PALLADACYCLES:
SYNTHESIS AND CATALYSIS

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ingestelde commissie,
in het openbaar te verdedigen in de Agnietenkapel
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PALLADACYCLES : SYNTHESIS AND CATALYSIS

Thèse de Doctorat pour obtenir le grade de
Docteur de l'Université Louis Pasteur Strasbourg I
présentée par

Alexandre Holuigue

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Table of Contents

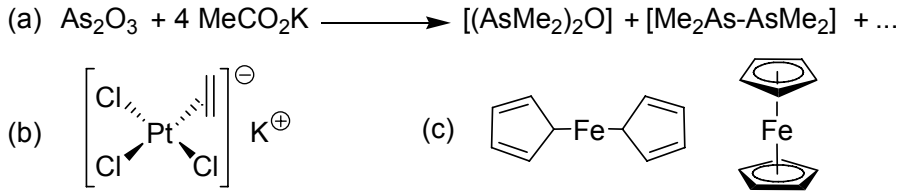
Chapter 1

General Introduction

1.1 Coordination and Organometallic complexes

Organometallic and coordination chemistry are two domains of chemistry that are complementary. Coordination complexes consist of one or more metals centres surrounded by ligands, organic or inorganic, ions or molecules, that can have an independent existence. The organometallic chemistry is defined as the chemistry of compounds containing metal–carbon bond, however, in general manner this term is attributed to the chemistry made of organic transformations assisted by metals.[1]

The rise of the modern organometallic chemistry occured in the 50's, after the discovery of the ferrocene (1951) by Pauson[2a] and Miller[2b] and the elucidation of its structure (1952) by Wilkinson[2c] and Fischer[2d]. However, it is in 1757 that the origin of the organometallic chemistry can be traced back when Cadet de Gassicourt discovered the "Cadet's fuming liquid" which was a mixture of cacodyl oxide and tetramethyldiarsine during his work on ink made of cobalt salts containing arsenic.[1c,4] The first organometallic complex containing a transition metal was a π complex synthesized by Zeise (1827).[5] Two decades later Frankland prepared a series of air sensitive metal–alkyl complexes *i.e.*: $ZnEt_2$ (1849), $HgMe_2$ (1852),[6] which have been used to synthesize various main group organometallic compounds as the organochlorosilanes of Friedel and Crafts (1863).[7]

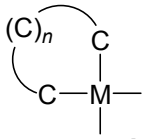


Scheme 1-1. (a) Reaction leading to the "fuming liquid of Cadet"; (b) Zeise's salt; (c) Ferrocene of Pauson followed by the ferrocene of Wilkinson and Fischer.

1.2 Metallacyclic and Cyclometallated Compounds of the Transition Elements

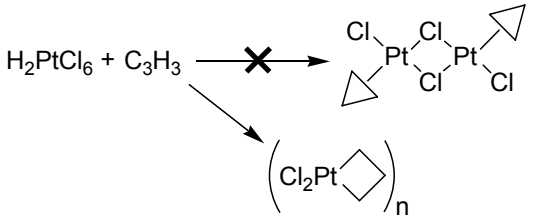
1.2.1 Metallacyclic compounds

A metallacycle can be defined as "a carbocyclic system with one or more atoms replaced by a transition metal".[8] This definition means that metallacycle should be restricted to those compounds, of type **I**, that have the transition metal atom incorporated in the ring *via* two carbon–metal *σ*-bonds, and therefore excludes simple complexes containing chelating PP, NN ligands, cyclometallated complexes and any other cyclic complex in which the metal is bound to a heteroatom.



I

The first metallacyclic complex was prepared by Tipper[9] in 1955 (Scheme 1-2). He treated hexachloroplatinic acid with cyclopropane in acetic anhydride to give a compound of formula $[PtCl_2(C_3H_6)]_n$. The complex was later shown to be a chloride bridged tetramer,[10] with a structure analogous to Pt(IV) alkyls, in which platinum has inserted into the cyclopropane ring and not a dimeric structure analogous to Zeise's dimer, as it was initially suggested.

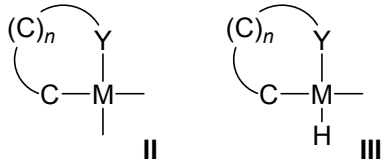


Scheme 1-2. Synthesis of the polymeric platina(IV)cyclobutane of Tipper and the dimeric structure initially proposed.

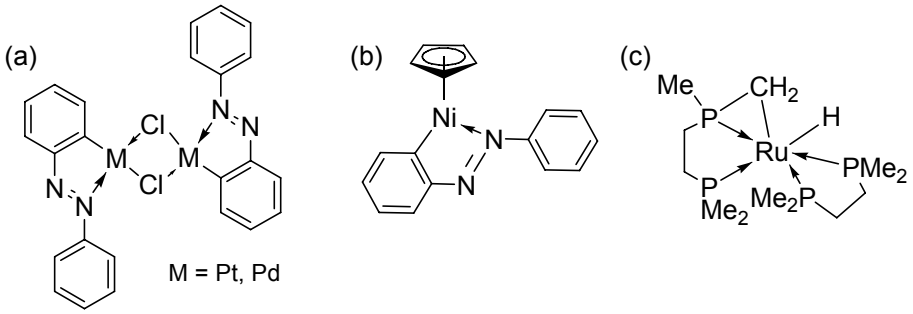
However, despite their discovery in the mid-fifties, metallacyclic compounds did not become intensively studied until their role in catalysis was appreciated. It is in the 1970s that the metallacyclic compounds of the transition elements have been the subject of considerable research as it was recognised that they were playing an important role in a number of catalytic reactions, *e.g*. alkene metathesis,[11] isomerization of strained carbocyclic rings,[12] cycloaddition of alkenes,[13] oligomerization of dienes[14] and in polymerisation reactions.[15]

1.2.2 Cyclometallated compounds

Cyclometallated compounds can be defined as being metallacyclic compounds in which a carbon atom is substituted by a heteroatom Y directly bound to the metal through a two electrons lone pair. Cyclometallated complexes of the type **II**, in which Y is typically a Lewis base and the chelate ring generally possesses three to seven members, with the five-membered ring being most prevalent. Precious metals are most common, although other transition metals can cyclometallate. Cyclometallated complexes of the type **III**, result of an hydrogen transfer from a coordinated ligand to a metal atom.



It is in the mid sixties that the first cyclometallated complexes were prepared by Cope *et al*.[16] by reacting aromatic azo compounds and potassium tetrachloroplatinate(II) or palladium(II) dichloride. However, two years before a cyclopentadienyl nickel compound with similar azobenzene ligand was obtained by Dubeck *et al*.[17] but they assigned the wrong structure to this compound as they proposed that the N=N double bond was π coordinated to nickel (Scheme 1-3). The first report of metal insertion in a C–H bond, leading to cyclometallated complexes of the type **III**, was made in a bis dimethylphosphinoethane (dmpe) complex of ruthenium [Ru(dmpe)$_2$], yielding a [HRu($CH_2PMe(CH_2)_2PMe_2$)(dmpe)] complex.[18]



Scheme 1-3. (a) Cycloplatinated and cyclopalladated complexes of Cope.[16] (b) Cyclopentadienyl azobenzene nickel compound of Dubeck.[17] (c) Formation of a cycloruthenated complex by insertion into a C–H bond of a methyl group of the coordinated ligand.

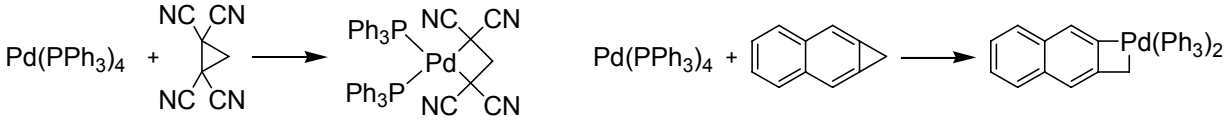
Despite the fact that the cyclometallation reactions under C–H activation have been known for more than thirty years[19] and represent one of the best developed

areas of organometallic chemistry, it is only almost two decades later that L. Lewis disclosed the discovery that cycloruthenated compounds displayed enhanced catalytic activity. Thus, olefin hydrogenation[20a] and the double alkylation of phenol with ethylene selectively in the *ortho* positions were performed with an *ortho*-ruthenated phosphite complex.[20b]

1.3 Formation of Palladacyclic Compounds

1.3.1 Insertion into C–C bonds

Oxidative addition of a C–C bond of cyclopropane to a metal centre provides a facile synthesis of metallacyclic complexes of a variety of transition metals. Regarding the group 10 of transition metal, most of the studies refer to the insertion of a metal in cyclopropane derivatives leading to metallocyclobutane.[21] The C–C bond cleavage of carbocyclic rings larger than cyclopropane or cyclopropene is less common, although it is known that cyclobutene derivatives can undergo this reaction. As may be expected, reactions with palladium are much less common than for platinum due to the fact that palladium is less able to accept electron density from the ring. Contrary to the reaction with Pt(II), in which an electrophilic attack on the organic ring has been proposed, the Pd^0 behaves as a nucleophilic moiety. Hence it is found that palladium will only insert into cyclopropanes containing good electron withdrawing substituants. Lenarda *et al.*[22] have demonstrated the formation of palladacyclobutanes **1** from tetracyanocyclopropane and tetrakis(triphenylphosphine)palladium (0), the latter inserting into the C–C bond containing the CN substituants (Scheme 1-4). Further investigations of tetrakis(triphenylphosphine)palladium(0) insertion into cycloproparenes has led to the preparation of an unstable palladacyclobuta[b]naphthalene **2**[23] product illustrated in Scheme 1-4.

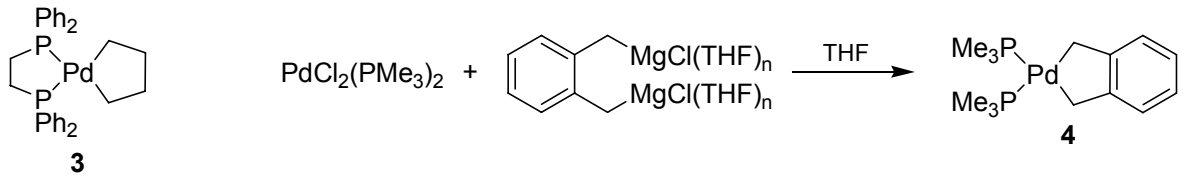


1 **2**

Scheme 1-4. Formation of palladacyclobutane derivatives *via* oxidative addition of C–C bond.

1.3.2 Reaction with dilithio and di-Grignard reagents

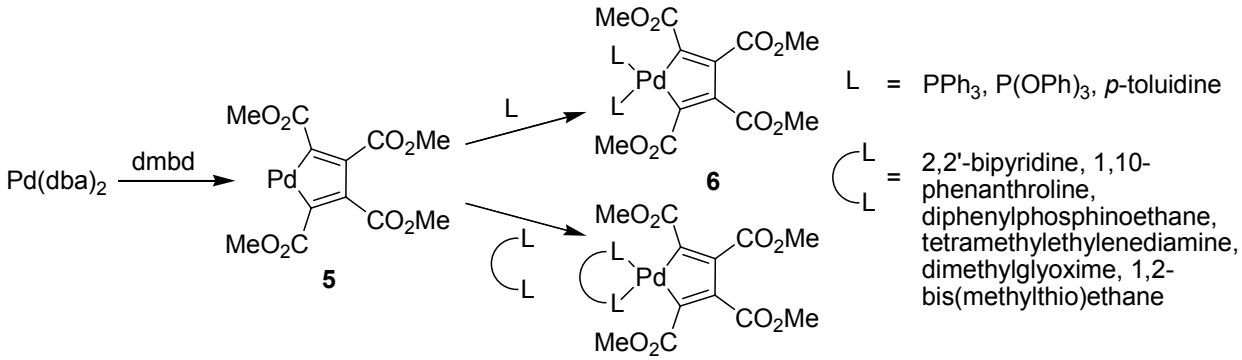
The most frequently synthesized palladacycles by transmetalation reaction are the five-membered rings, although in principle any ring size can be obtained. Reaction of 1,4-dilithiobutane with $[PdCl_2(dppe)]$[24a,b] at -70°C leads to the formation of the palladacyclopentane **3** (Scheme 1-5). This compound is thermally very stable considering that it contains *β*-hydrogen atoms available for hydride elimination and decomposes in about 12 hours in toluene whereas $[Pd(n\text{Bu})_2(dppe)]$ decomposes in about 1 hour. The use of the α,α-xylil di-Grignard reagent with $[PdCl_2(PMe_3)_2]$ yielded the formation of benzo[c]palladacyclopentene **4**[25] (Scheme 1-5).



