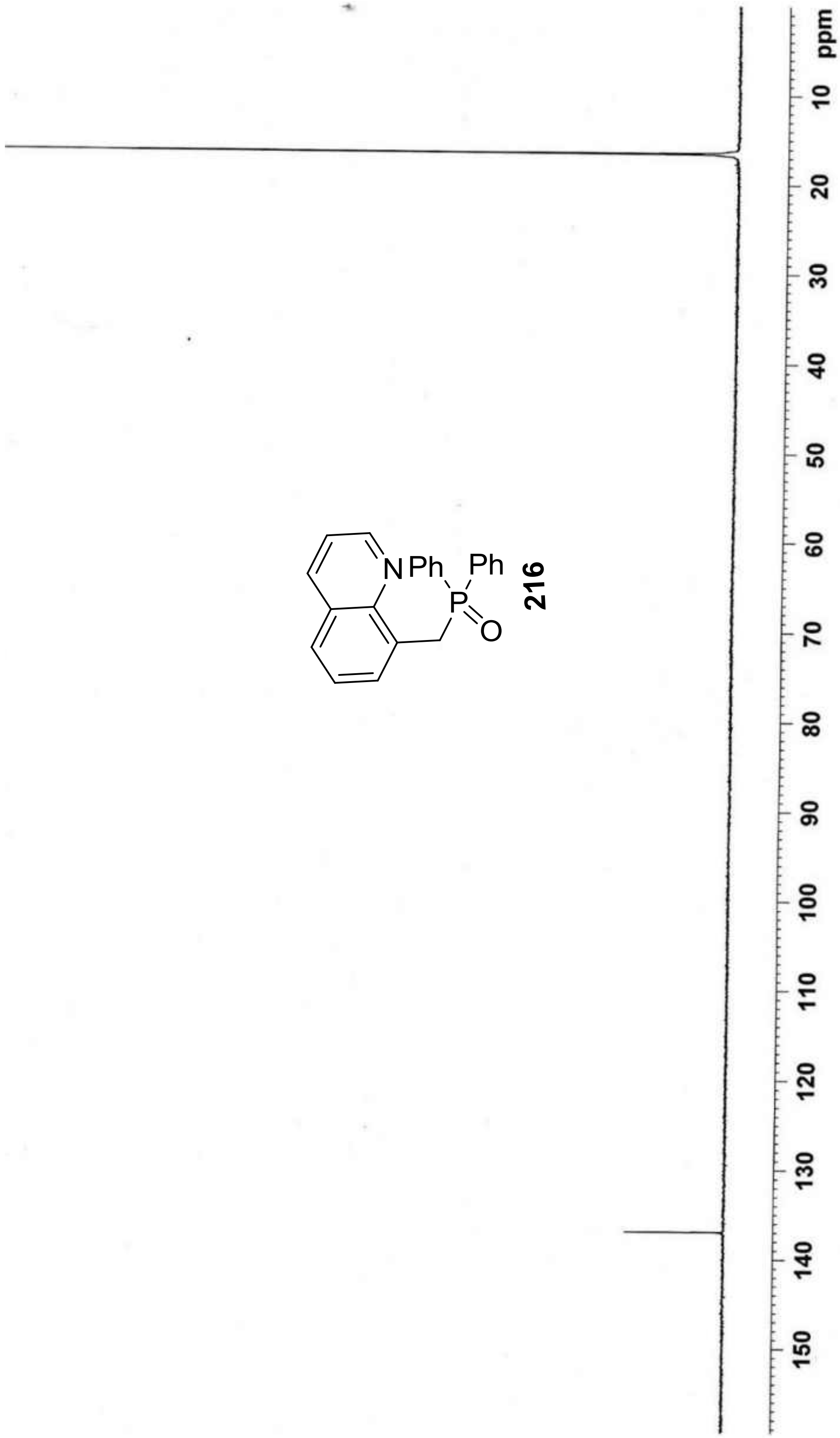

Figure 49. $^{31}P\{^{1}H\}$ NMR spectrum of **216**.