Scheme 1-5. (**3**) Palladacyclopentane obtained by reaction of 1,4-dilithiobutane[24] and (**4**) benzo[c]palladacyclopentene synthesized from α,α-xylil di-Grignard reagent.[25]

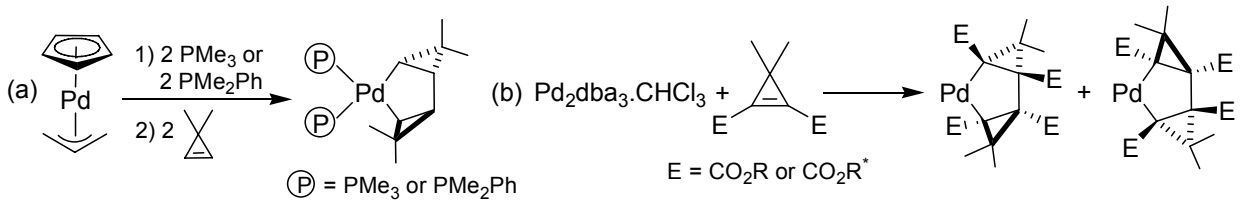
1.3.3 Palladacycles derived from homocoupling reactions of alkynes or alkenes

Reactions of metal complexes with alkenes giving metallacycloalkanes, or alkynes giving metallacycloalkadienes represent the most common and useful methods for synthesis of metallacyclic compounds. In the 1970s a series of palladacyclopentadienes has been made by Maitlis *et al*.[26] and Ishii *et al*.[27] using a zerovalent palladium starting material. Thus, reaction of dibenzylideneacetonepalladium, $[Pd(dba)_2]$ or $[Pd_2(dba)_3]$, with dimethyl-2-butynedioate (dmbd) at room temperature led to the formation of **5** which forms adducts **6** with either monodentate or bidentate donor ligands (Scheme 1-6). The quantitative oxidative-addition/coupling toward palladium(0) olefin complexes requires the electron-deficiency of the alkyne. Fewer examples are known of reactions with alkynes leading to palladacyclopentadienes[28,29,30] as palladium generally prefers to form monoalkyne complexes which tend to be inert to further acetylenic attack. This method of synthesis yields almost exclusively five membered ring systems.



Scheme 1-6. Formation of palladacyclopentadienes from dmbd reported 1970s.

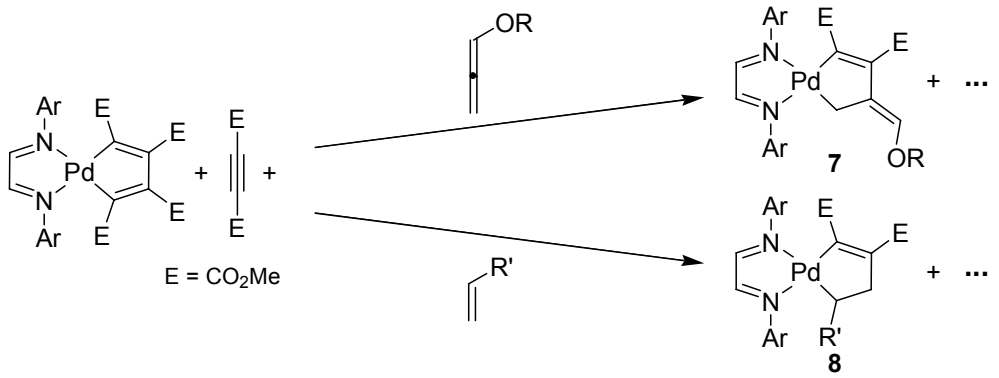
Besides electron deficiency, structural strain can also lead to the activation of an unsaturated molecule towards the cycloaddition reaction, *i.e*. the cycloaddition of cyclopropene derivatives (Scheme 1-7) on the in situ generated $[Pd(PR_3)_2]$[31] and the regioselective oxidative cyclization of C_2-symmetrical, chiral cyclopropene derivatives on $[Pd_2dba_3.CHCl_3]$.[32]



Scheme 1-7. (a) Cycloaddition of cyclopropene by Binger *et al*.[31] (b) Formation of *trans*-5-palladatricyclo[4.1.0.$0^{2,4}$]heptanes described by Hashmi *et al*..[32]

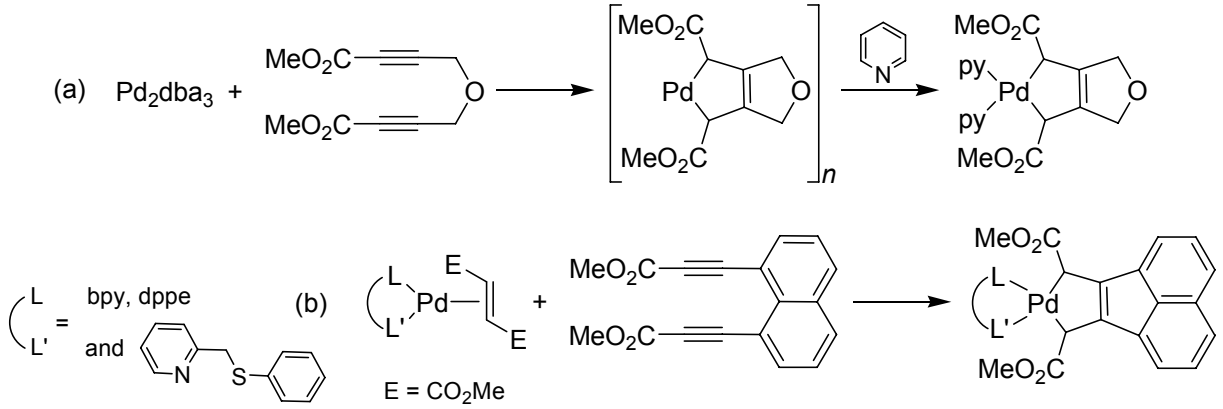
1.3.4 Palladacycles derived from heterocoupling reactions of unsaturated molecules or polyalkene or polyalkyne reactions

During their studies on co-cycloaddition of methoxyallene and dimethyl-2-butynedioate (dmbd) on a diazadiene palladium(0) fragment to form tetrahydronaphthalene derivatives, tom Dieck *et al*. noticed that the use of allenic ethers with better leaving groups was not resulting in improved yields but instead in the formation of stable palladacyclopentenes **7** (Scheme 1-8).[33a] The formation of palladacyclopentene **8** from dmbd and alkene was also successful, however, a considerable excess of alkene was necessary to compete with the oxidative coupling reaction of the second molecule of dmbd.[33b]



Scheme 1-8. Palladacyclopentene resulting of the heterocoupling reaction of dmbd with allenic ethers and dmbd with alkene.

Yamamoto *et al.*[34] and Canovese *et al.*[35] recently reported the synthesis of palladacyclopentadienyl derivatives from diyne diester. In both cases, the formation of a bicyclopalladacycle is observed as illustrated in Scheme 1-9.

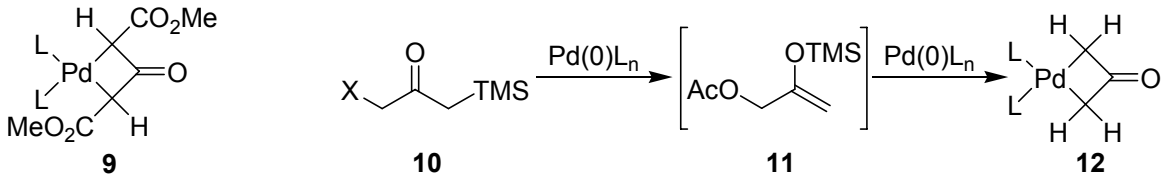


Scheme 1-9. Palladacyclopentadienyl derivatives issued of (a) flexible[34] and (b) rigid[35] diyne diester.

1.3.5 Formation of palladacycles *via* palladacyclization reactions

Metallacyclization involving coordinated ligands has been known for a long time (1970s)[19a] but it is only few years later that its application to hydrocarbyl systems has been recognized. Cyclization can be observed *via* oxidative addition to a distal C–H bond of functionalized alkyl groups. This reaction has been observed in palladium complexes by Clarke *et al.*[36] whereby dimethyl 3-oxoglutarate reacts with the zerovalent complex [PdL_4] (L = PPh_3) to give **9**. One decade later, Trost investigated

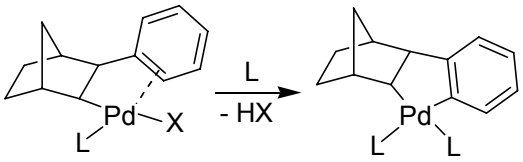
the scope and reactivity of the complexes obtained from reaction of Pd^0 with 1-acetoxy-3-(trimethylsilyl)propanone **10** and suggested that the Pd^0 would be at the origin of a Brook rearrangement to form the silyl enol ether **11** and after a catalytic oxidative addition into the allyl acetate, the acetate-induced desilylation would form palladacyclobutanone **12** (Scheme 1-10).[37]



Scheme 1-10. Palladacyclobutanones described by Clark *et al.* **9**[36] (L = PPh_3) and Trost **12** (L = PPh_3, $P(C_2H_5)_3$).[37]

Thermal palladacyclization was observed from dialkyl complex, palladacyclobutane has been prepared by intramolecular C–H insertion reaction of the corresponding dineopentyl palladium complex $[Pd(CH_2CMe_3)_2(PPh_3)_2]$.[38]

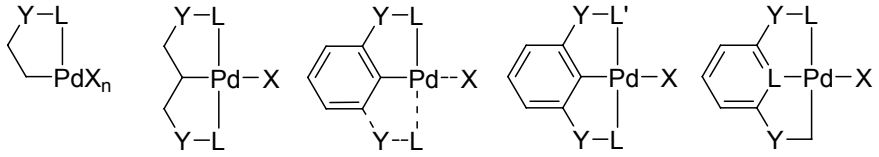
Electrophilic palladacyclization is an electrophilic substitution at the unactivated *ortho* aromatic carbon, the reaction being favored by the presence of electron-donating substituents on the aromatic ring (*para* to the palladium-carbon bond to be formed) of the open precursor.[39] The reaction corresponds to activation of a usually inert aromatic C–H bond *i.e*. Catellani and co-workers have showed that the ring closure readily occurs under very mild conditions with arylnorbornylpalladium complexes (Scheme 1-11),[39,40] that is probably favored by the previous coordination of the aromatic ring to the metal which provides the right steric arrangement.[41,42]



Scheme 1-11. Palladacyclization of arylnorbornylpalladium *via* activation C–H (L = mono- or bidentate nitrogen ligands or PPh_3).