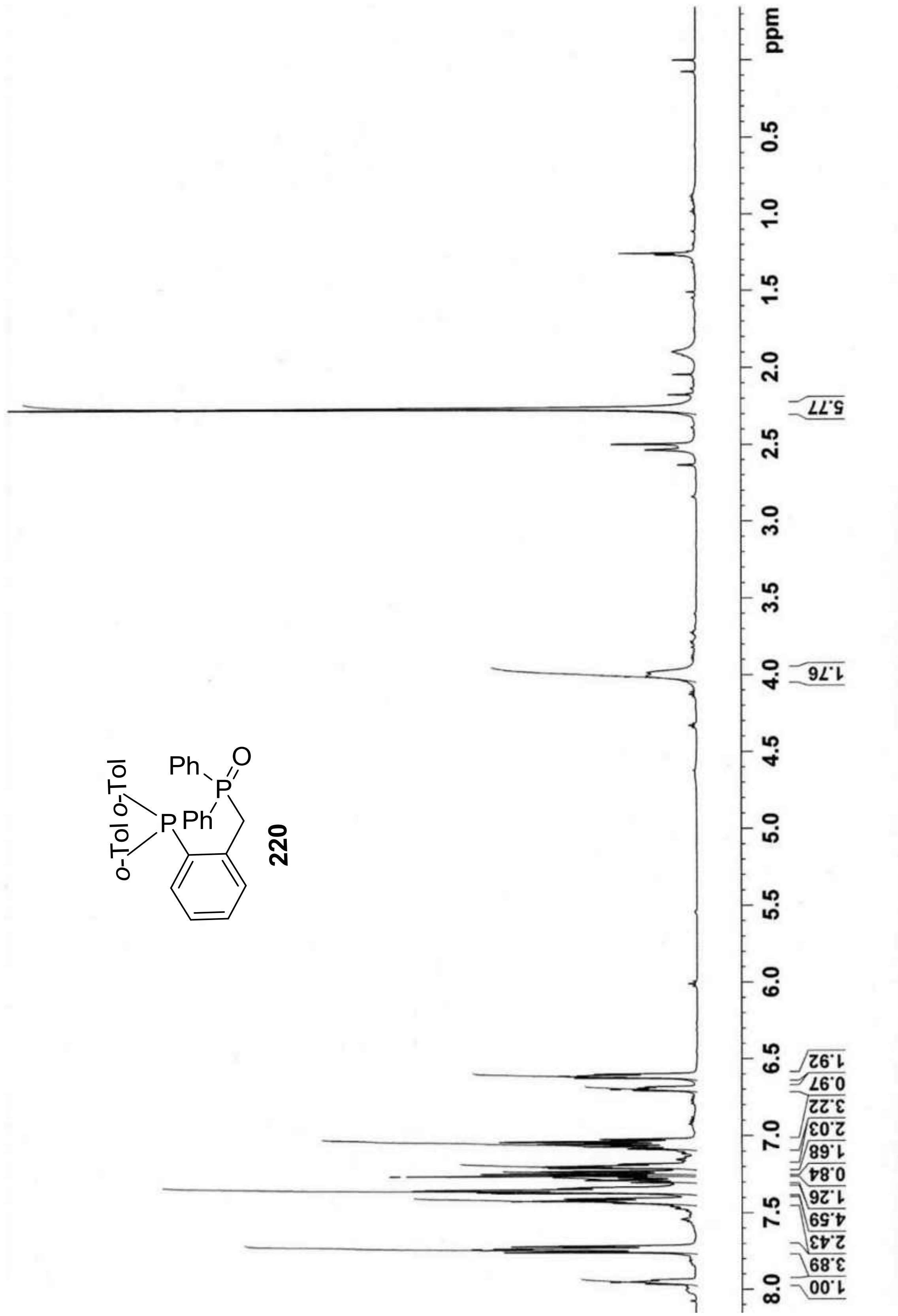

Figure 50. ^{1}H NMR spectrum of **220**.