1.4 Formation of Cyclopalladated Compounds

The vast majority of these complexes possess anionic four-electron (bidentate) or six-electron (tridentate) donor ligands, with five-membered nitrogen-containing rings being the most common (Scheme 1-12). In syntheses prior to 1980, the C-donor was sp^2-hybridized and primarily part of an aromatic ring, nowadays cyclopalladated compounds are known, for nearly all classes of ligands using different methods of preparation[43] and to be formed by a variety of mechanisms.[44a] Their synthesis is facile and it is possible to modulate their electronic and steric properties simply by changing (i) the size of the metallacyclic ring (3-10 membered), (ii) the nature of the metallated carbon atom (aliphatic, aromatic, vinylic, etc.), (iii) the type of donor group L (N-, P-, S-, O containing group, etc.) and its substituents (alkyl, aryl, etc.), or (iv) the nature of the X ligands (halide, triflate, or solvent, *i.e*. THF, H_2O). These factors determine whether the complex is dimeric, monomeric, neutral, or cationic. This flexibility confers a plethora of potential applications upon this class of compounds.



IV **V** **VI** **VII** **VIII**

Scheme 1-12. General cyclopalladated complexes structures (with L = donor and Y = linker group), cyclopalladated complexes (**IV** and **VI**), symmetric pincer type cyclopalladated complexes[45] (**IV** and **V**), dissymmetric pincer type cyclopalladated complexes (**VII** and **VIII**).

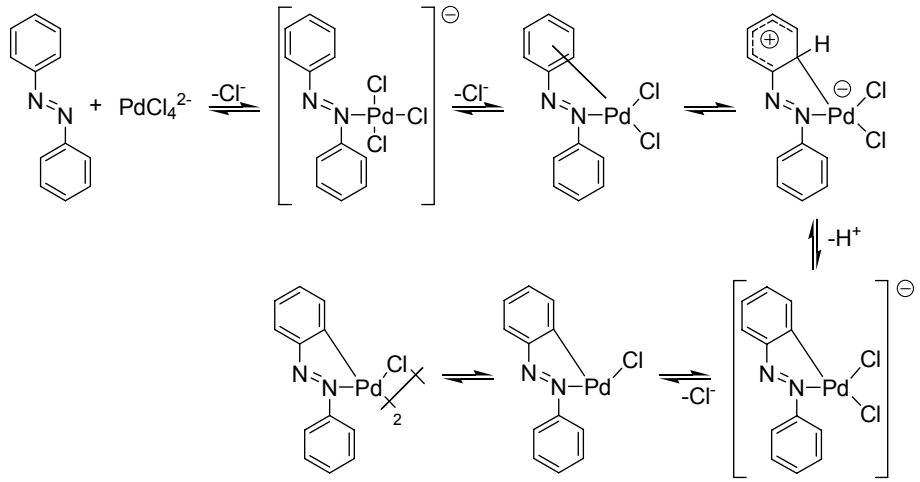
1.4.1 Cyclopalladation by orthopalladation and similar reactions

Cyclopalladation or bis-cyclopalladation was successfully used as early as 1965 for the complexation of Pd with C^N ligands,[16] and 1976 for the complexation of Pd with P^C^P ligands.[46]

The direct cyclopalladation, promoted by the chelate effect, is the most simple and there has been a considerable interest in the synthesis of these cyclopalladated complexes. This allows the use of simple organic starting materials and hence is

much more economic than those reactions that require the use of expensive and air-sensitive organometallic precursors (*e.g.*, RLi). The classical methods are the use of tetrachloropalladated salts with base[47] or palladium acetate in acetic acid, benzene or toluene.[48]

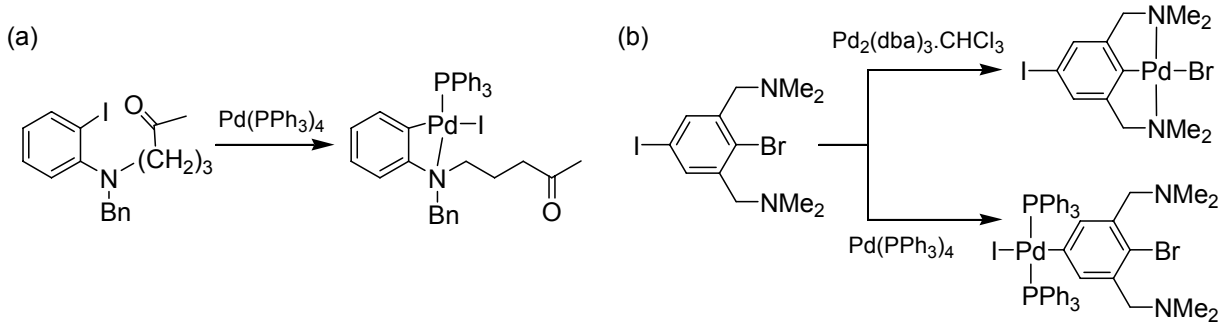
The cyclopalladation also termed orthopalladation means usually an intramolecular coordination of donor groups on the ligand precursor prior to formation of the Pd–C σ bond (Scheme 1-13).[19a,2] This method of cyclopalladation is quite similar to the palladacyclization of the arylnorbornylpalladium complexes[39,40] represented in Scheme 1-11.



Scheme 1-13. Proposed mechanism for the cyclopalladation of aromatic ligand, *i.e.* the azobenzene ligand of Cope[16].

1.4.2 Cyclopalladation *via* oxidative addition

In contrast to direct cyclometallation, oxidative addition to carbon–halogen bonds has hardly been explored, presumably because C–H activation has been a successful method for complexation. This method is used to generate cyclopalladated complexes which are not usually accessible by direct C–H bond activation, *i.e.* the syntheses of three-membered ring cyclopalladated compounds $[(PPh_2R)_2Pd(CH_2SR')Cl]$,[49a] by oxidative addition of $R'SCH_2Cl$ to $[Pd(PPh_2R)_4]$ and the formation of four-membered ring cyclopalladated compounds (Scheme 1-14).[49b]

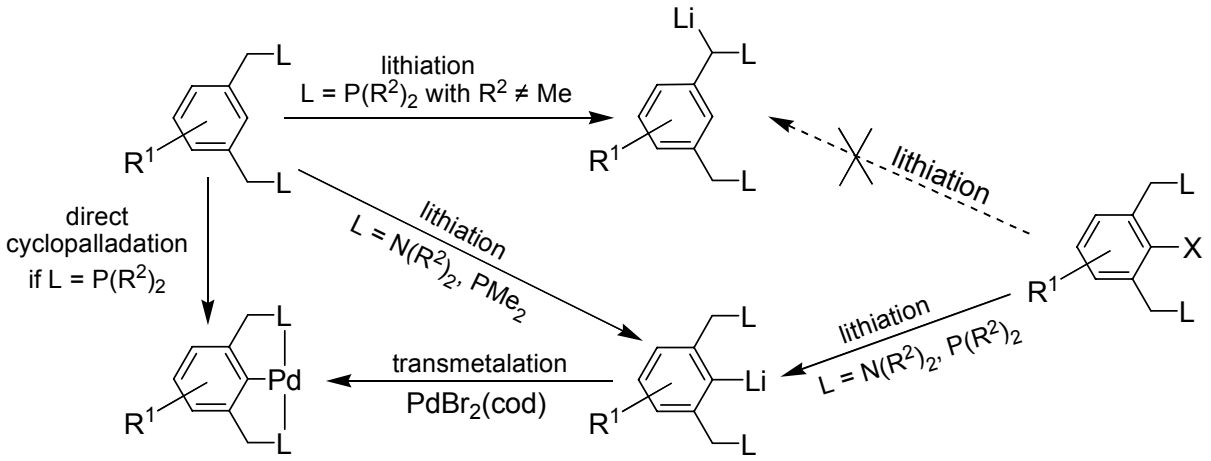


Scheme 1-14. (a) Formation of the unfavourable four-membered cyclopalladated complex.[49b] (b) Chemoselective palladation of the bifunctional pincer N^C^N ligand.[50]

The method might become more important when further functionalization on the ligand is required. Van Koten achieved the chemoselective palladation on pincer ligand at the C_{aryl}–I or C_{aryl}–Br bonds (Scheme 1-14).[50] In this way a series of bis-cyclopalladated complexes were prepared that have a second functional group available for further reactions such as a second metallation in order to obtain (hetero)bimetallic complex.

1.4.3 Cyclopalladated compounds formed by transmetallation reaction

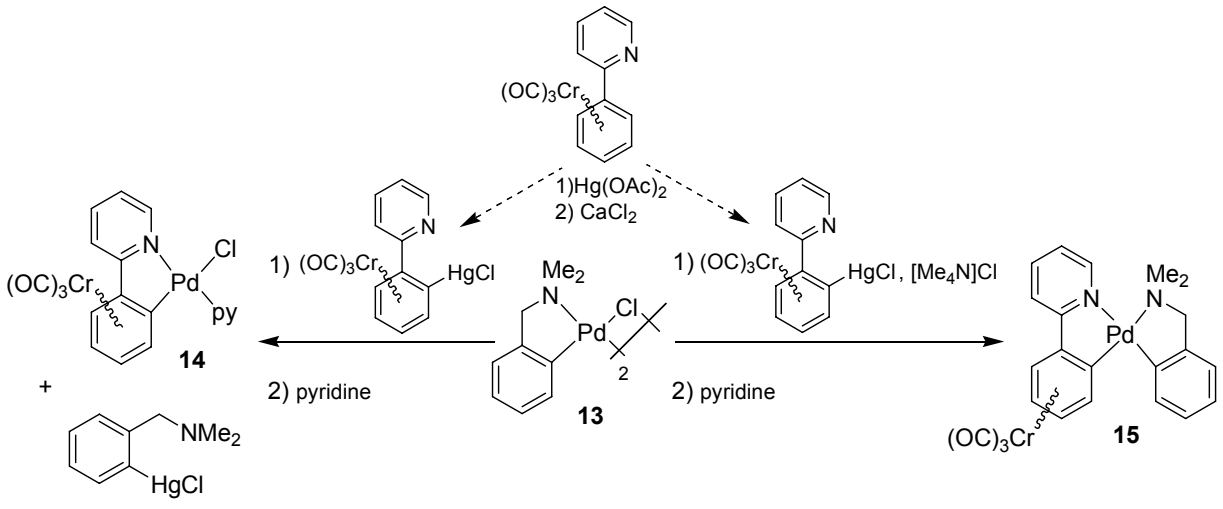
The transmetallation methodology involves in most cases organolithium or organomercury as transmetallating agents and is often-used to achieve bis-cyclopalladation. Similarly to the oxidative addition, the transmetallation could be used to generate cyclopalladated complexes which are not usually accessible by direct C–H bond activation, *i.e*. it has been used for the bis-cyclopalladation of N^C^N pincer ligands.[51] The lithiation of P^C^P or N^C^N pincer ligands has been studied and the use of an aryl halide precursor improves the selectivity, since Li/halide exchange is quantitative. In case of P^C^P pincer ligand, methyl substituants, on the phosphorus atoms, have to be used to prevent an isomerization into benzyllithium (Scheme 1-15).[52]



Scheme 1-15. Lithiation of N^C(H or X) (N and P(C(H or X) (P pincers ligands.