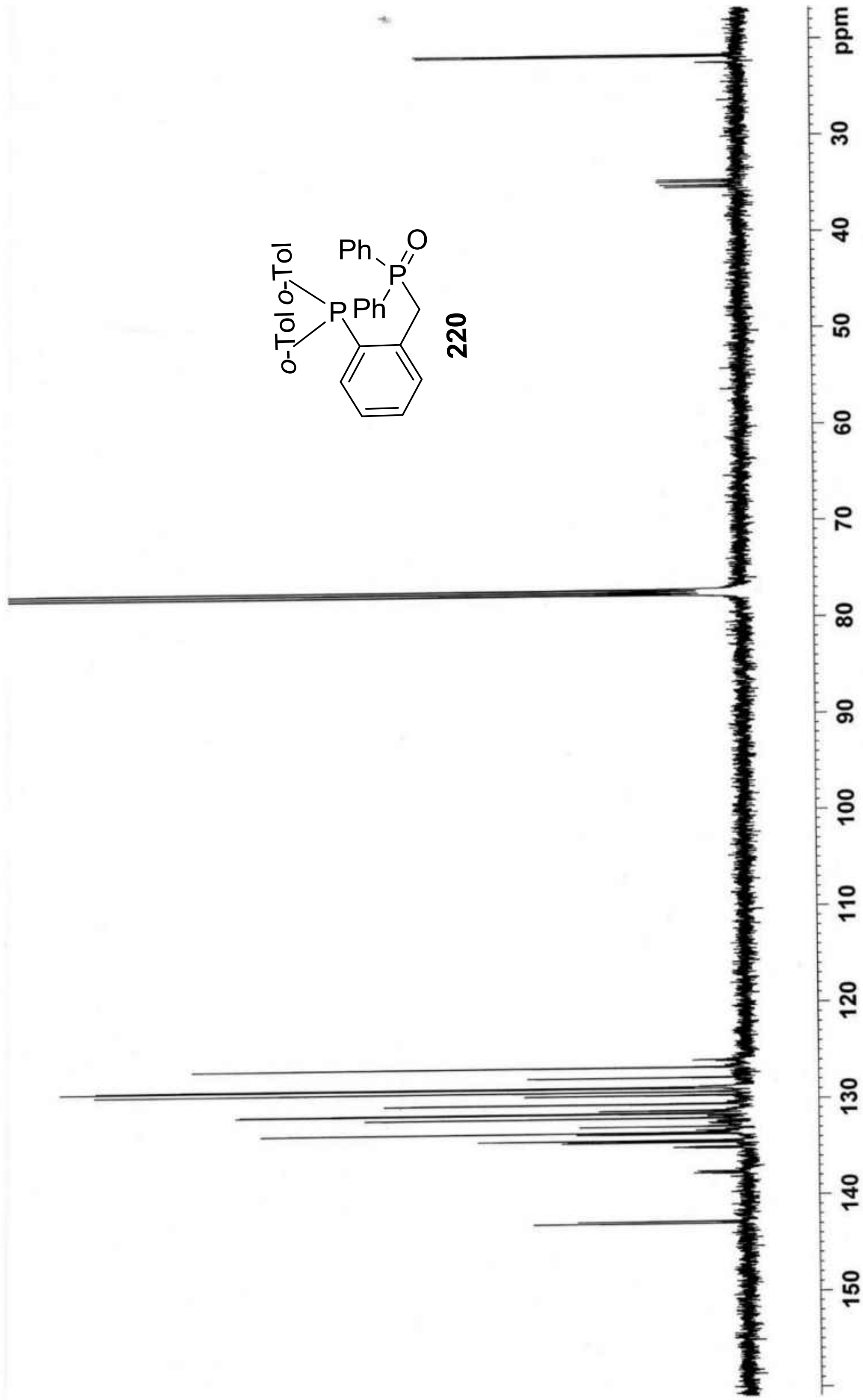

Figure 51. $^{13}C\{^{1}H\}$ NMR spectrum of **220**.