The formation of [Pd(C(N)(C'(L')] (with L' = N or O), an other type of bis-cyclopalladated compound, is easily realized by reacting organolithium or organomercury compounds (Li–C'(L' or HgCl–C'(L') with halogen dimer cyclopalladated complex (Scheme 1-16).53,54

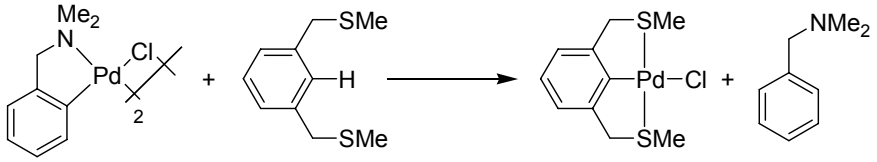
The synthesis of planar chiral cyclopalladated complexes containing the Cr(CO)3 moiety via transmetallation with organomercury compounds has been explored by Berger et al. since the cyclopalladation under C–H bond activation yielded irreversibly to the decomposition in Cr0 (Scheme 1-16).54



Scheme 1-16. Synthesis of the chiral planar palladacycle **14** and of the bimetallic heteroleptic *cis* bis-chelated Pd(II) complex **15** by a transmetallation reaction of the orthomercurated 2-[tricarbonyl(η^6-phenyl)chromium]pyridine.[54]

1.4.4 Cyclopalladated compounds formed by transcyclometallation reaction

Accordingly, transcyclometallation describes the substitution of one cyclometallated ligand by another one without the formation of significant and detectable amounts of purely inorganic compounds (dissociated metal salts). Transcyclometallation reactions were initially investigated with bidentate coordinating ligands,[55] but the concept has subsequently been extended also to terdentate-binding pincer ligands. Preliminary results included the reaction of the pincer ligand precursor S^C(H)^S with half an equivalent of the chloro-bridged cyclopalladated dimer of *N*,*N*-dimethylbenzylamine **13** which afforded the biscyclopalladated palladium complex [PdCl(S^C^S)] **16** and the free *N*,*N*-dimethylbenzylamine (Scheme 1-17).



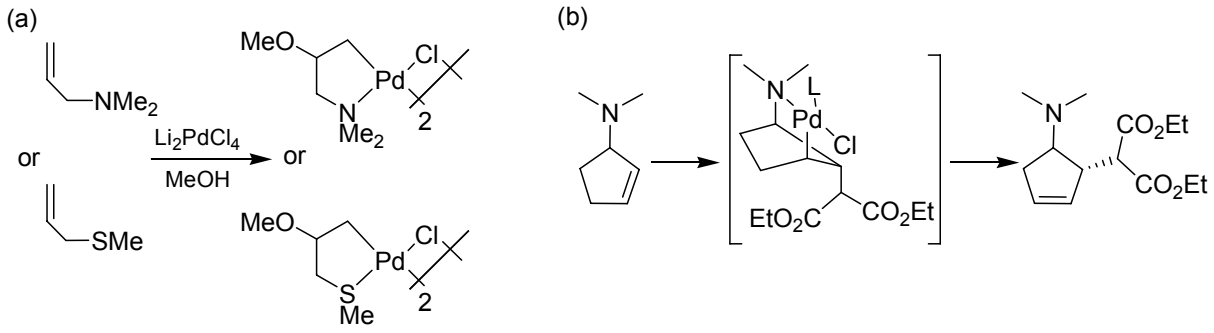
13 **16**

Scheme 1-17. Transcyclometallation reaction.

1.4.5 Cyclopalladation *via* carbopalladation of alkenes and chloropalladation of alkynes

1.4.5.1 Alkoxy- and carbopalladation of allylic amines and thioethers

The regiospecific carbopalladation of allylic and homoallylic amines and thioethers by stabilized enolates or carbanions and [Li_2PdCl_4] invariably provides stable five-membered cyclopalladated complexes.[56a,b] It has been demonstrated that the carbopalladation process occurs in a stereospecific manner, introducing malonate and palladium in a *trans* fashion across the unsaturated linkage (Scheme1-18).[56c] The reaction proceeds *via* external nucleophilic addition of the alkoxy anion onto the allylamines coordinated to the metal centre through the C=C bond and the nitrogen lone pair to produce the thermodynamically more stable five-membered cyclopalladated complexes.[57]

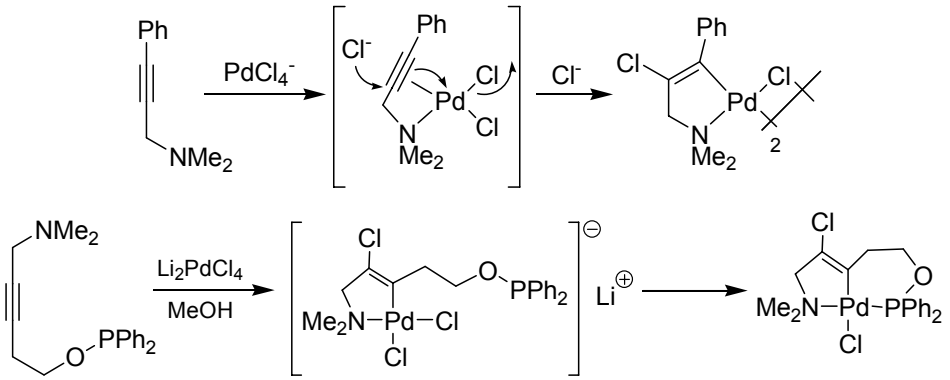


Scheme 1-18. (a) Alkoxypalladation and allylamine or thioether leading to cyclopalladated complexes. (b) *Trans*-carbopalladation of alkene.

1.4.5.2 *Trans*-chloropalladation of heterosubstituted alkynes

The reaction of propargyl amines and thioethers with [Li_2PdCl_4] occurs readily to afford exclusively the air-stable five-membered cyclopalladated compounds containing a palladium–vinyl bond resulting formally from the *trans* nucleophilic addition of the chlorine anion onto the C≡C bond (Scheme 1-19).[58a] This method tolerates a variety of alkyne functional groups (amines, pyridine, thioethers, phosphines, and phosphinites) and allows the preparation of palladacycles containing various metalate ring sizes.

Thus the reaction of [Li_2PdCl_4] with hetero-substituted alkynes $Me_2NCH_2C{\equiv}CCH_2CH_2L$ (L = S-*t*-Bu, NMe_2, PPh_2, and $OPPh_2$) affords the “pincer” cyclopalladated compounds (Scheme 1-19). This chloropalladation reaction is an interesting method for the generation of unsymmetrical pincer type cyclopalladated complexes. The following mechanism was proposed, the chloropalladation reaction proceeds through the coordination of only one donor group followed by coordination of the C≡C bond to the palladium. Selective intermolecular chloride nucleophilic addition on this activated triple bond affords the more thermodynamically stable cyclopalladated ring. Finally, coordination of the second donor group to the Pd centre yields the “pincer” palladacycles.[58b]



Scheme 1-19. *Trans*-chloropalladation of heterosubstituted alkynes.

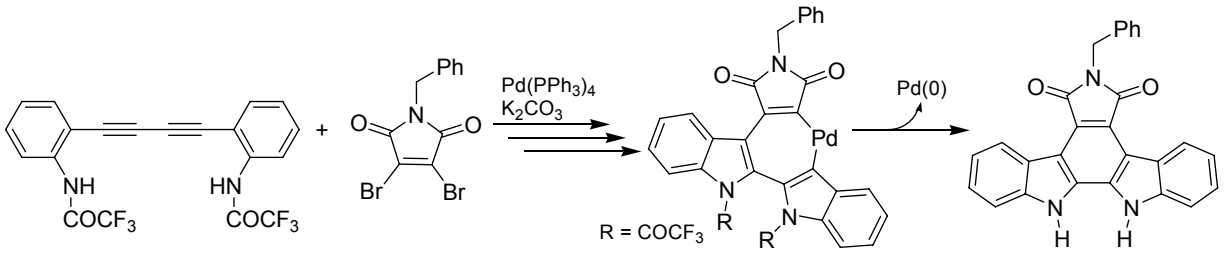
1.5 Palladacyclic and Cyclopalladated Compounds in Catalysis

1.5.1 Palladacyclic compounds

Palladacyclic compounds are most of the time intermediate species in catalytic processes[59] such as palladium-mediated cycloaddition reactions. Palladacycles are key intermediates in other types of palladium-catalyzed reactions, such as coupling reactions *via* C–H activation and the intramolecular Stille reaction but they are also assumed to be intermediates in Heck type cyclization reactions when the crucial reaction step, the *β*-hydrogen elimination, is inhibited.[60] They can be formed in the course of a sequence by C–H activation of usually inert groups, by oxidative coupling and they can also be demolished in the course of the same reaction sequence during which they have been formed. The cyclopalladation of alkyl(aryl) ligands is frequently invoked in palladium-catalyzed cyclization reaction.[61]

1.5.1.1 Palladacycles as intermediates: 6-membered rings and larger rings

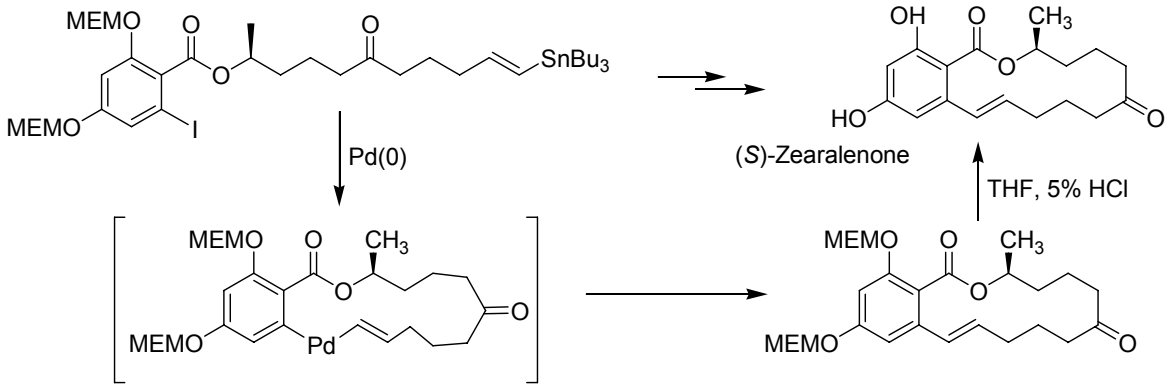
The typical reaction that 6-membered rings and larger palladacycles with two carbon-palladium *σ* bonds undergo is reductive elimination, *e.g*. the synthesis of the indolo[2,3-a]carbazole alkaloid ring system present in several active molecules such as arcyriaflavin A and the potent antitumor agent rebeccamycin (Scheme 1-20).[62] This is a facile process, thus explaining why it is difficult to detect these reactive intermediates.



Scheme 1-20. The polyannulation reaction, leading to the indolo[2,3-a]carbazole alkaloid ring system, is assumed to proceed *via* a palladacycloheptatriene.

For some palladium-catalyzed reactions their role as key intermediates is based on compelling mechanistic considerations (*e.g.* for the intramolecular Stille coupling reaction). Intramolecular palladium-catalyzed processes that involve a sequence of oxidative addition at aryl or vinyl halides, followed by a transmetallation step, generally proceed *via* palladacycles. This type of processes have found widespread application in the synthesis of naturally occurring macrocycles. An intramolecular Stille coupling reaction was the key step in the synthesis of (*S*)-zearalenone, a macrocyclic lactone (Scheme 1-21).[63]

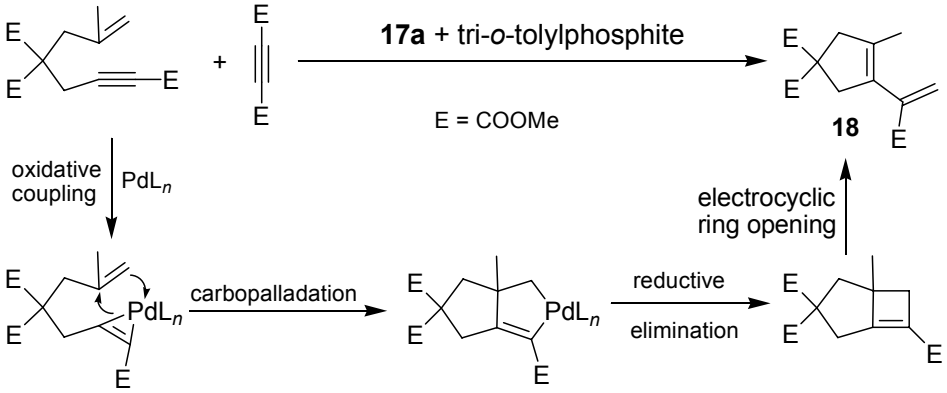
For some other reactions the presence of 6-membered rings and larger palladacycles as intermediates has to be regarded as a working hypothesis that is challenged by alternative mechanistic explanations.