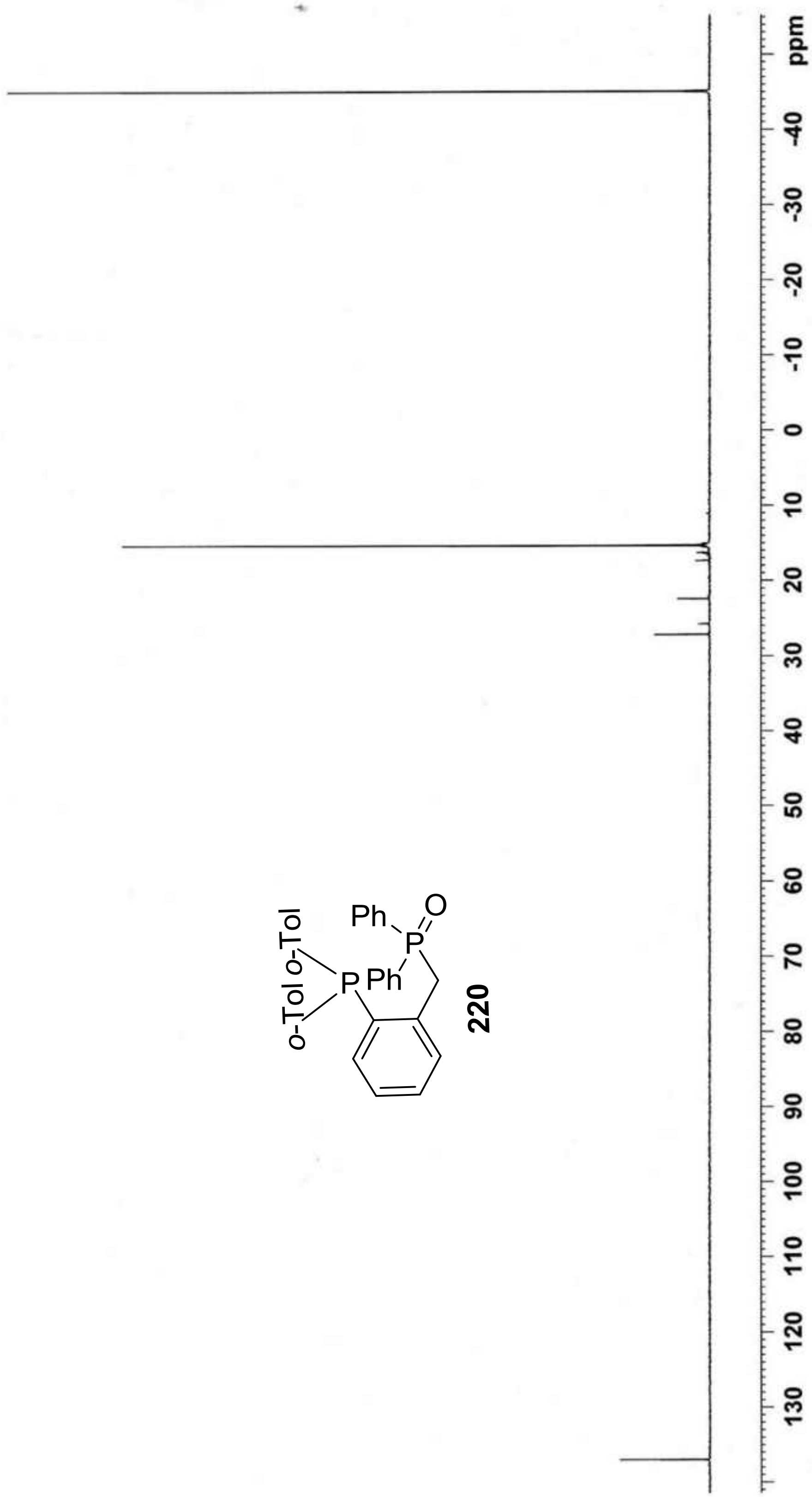

Figure 52. ${}^{31}P\{{}^{1}H\}$ NMR spectrum of **220**.

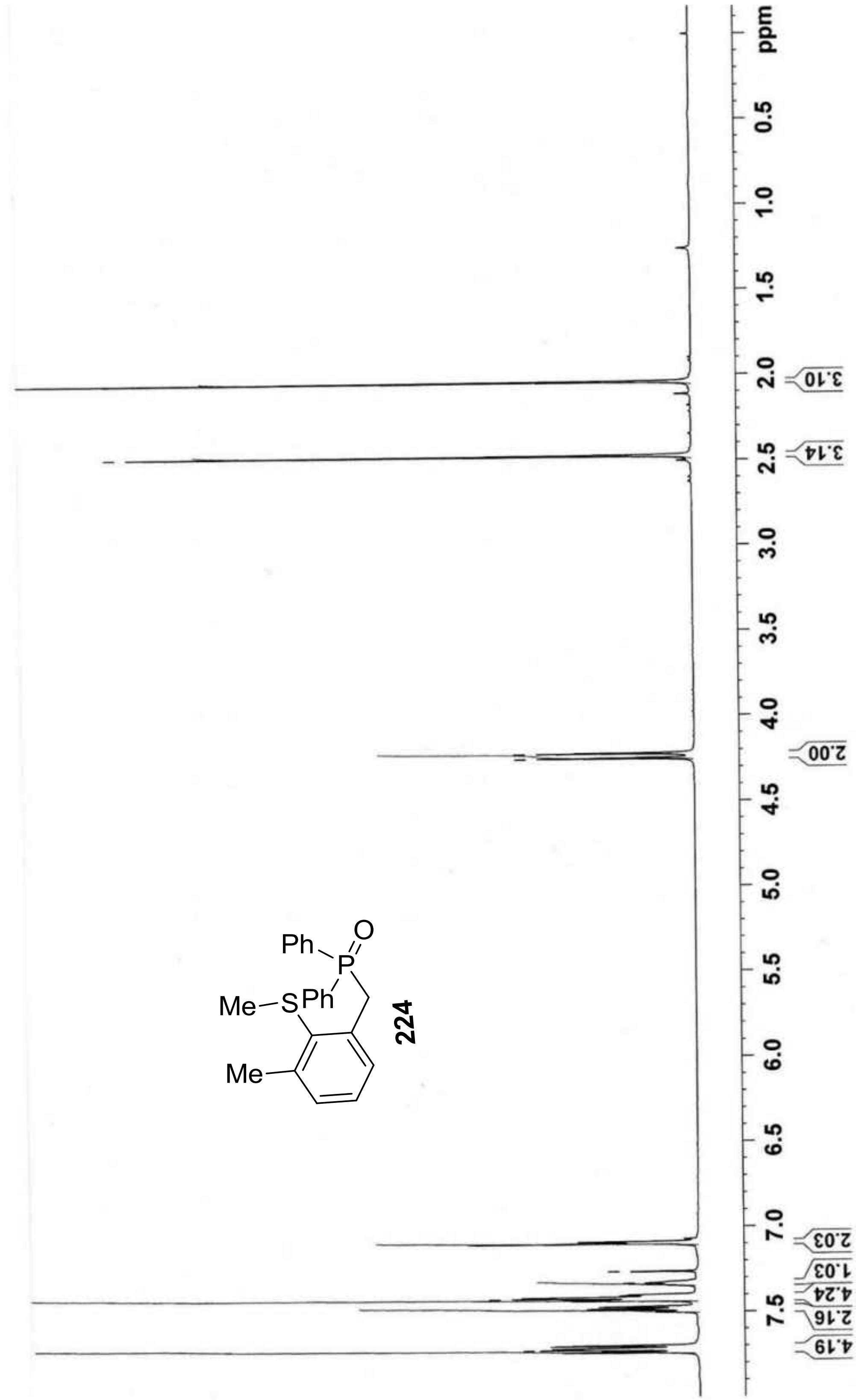

Figure 53. ^{1}H NMR spectrum of **224**.

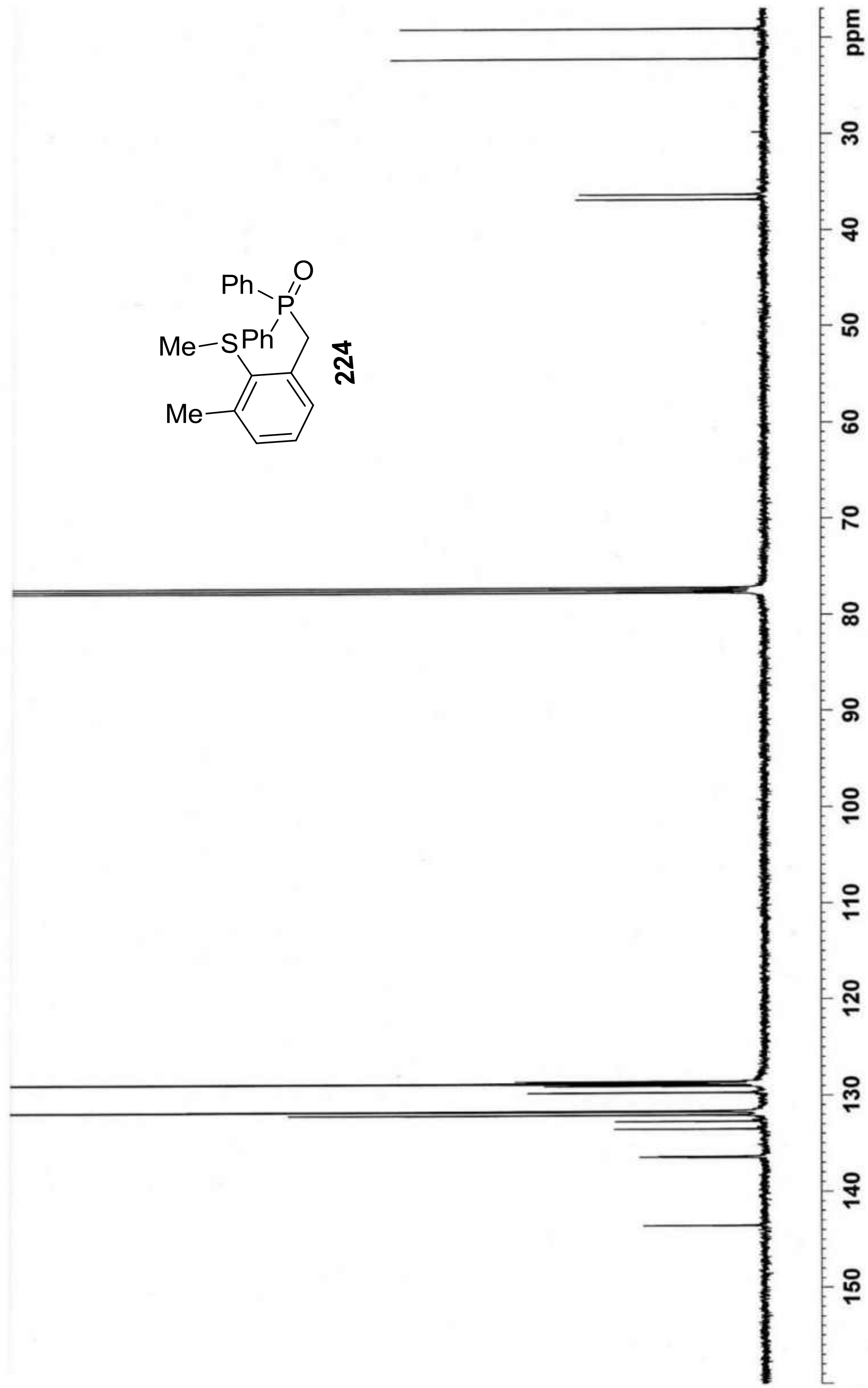

Figure 54. $^{13}C\{^1H\}$ NMR spectrum of **224**.