Scheme 1-21. Oxidative addition of the supported Pd^0 catalyst to the aryl iodide bond, and transmetallation with the vinylstannane, to give the 15-membered palladacycle which lead, after reductive elimination and deprotection to (*S*)-zearalenone.

1.5.1.2 Palladacycles as intermediates: 5-membered rings and smaller rings

No matter how 6-membered rings and larger palladacycles are formed, they generally undergo a facile reductive elimination. 5-Membered palladacycles behave differently; the formation of 4-membered rings *via* reductive elimination is unfavourable and restricted to special cases. Instead, 5-membered palladacycles can react with a second equivalent starting material, or with added reagents resulting in domino processes[64] *i.e*. [2+2+2] cycloaddition reaction[61a,65] such as cyclo- and cyclocotrimerization of acetylenes,[26a,28,34,66] arynes,[67] or dimerization-carbostannylation of alkynes.[68]



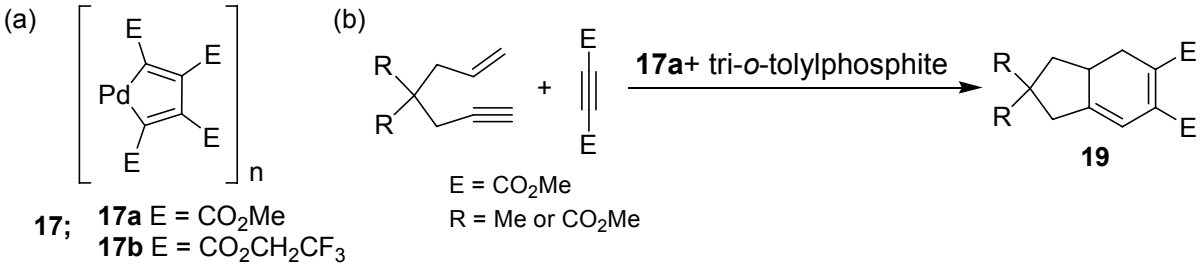
Scheme 1-22. Treatment of 1,6-enyne in presence of palladacyclopentadiene **17a** and tri-*o*-tolylphosphite and dimethyl-2-butynedioate (dmbd) leads to vinylcyclopentene **18**.[61b,69]

The three-membered organopalladium intermediates, resulting from the oxidative coupling of Pd^0 complexes with C=C or C≡C bonds of alkenes, alkynes, allenes, conjugated dienes, and other C–C multiple bonds including even arenes, are involved or suggested in various process such as oligomerization reaction of conjugated diene *via* the production of a bis(allyl)palladium[70] or in the conversion of enynes into vinylcyclopentene derivatives[69] (Scheme 1-22).

1.5.1.3 Palladacycles as catalysts

Thermodynamic, as well as kinetic stability is necessary for palladacycles to be applicable as catalysts. 5-Membered palladacycles that fulfil these requirements are

the derivatives of the polymeric tetrakis(alkoxycarbonyl)palladacyclopentadiene (TCPC) **17**, and the chiral palladatricycloheptane THC-catalysts[32a] (see (b) Scheme 1-7). Reductive elimination is unfavourable in both cases. The polymeric pre-catalysts TCPC **17** required an activation such as the addition of a ligand to break down the insoluble polymer to create the active specie. Trost has reported that ene-diyne [2+2+2] cycloaddition with an electron-deficient alkyne, leading to cyclohexadiene derivatives such as **19**, is catalyzed by **17a** in presence of tri-*o*-tolylphosphite (Scheme 1-23).[71] In contrast, with the TCPC catalyst **17b** that achieved an intramolecular enyne metathesis.[72] Other reactions of [2+2+2] cycloaddition catalyzed by TCPC type of catalyst have been reported such as co-cyclotrimerization of various alkynes,[28] of acetylenes with alkenes.[8a]

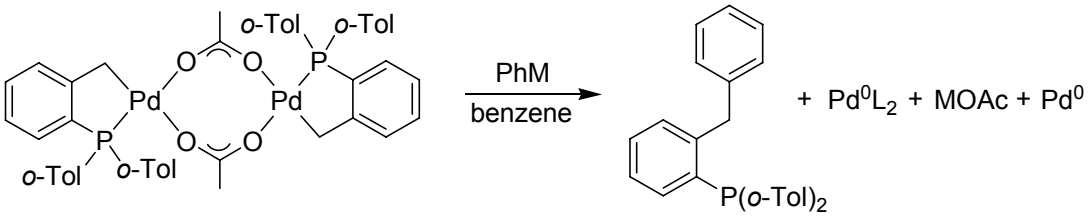


Scheme 1-23. (a) The polymeric tetrakis(alkoxycarbonyl)palladacyclopentadienes **17**. (b) The ene-diyne [2+2+2] cycloaddition with dmbd catalyzed by **17a**.[71]

Other reactions catalyzed by TCPC derivatives are cycloaddition reactions with intermediary palladadienes,[73] three-component synthesis of conjugated dienes,[74] the dimerization of allenyl ketones leading to functionalized furans,[75] hydrostannation of cyclopropene[76] and in Stille cross-coupling reaction.[77]

1.5.2 Cyclopalladated compounds

Cyclopalladated complexes are amongst the most active catalysts in Heck-type carbon–carbon bond formation and related carbon–heteroatom bond forming reactions.[78,45c] Heck type reactions are generally believed to work *via* a Pd(0)/Pd(II) catalytic cycle.[8] Starting with cyclopalladated pre-catalyst in the oxidation state +II a reduction step prior to catalysis would be necessary.

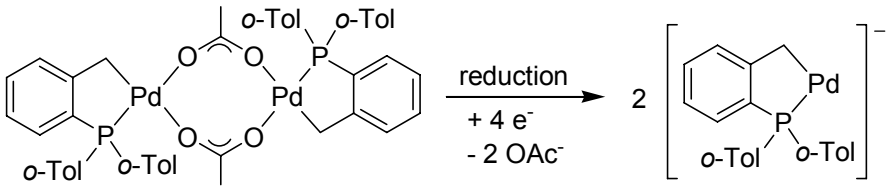


PhM with M = $SnMe_3$, MgBr, ZnCl

Scheme 1-21. Reduction of the Herrmann's cyclopalladated catalyst to Pd^0 species.

In the cases of the Stille, Grignard, Negishi and Suzuki-Miyaura cross coupling reactions, the reduction mechanism of the Herrmann's palladacycle into a catalytically active Pd^0 species has been elucidated by Hartwig[79] and extended by Böhm[80] (Scheme 1-21). Regarding the Mizoroki-Heck reaction a Pd(II)/Pd(IV) cycle was initially proposed since the cyclopalladated catalyst was recovered unchanged in good yield at the end of the reaction.[78a] However, after these initial speculations, all experimental evidence available to date speaks against such Pd(II)/Pd(IV) cycle.[81] It is now accepted that in most of the cases, the catalytically active species involved in these reactions are based on Pd^0 and that the reaction proceeds through a Pd(0)/Pd(II) catalytic cycle.[82,83]

How act the cyclopalladated compounds in Mizoroki-Heck reaction? Consorti *et al*. described their C^N cyclopalladated pre-catalyst as a reservoir of the catalytically active Pd^0 species, *i.e*. Pd colloids, or highly active forms of low ligated Pd^0 species,[84] and Herrmann and co-workers described a cyclometallated anionic palladium(0) as the catalytically active species (Scheme 1-22) assuming the reduction of the dimeric pre-catalyst without cleavage of the metallacycle.[83]



Scheme 1-22. Reduction of the Herrmann's pre-catalyst without rupture of the carbon–palladium bond.

1.6 Aim and Outline of this Thesis

The research described in this thesis ranges from the study of the formation of palladacycles and cyclopalladated complexes (Chapters 2,3 and 4) and the investigation of their catalytic properties (Chapters 3 and 4) to the study of the cyclic palladium(0)-complexes, containing chelating *α*-diimines ligands, in catalytic semi hydrogenation of allenes to (*Z*)-alkenes (Chapter 5).

In *Chapter 2* the synthesis of palladacyclopentadienes complexes from $[Pd(dba)_2]$ and dissymmetric electron-poor alkynes, such as methyl phenylpropynoate, methyl (4-methoxyphenyl)propynoate and methyl (4-nitrophenyl)propynoate with various bidentate *N*-ligands, 2,2'-bipyridine, 1,10-phenanthroline, tetramethylenediamine and bis(arylimino)acenaphtene is presented. X-ray crystal structures of dissymmetric and symmetric palladacyclopentadienes have been obtained. The regioselectivity and the stability of these complexes will be presented.

The kinetics, mechanistic aspects and the scope of the three-components synthesis of conjugated dienes from alkyne catalyzed by $[Pd(bis(arylimino)acenaphtene)(CCOOMe)_4]$ are described in *Chapter 3*. Based on the experiments, a general mechanism is proposed for this catalytic formation of dienes.

Chapter 4 deals with the synthesis and characterization of cyclopalladated and cycloplatinated complexes of the type $[M(C^{\wedge}N)(LL)]^+$ ($C^{\wedge}N$ = *N,N*-dimethylbenzylamine or benzo[*h*]quinoline and LL = 4,4'-bis(*tert*-butyl)-2,2'-bipyridine or bis(diphenylphosphino)ethane). X-ray crystal structure determinations of complexes have been determined. The complexes have been employed as pre-catalyst in the Sonogashira cross-coupling reaction and the results will be discribed. The tentatives about the preparation of cyclopalladated complex of type $[Pd(C^{\wedge}N)L_n)]^-$ and the use of biphosphinine as ligand to stabilize such anionic zerovalent palladium complex will be discussed

In the *Chapter 5* the palladium complexes of the type [Pd(bis(arylimino)acenaphthene)(η^2-alkene)], containing electron-poor alkenes, have been employed as pre-catalysts for the reaction of hydrogenation of different functionalized allenes. The results will be discussed and from these experiments a plausible reaction mechanism will be proposed.

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Chapter 2

Synthesis and Characterization of Palladacyclopentadienes Obtained from Dissymmetric Alkynes

Abstract

The complexes (1,3-dicarbomethoxy-2,4-diphenylbuta-1,3-dien-1,4-diyl)(N,N) palladium(II) and (1,3-dicarbomethoxy-2,4-di(4-methoxyphenyl)buta-1,3-dien-1,4-diyl)(N,N)palladium(II), where N,N = 2,2'-bipyridine, tetramethylenediamine, 1,10-phenanthroline have been obtained by reaction of [Pd(dba)$_2$] with the respective bidentate N-ligand and two equivalents of methyl phenyl or methyl (4-methoxyphenyl)propynoate via a completely regioselective head-to-tail coupling of the asymmetric acetylenes. Such regioselectivity, especially in conjunction with the high yield, is very unusual in the formation of palladacycles and has so far only been observed for head-to-head or tail-to-tail coupling. The reactions with methyl (4-nitrophenyl) or methyl (4-trifluoromethylphenyl)propynoate did not lead to complete regioselectivity. The X-ray crystal structures of (1,3-dicarbomethoxy-2,4-diphenylbuta-1,3-dien-1,4-diyl)(phen)palladium(II), (1,3-dicarbomethoxy-2,4-di(4-methoxyphenyl)buta-1,3-dien-1,4-diyl)(bipy)palladium(II) and (1,3-dicarbomethoxy-2,4-di(4-nitrophenyl)buta-1,3-dien-1,4-diyl)(bipy)palladium(II) were obtained and revealed pseudo square planar metal centres, the palladacycles and chelate rings being essentially planar.

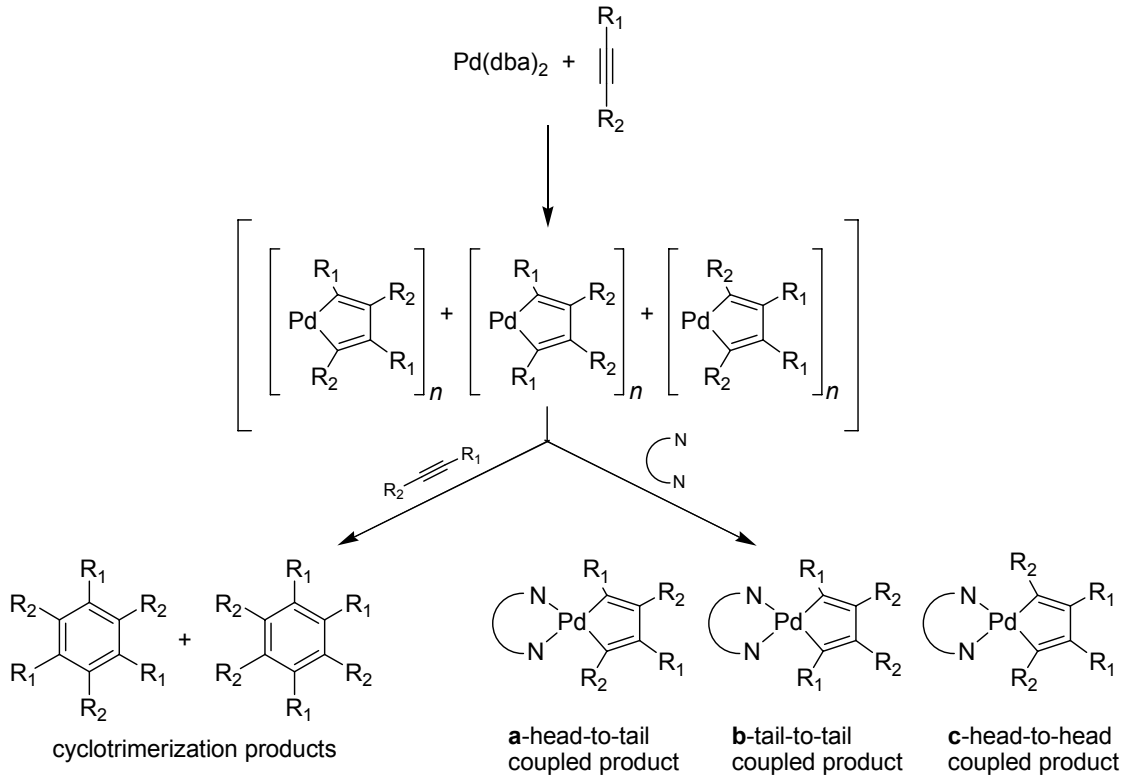
2.1 Introduction

Metallocyclopentadiene complexes, $[MC_4R_4]L_n$, are key intermediates in the oligomerization, cyclooligomerization or cyclocooligomerization of various alkynes using transition metal catalysts as Ti,[1] Zr,[2] Co,[3] Rh and Ir,[4] Ni, Pd and Pt,[5] Cr,[6] Ta[7] and Ru[8]. These intermediates are involved in the carbometallation mechanism or more frequently in the [2+2+2] cycloaddition mechanism of these catalytic processes. In the 1970s, Maitlis *et al*.[9-11] and Ishii *et al*.[12] have independently reported the formation of oligomeric tetracarboalkoxy palladacyclopentadiene from a palladium(0) dibenzylidenacetone (dba) complex and two molecules of dimethyl-2-butynedioate (dmbd), $[Pd(CCOOMe)_4]_n$. The latter can be converted into several derivatives including dienes, mellitates, and palladacyclopentadienes $[PdL_2(CCOOMe)_4]$ respectively by addition of bromine, an excess of dmbd or an excess of ancillary ligands (L). The palladacyclopentadienes, $[PdL_2(CCOOMe)_4]$, can be also formed *via* a complex $[PdL_2(\eta^2\text{-dmbd})]$. However, π-acetylenic complexes are more stabilized with increasing the π-acceptor character of L and/or the bulkiness of the ancillary ligand. Phosphines and bidentate N-ligands allow the oxidative cyclization, the insertion of a second acetylene to produce the palladacyclopentadiene. This is contrary to phosphites or to the very bulky *N*,*N'*-di-*tert*-butyldiazadiene, which yield an unreactive π-acetylenic intermediate.[13,14]

Palladium-catalyzed reactions involving unsaturated molecules and palladacyclopentadienyl derivatives have attracted much attention; for instance, cyclocotrimerization of acetylenes,[9,14] cyclocotrimerization of acetylenes with alkenes,[15,16] cycloaddition of enynes,[17] three-component synthesis of conjugated dienes,[18] dimerization-carbostannylation of alkynes,[19] cyclocotrimerization of diynes and alkynes,[20] cyclotrimerization of arynes,[21] cyclocotrimerization of arynes and alkynes[22] or alkenes[23] and Stille coupling[24] are well known. However, despite the importance of palladacyclopentadienyl derivatives, the first detailed mechanistic study on the formation of these compounds has been published only recently by Canovese *et al*.[25]

The regiochemical outcome of the formation of palladacyclopentadienes involving dissymmetric alkynes is difficult to predict a priori, due to the two possible, often rather similar, orientations of the incoming alkyne during the insertion into the putative

Pd(η^2-alkyne) intermediate (Scheme 2-1). The aim of this work is to study the feasibility and selectivity, if any, of the formation of palladacyclopentadienes starting from dissymmetric alkynes.



Scheme 2-1. Regioselectivity of oxidative cyclization of asymmetric alkyne on palladium.

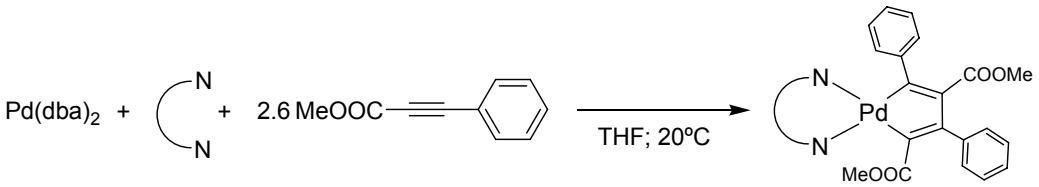
2.2 Results

Initially, the synthesis of palladacyclopentadienes from alkynes in the presence of various chelating bidentate nitrogen ligands (NN) was executed by reaction of [Pd(dba)$_2$], the relevant alkyne and the specific NN ligand in acetone. However, after product formation, consecutive decomposition was observed in most cases. The palladacycles were successfully synthesized by reaction of [Pd(dba)$_2$] with 1.0 equivalent of the NN ligand and 2.6 equivalents of the respective acetylenic compound in THF for 1 to 3 hours at 20ºC. The new compounds are air-stable solids, which are very soluble in chloroform and dichloromethane. They have been analyzed by elemental analysis or mass spectroscopy and by ^{1}H and ^{13}C NMR spectroscopy in solution. The most characteristic chemical shifts of all complexes, in ^{1}H NMR, are the

ones that correspond to the methoxycarbonyl groups (Scheme 2-1; R_1 = COOMe). They can act as a probe for the stereochemistry of compounds **1**-**10**, *i.e*., symmetric complexes (of types **b** and **c**) show one peak for the methoxycarbonyl groups and the asymmetric one (type **a**) shows two resonances for the methoxycarbonyl groups. The results of the reaction of [Pd(dba)$_2$], acetylenic and several NN ligands are compiled in Table 2-1.

2.2.1 Synthesis of palladacyclopentadienes from methyl phenylpropynoate

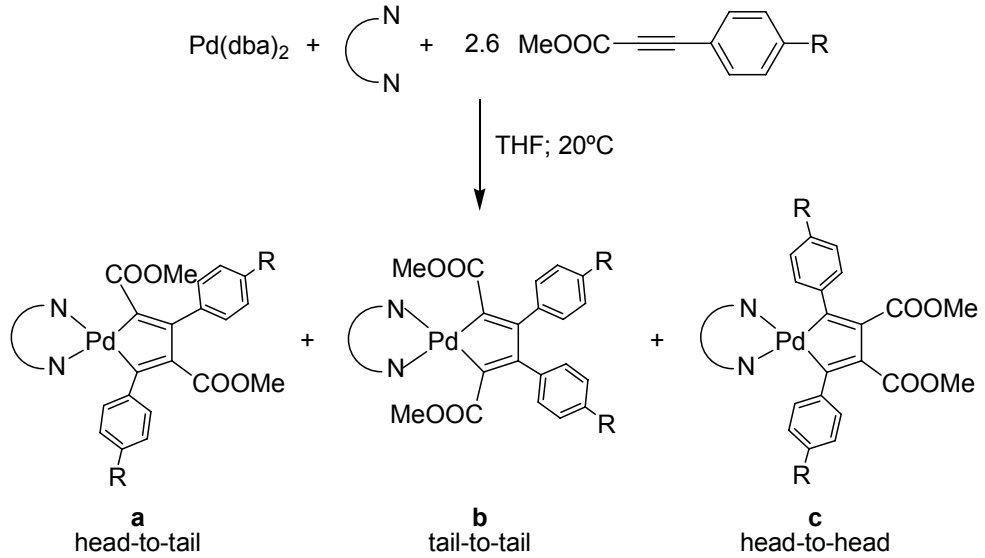
The palladacycles **1a**-**3a** were synthesized in good yield (35-70%) by reaction of [Pd(dba)$_2$] with 1.0 equivalent of the specific NN ligand such as 2,2'-bipyridine (bipy), *N*,*N*-tetramethylethylenediamine (tmeda), 1,10-phenanthroline (phen) and 2.6 equivalents of methyl phenylpropynoate in THF (Scheme 2-2). In all cases a stable orange-yellow solid was obtained and their ^{1}H NMR spectrum evidenced the presence of a single palladacycle in each case. The palladacyclopentadienes **1a**-**3a** were obtained as pure regioisomers *via* a completely regioselective 'head-to-tail' coupling of the two dissymmetric alkynes involved. Unfortunately the bis(*p*-tolyl)acenaphtenequinonediimine (*p*-tolyl-bian) ligand proved to be unsuitable, no complex could be isolated from the reaction with [Pd(dba)$_2$] and methyl phenylpropynoate in this case.



1a; NN = bipy
2a; NN = tmeda
3a; NN = phen

Scheme 2-2. Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-diphenylcyclopentadiene **1a**-**3a**.

2.2.2 Synthesis of palladacyclopentadienes from methyl (4-methoxyphenyl) propynoate



4; NN = bipy; R = OMe
5; NN = tmeda; R = OMe
6; NN = phen; R = OMe
7; NN = bipy; R = NO_2
8; NN = tmeda; R = NO_2
9; NN = phen; R = NO_2
10; NN = p-tolyl-bian; R = NO_2

Scheme 2-3. Synthesis of palladacyclopentadienes with methyl (4-methoxyphenyl)propynoate, methyl (4-nitrophenyl)propynoate and their three possible regioisomers.