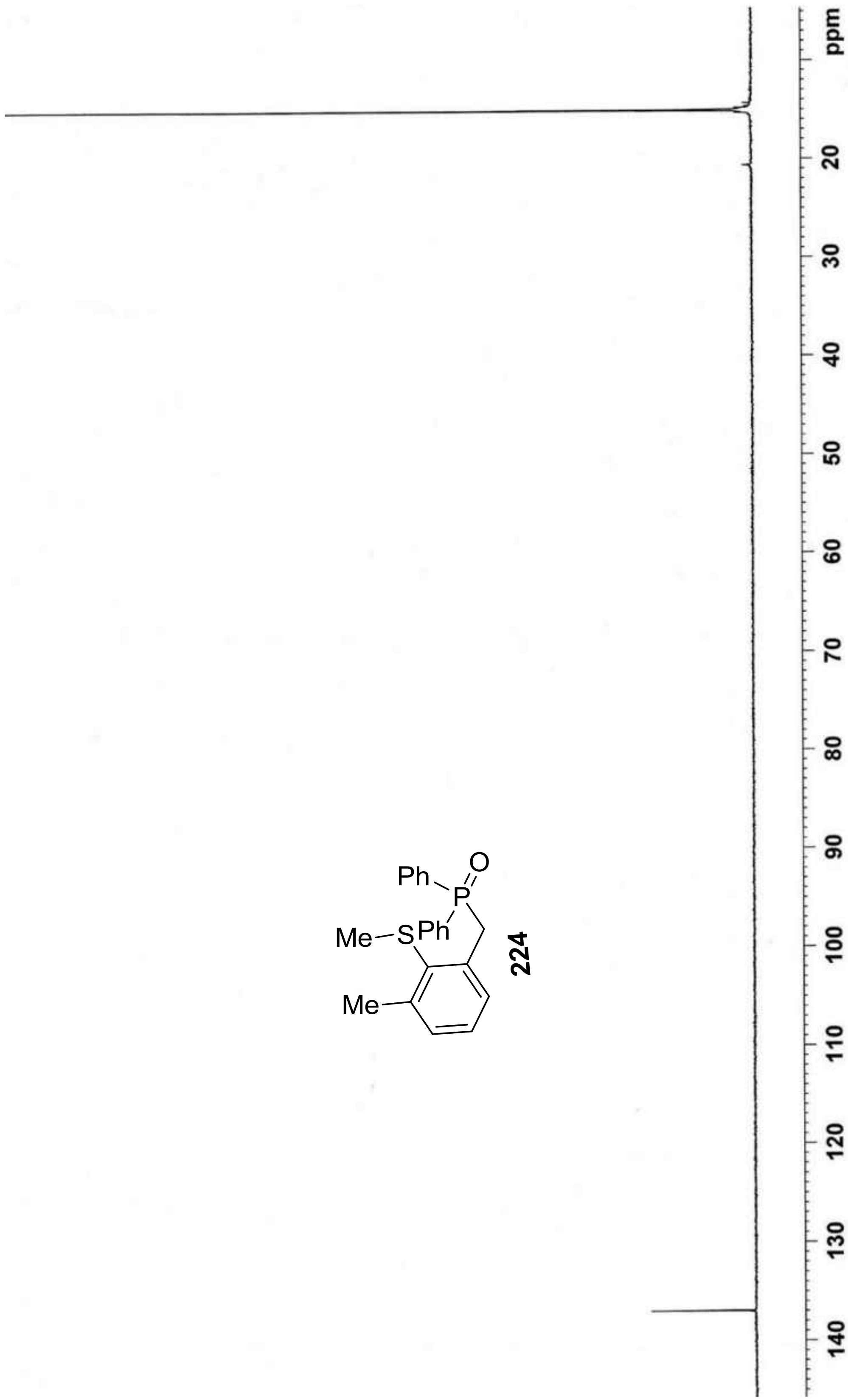

Figure 55. $^{31}P\{^{1}H\}$ NMR spectrum of **224**.