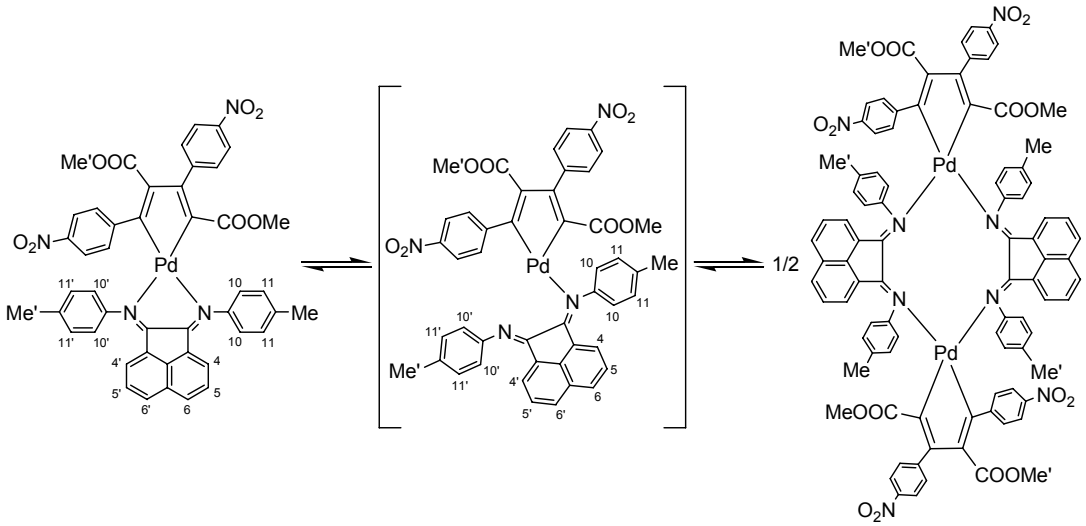
The palladacycles **4a**-**5a** (Scheme 2-3) were also obtained in good yield (35-70%) by a completely regioselective 'head-to-tail' coupling of methyl (4-methoxyphenyl)propynoate. The reaction with phenanthroline as the ligand did lead only to the formation of a trace of product. From the NMR of the crude mixture this could be identified as the 'head-to-tail' coupled regioisomer **6a**. The use of the bulkier *p*-tolyl-bian ligand does not lead to the formation of palladacyclic compounds of the type obtained above.

2.2.3 Synthesis of palladacyclopentadienes from methyl (4-nitrophenyl)propynoate

The palladacycles **7**-**10** were synthesized in good yield (35-70%) but, contrary to the previous cases, the reaction does not occur *via* a completely regioselective 'head-

to-tail' coupling. A mixture of two regioisomers out of the possible three is obtained (Scheme 2-3), but the 'head-to-tail' coupled product is still the major one. Is the second regioisomer obtained from a 'head-to-head' or 'tail-to-tail' coupling?

It is difficult to predict the nature of the coupling since no significant steric repulsion is involved in comparison to the previous examples. No discrimination between symmetric regioisomer, **b** or **c**, could be made based on NMR. The structural assignment as the 'tail-to-tail' coupling product **b** has finally been based on the X-ray crystal structure determination of **8b** (Figure 2-1). It is important to note that, contrary to the previous cases, the use of *p*-tolyl-bian does lead to the formation of palladacyclopentadienes and the 'head-to-tail' coupled product **10a** has been obtained as the single regioisomer. This complex shows fluxional behaviour on the NMR time scale involving the atoms on the *ortho* (H10) and *meta* (H11) positions of the *N*-phenyl rings of the bian ligand and can be ascribed to hindered rotation around the *N*-aryl axis of the bian ligand, by which process the diastereotopic *ortho* (and *meta*) atoms interconvert. This behaviour was not observed for the [Pd(*p*-tolyl-bian)$(CCOOMe)_4$] analogue,[26] in which case protons H(4), H(5) and H(6) are also averaged at room temperature and de-coalesce at low temperature. The process involved is most likely a chelate dissociation, where the N-ligand coordinates in a monodentate fashion, facilitating rotation. A similar case involving *p*-anisyl-bian has been reported.[27]



Scheme 2-4. Formation of a dimer of **10a**.

The chelate dissociation could lead to the formation of a dimeric species as observed for [Pd(bipy)$(CCOOMe)_4$][26] *via* a mono-coordinated intermediate (Scheme 2-4) or *via*

the dimeric form with a bridging C=O as reported for [Pd(*o,o'*-dimethylpyridine)$_2$(CCOOMe)$_4$].[28] The dimer formation was confirmed by the concentration-dependent dynamic behaviour observed for **10a**, which indicates an equilibrium between a mono- and a binuclear species.

Table 2-1. Observed regioselectivity for the various cases studied.

Entry	Compound nº	Ligand NN	E≡—C$_6$H$_4$—R R	Regioisomer (%)[a]			Note
				a	**b**	**c**	
1	**1a**	bipy	H	>99	-	-	
2	**2a**	tmeda	H	>99	-	-	
3	**3a**	phen	H	>99	-	-	
4	**–**	*p*-tolyl-bian	H	-	-	-	[b]
5	**4a**	bipy	OMe	>99	-	-	
6	**5a**	tmeda	OMe	>99	-	-	
7	**6a**	phen	OMe	>99	-	-	[c]
8	**–**	*p*-tolyl-bian	OMe	-	-	-	[b]
9	**7**	bipy	NO_2	66	33	-	[d]
10	**8**	tmeda	NO_2	95	5	-	
11	**9**	phen	NO_2	66	33	-	
12	**10**	*p*-tolyl-bian	NO_2	>99	-	-	
13	**12**	bipy	CF_3	89	11	-	

[a] ^{1}H NMR was done on the crude mixture before work up. [b] No palladacyclopentadiene formed. [c] Only traces were observed by ^{1}H NMR. [d] The benzenic derivatives arising from the cyclotrimerization product of the alkyne was also observed.

2.2.4 X-ray Crystal Structures of 3a, 4a, 7a and 8b

The adopted numbering schemes of the molecular structures of **3a**, **4a**, **7a** and **8b** are depicted in Figures 2-1 to 2-4; selected bond distances, bond angles and torsion angles have been compiled in Table 2-2. All complexes **3a**, **4a**, **7a** and **8b** are characterized by a distorted square-planar coordination around the metal centre. The palladacycle itself and the chelate ring are essentially planar as indicated in **3a**, **4a** and **7a** by the small deviations from the least-squares planes, which are 0.01(1) and

0.02(1) Å for C16 and C13 of **3a**, 0.05(1) and -0.06(1) Å for C14 and C6 of **4a** and 0.05(1) and -0.07(1) Å for C14 and C6 of **7a**.

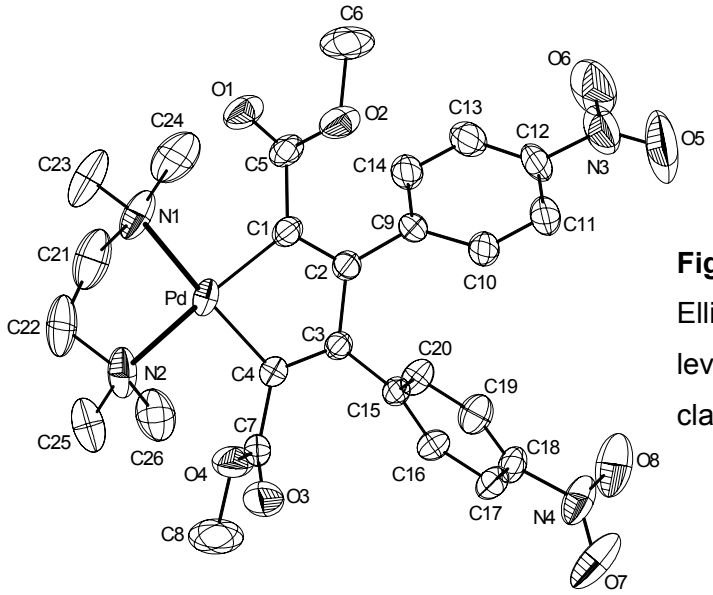


Figure 2-1. Crystal structure of **8b**. Ellipsoids are at the 50% probability level; hydrogen atoms are omitted for clarity.

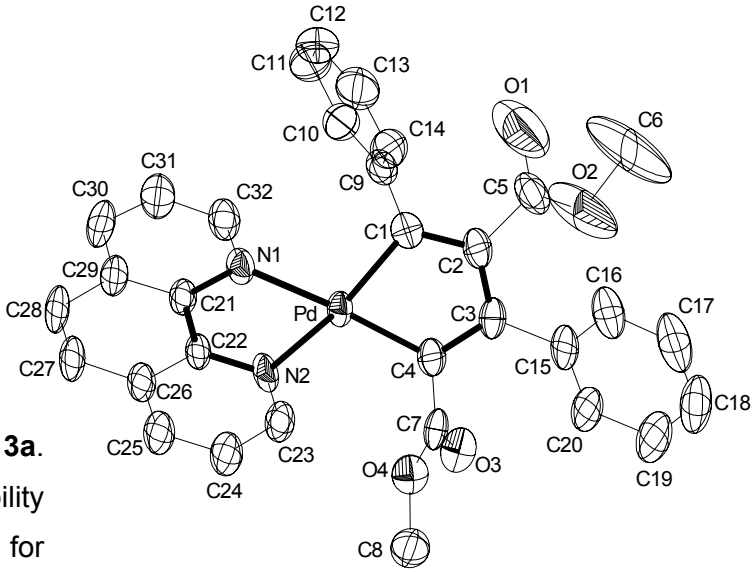


Figure 2-2. Crystal structure of **3a**. Ellipsoids are at the 50% probability level; hydrogen atoms are omitted for clarity.

The distortion from square planarity is reflected by the dihedral angle between these planes, amounting to 21.6(3)º, 23.2(1)º and 19.0(1)º for **3a**, **4a**, **7a**, respectively. These are comparable to those of other palladacyclopentadiene complexes, *i.e.*, for (bipy)pallada-2,3,4,5-tetrakis(carbomethoxy)-2,4-cyclopentadiene and its phenyl-bip analogue where a dihedral angle of 15.6(4)º and 27.1(4)º, respectively, has been observed.[26] Considering **3a**, we can explain the dihedral angle by an intermediate interaction of the phenanthroline, as compared to the bipy and phenyl-bip, with the ester group and the phenyl group on the palladacycle. The **3a**

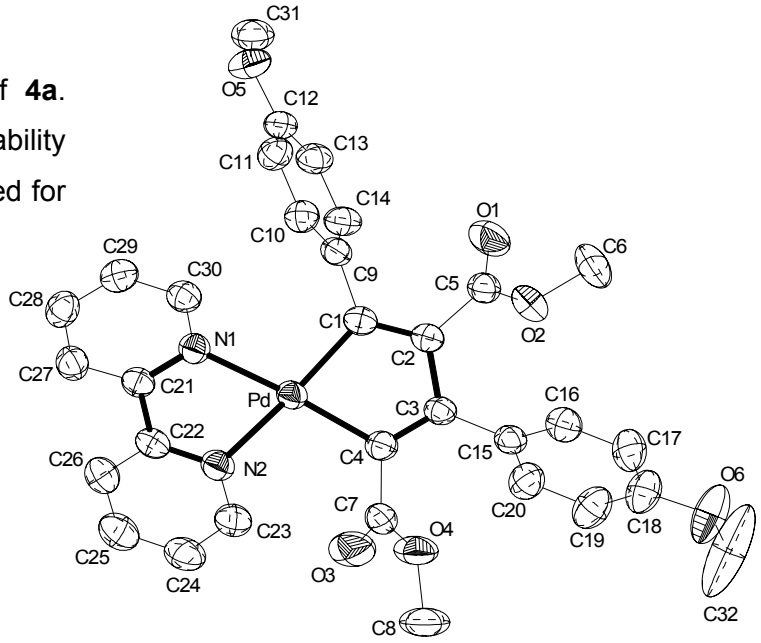
bite angle, N12–Pd–N1 of 78.1(3)º, is somewhat smaller than the similar bite angle in the palladium bis(methoxycarbonyl) coordination compound $[Pd(phen)(CO_2CH_3)_2]$[29] (82.5(3)º), due to a larger steric encumbrance of the palladacycle compared to the two mutually *cis* carbomethoxy groups.