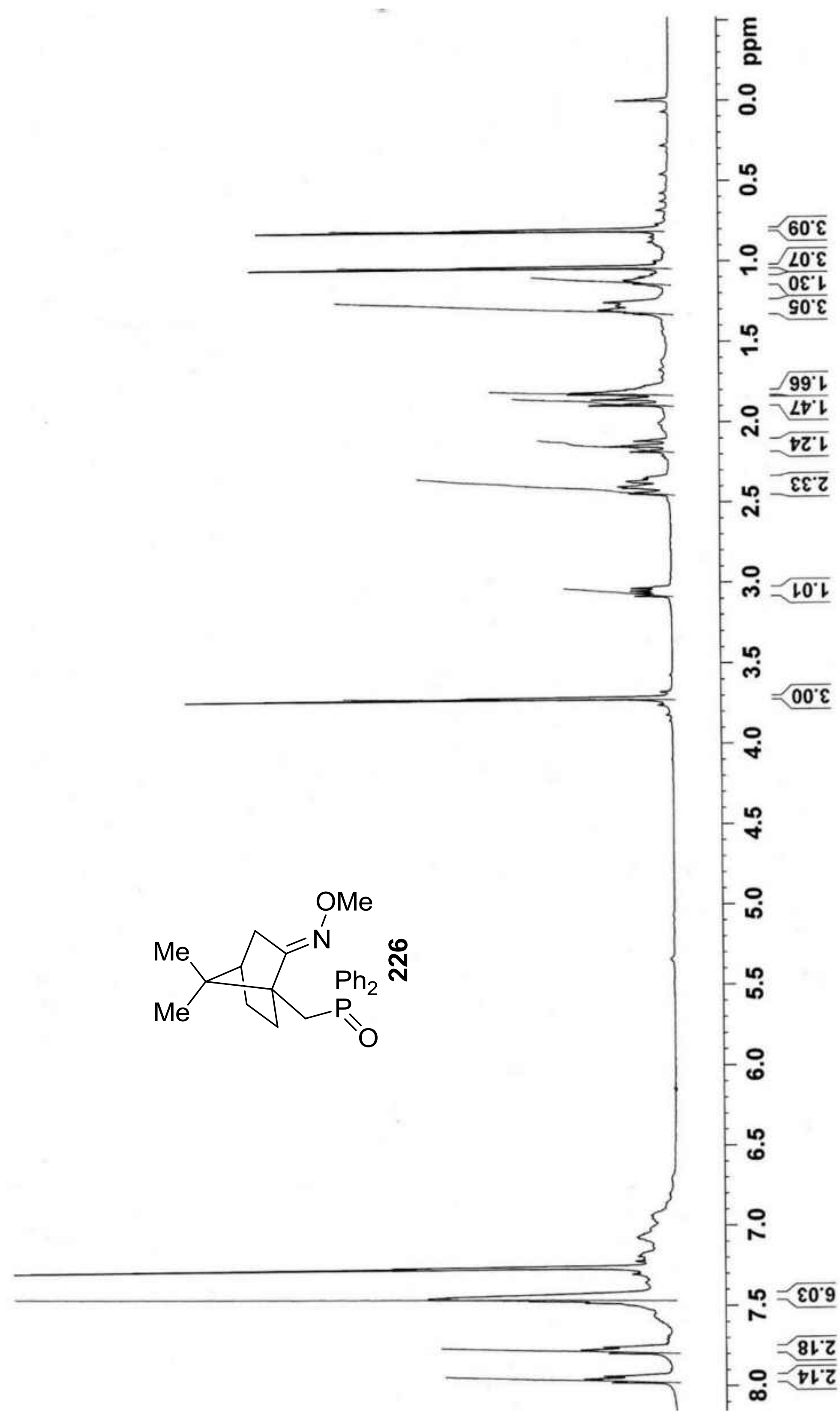

Figure 56. ^{1}H NMR spectrum of **226**.

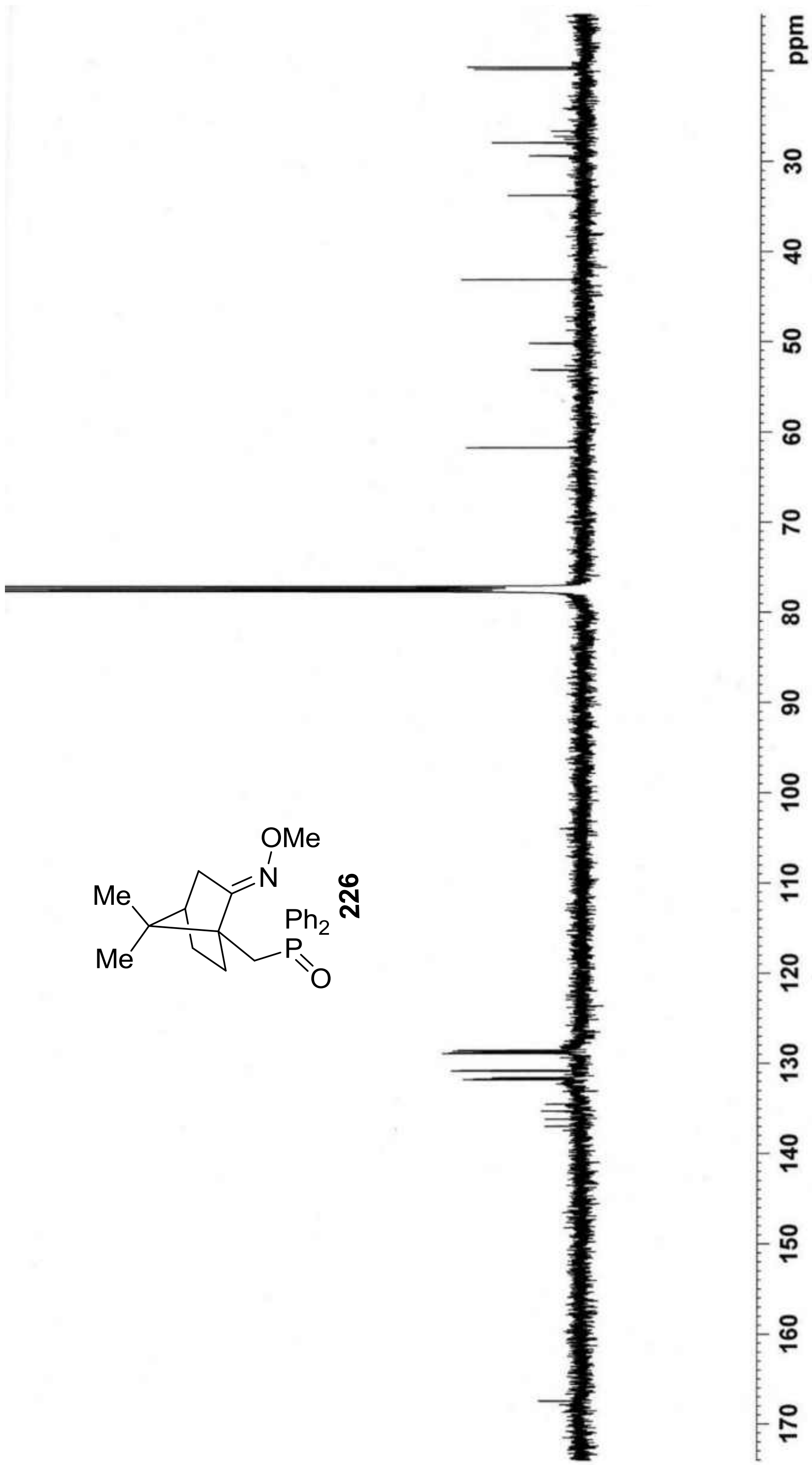

Figure 57. $^{13}C\{^{1}H\}$ NMR spectrum of **226**.

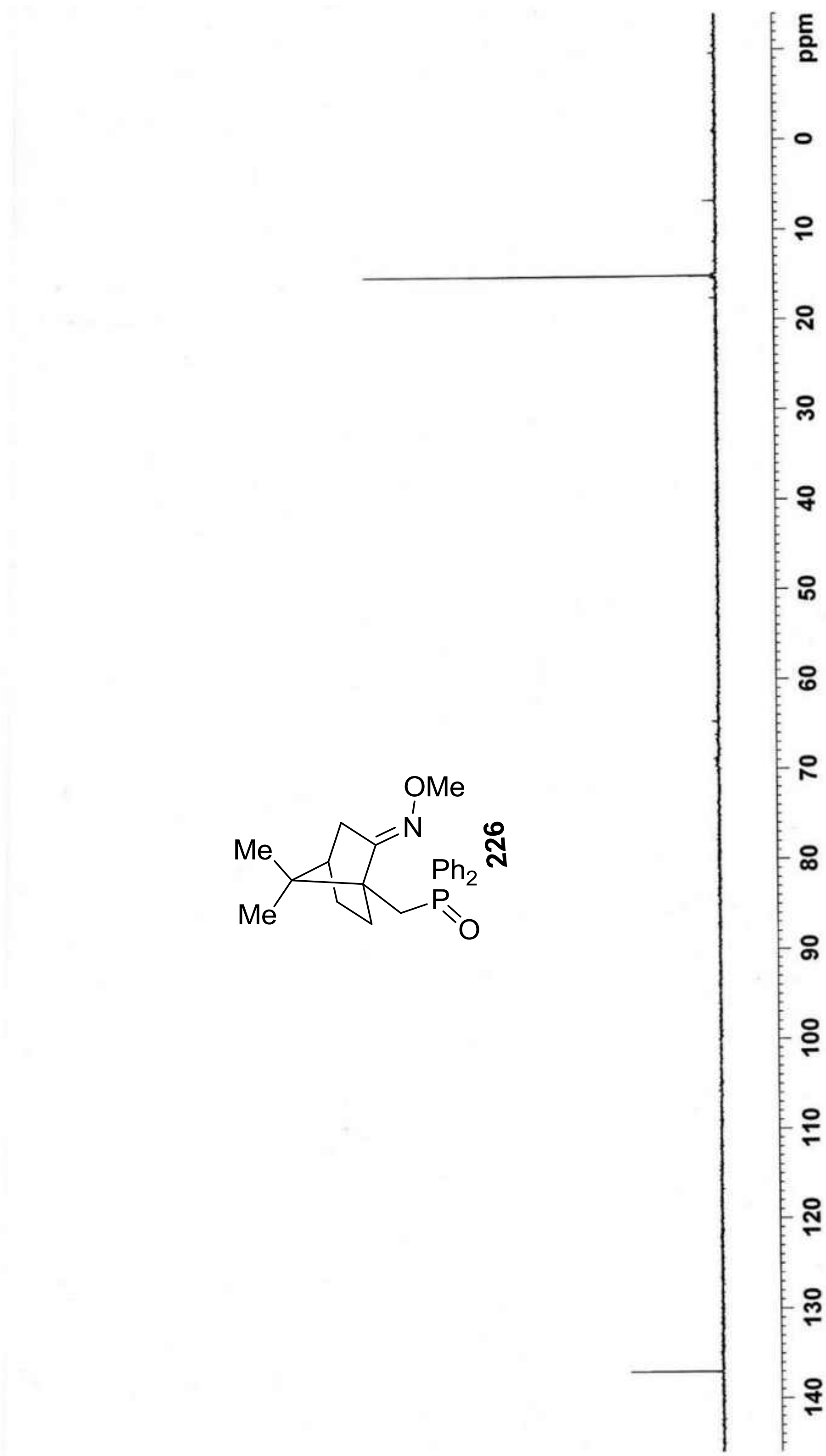

Figure 58. $^{31}P\{^1H\}$ NMR spectrum of **226**.

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