Table 2-2. Selected distances [Å] and angles (º) of **3a**, **4a**, **7a** and **8b** with esd's in parenthesis.

	3a	**4a**	**7a**	**8b**
atoms		**distance**		
Pd-N1	2.143(8)	2.152(3)	2.122(6)	2.188(4)
Pd-N2	2.194(7)	2.162(3)	2.167(7)	2.192(4)
Pd-C1	2.037(9)	2.008(3)	2.032(7)	2.023(3)
Pd-C4	1.997(9)	2.015(4)	1.999(7)	2.027(3)
C21-C22	1.427(12)	1.492(5)	1.473(11)	1.483(9)
C1-C2	1.390(13)	1.346(6)	1.337(10)	1.357(5)
C2-C3	1.454(13)	1.483(5)	1.472(10)	1.473(5)
C3-C4	1.386(13)	1.348(5)	1.363(10)	1.354(5)
atoms		**bond angle**		
N1-Pd-N2	78.1(3)	76.20(12)	77.2(3)	82.94(15)
C1-Pd-C4	80.8(4)	78.51(14)	79.3(3)	79.07(13)
N1-Pd-C4	172.3(3)	167.90(15)	167.5(3)	176.92(13)
N1-Pd-C1	101.3(3)	104.17(13)	101.3(3)	99.13(14)
N2-Pd-C4	102.2(3)	104.41(14)	104.3(3)	98.74(14)
N2-Pd-C1	162.0(3)	164.62(14)	170.1(3)	176.38(13)
Pd-N1-C21	113.3(6)	115.8(2)	116.0(5)	103.3(3)
Pd-N2-C22	111.8(6)	115.4(2)	113.1(5)	106.0(3)
Pd-C1-C2	112.7(6)	116.9(3)	115.0(5)	116.4(2)
Pd-C4-C3	117.0(7)	118.0(3)	117.1(5)	116.1(2)
C1-C2-C3	117.2(7)	114.4(3)	115.8(6)	113.8(3)
C4-C3-C2	112.3(8)	111.9(4)	112.3(6)	114.3(3)
atoms		**torsion angle**		
N1-C21-C22-N2	-2.3(13)	14.5(5)	-12.5(11)	59.1(6)
C1-C2-C3-C4	1.5(12)	5.5(5)	0.8(10)	-0.2(4)

Regarding **4a** and **7a** (Figure 2-3 and 2-4), the direct comparison with the $[Pd(bipy)(CCOOMe)_4]$ analogue confirms the origin of the intermediate torsion indicated above. The bite angles N1–Pd–N12 of 76.2(12)º and 77.2(3)º of **4a** and **7a**, respectively, are similar to that of the $[Pd(bipy)(CCOOMe)_4]$ analogue (77.6(3)º). Meanwhile, it is smaller than the one of di-(η^1-C) carbamoyl-palladium coordination compound $[Pd(CON(CH_2)_4CH_2)_2(bipy)]$[30] (78.8(6)º) due to a larger steric encumbrance of the palladacycle compared to the two mutually carbon sp^2 from the *cis* carbamoyl groups.

Figure 2-3. Crystal structue of **4a**. Ellipsoids are at the 50% probability level; hydrogen atoms are omitted for clarity.



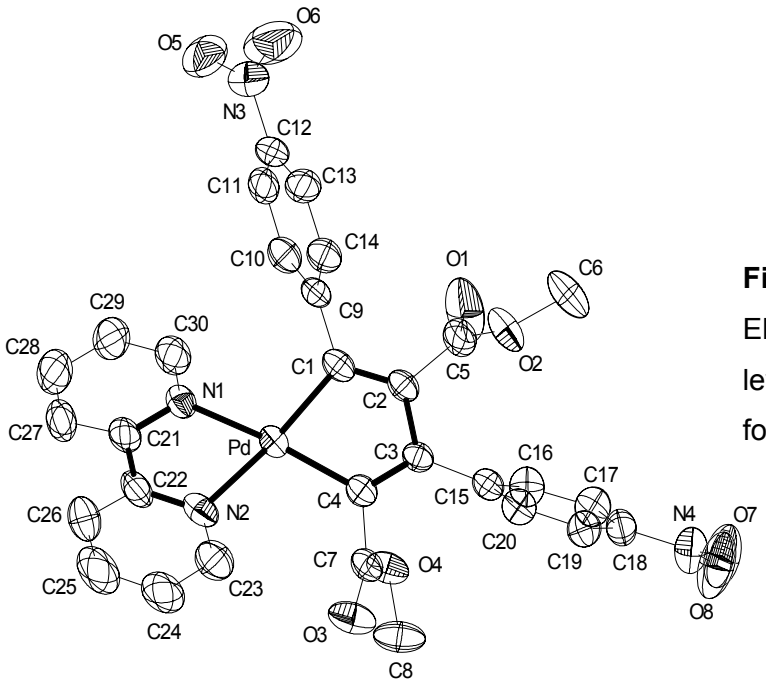


Figure 2-4. Crystal structure of **7a**. Ellipsoids are at the 50% probability level; hydrogen atoms are omitted for clarity.

Regarding **8b** (Figure 2-1), the bite angle C1–Pd–C4 of 79.07(13)º is somewhat smaller than the one in the diarylpalladium coordination compound [Pd(tmeda)(2,4,6-F_3-C_6H_2)(4-MeO-C_6H_4)][31] (85.4(1)º), due to a larger steric encumbrance of the palladacycle compared to the two mutually *cis* aryl groups. However this angle is similar to the one found in **2a** (79.3(3)º)[32] despite the repulsion that the two aryl groups, located on two vicinal carbons, generate.

2.3 Discussion

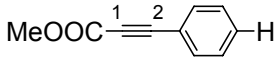
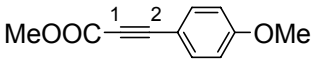
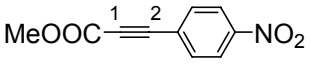
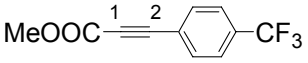
2.3.1 Regioselectivity of the second alkyne insertion

First of all, we observe a reaction leading to palladacycles for the reactions between the palladium(NN) complexes, as far as bipy, tmeda and phen are involved, with all three alkynes, irrespective of the specific bidentate N-ligand used (Table 2-1). However, in case of the Ar-bian ligand, the reaction is only observed for methyl (4-nitrophenyl)propynoate. This reaction requires electron-poor alkynes due to the strong nucleophilic nature of the dba-palladium complexe.[9,26] This would mean that slightly electron poor alkynes are electrophilic enough for this reaction in these cases if the ligands are sterically not very large. Whereas, in the case of the larger Ar-bian complex, an electron-poorer alkyne is needed in order to obtain a palladacycle. The steric aspect appears to be secondary since a small difference in bite angles between **4a**, **7a** on one hand and the [Pd(bipy)(CCOOMe)$_4$] analogue on the other, indeed confirm the comparable sterics of the alkynes. It is important to note in this context that, contrary to Van Belzen *et al*., π-acetylenic intermediates could not be observed by NMR in any of the cases studied.[33] Probably, such putative intermediates are relatively unstable in the cases studied; their low stability may be due to the weak π-acceptor character of the ancillary ligands.[13]

It is striking that we nearly always obtain the regioselective formation of the 'head-to-tail' isomers of type **a**. Indeed, complete regioselectivity has been observed in the cases of two alkynes, *e.g.*, for methyl phenylpropynoate and methyl (4-methoxyphenyl)propynoate. This is explained by invoking the large mutual steric hindrance of the phenyl groups that would be vicinal when the 'tail-to-tail' compound of type **b** would be formed. However, the complete regioselectivity disappears when using methyl (4-nitrophenyl)propynoate as the substrate; in that case we observe the formation of a small amount of the 'tail-to-tail' compound of type **b** as well. As no major difference in steric encumbrance can be attributed to this alkyne compared to the other two, the involvement of electronic factors is evident. Obviously, electronic factors are operating in the other cases as well, since we never observe any formation of the 'head-to-head' isomer **c**. We think that a subtle interplay between steric and electronic factors is responsible for the overall selectivity (or non-selectivity) of the oxidative cyclization of a second molecule of alkyne with the

[Pd(NN)(η^2-alkyne)] intermediate formed. Only in this way could we explain the complete regioselectivity observed for methyl phenylpropynoate and methyl (4-methoxyphenyl)propynoate on one hand and the lower regioselectivity when using methyl (4-nitrophenyl)propynoate as the substrate on the other.

Table 2-3. DFT calculation of charge's repartition on the triple bond.[34]

Entry	Alkyne	Charge of atom C-1 (eV)	Charge of atom C-2 (eV)	Δ (eV)
1		0.0076	-0.0066	0.0142
2		-0.0062	-0.0078	0.0016
3		0.0286	-0.0121	0.0407
4		0.0113	-0.0004	0.0117

It has been stated that, among the palladacyclopentadienes **a**-**c** (Scheme 2-1), type **b** is the thermodynamically most stable isomer, because two electron-withdrawing ester groups are attached to carbons in α-position relative to the palladium atom.[35] In the current case, regarding the charge of carbon-1 of the different alkynes that we used, the positive charge on C-1 of methyl (4-nitrophenyl)propynoate is higher than the one of the other alkynes (Table 2-3, entry 3). This, combined with the small steric encumbrance generated by bipy, tmeda or phen, leads also to the formation of compound **b**. Only in case where the steric hindrance induced by the NN ligand is more important, like with the *p*-tolyl-bian ligand, completely regioselective formation of the 'head-to-tail' coupled product **a** is observed. The carbon 1 of the methyl (4-trifluoromethylphenyl)propynoate (Table 2-3, entry 4) has an intermediate positive charge comparing methyl phenylpropynoate and methyl (4-methoxyphenyl)propynoate on the one hand and methyl (4-nitrophenyl)propynoate on the other. The observed regioselectivity during the reaction with 2,2'-bipyridine is somewhat intermediate, the coupled product **b** is also observed but in lower proportion than in the previous case with the same ligand. In the other examples (Table 2-3, entries 1 and 2), C-1 shows a lower positive charge, which is not high enough to lead also to the formation of the 'tail-to-tail' product **b**.

2.3.2 Reactivity of palladacyclopentadienes towards alkynes

2.3.2.1 Stability of the regioisomers

We were interested by the study of the stability of the regioisomers since Shirakawa *et al*.[19b] proposed a catalytic cycle of their dimerization-carbostannylation process. They concluded that an equilibrium is established between a thermodynamic regioisomer and a kinetic one (Chart 2-1). Since they were unable to isolate any palladacyclopentadiene to confirm this hypothesis, they proposed the two regioisomeric structures shown in Chart 2-1 based on the regioisomers obtained in the respective catalytic reactions.

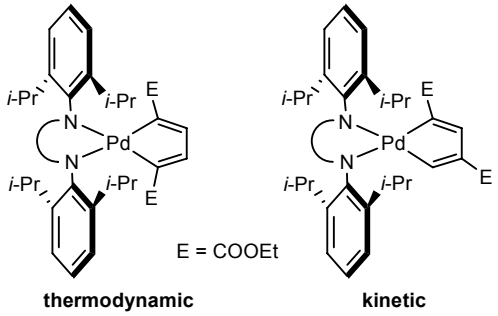
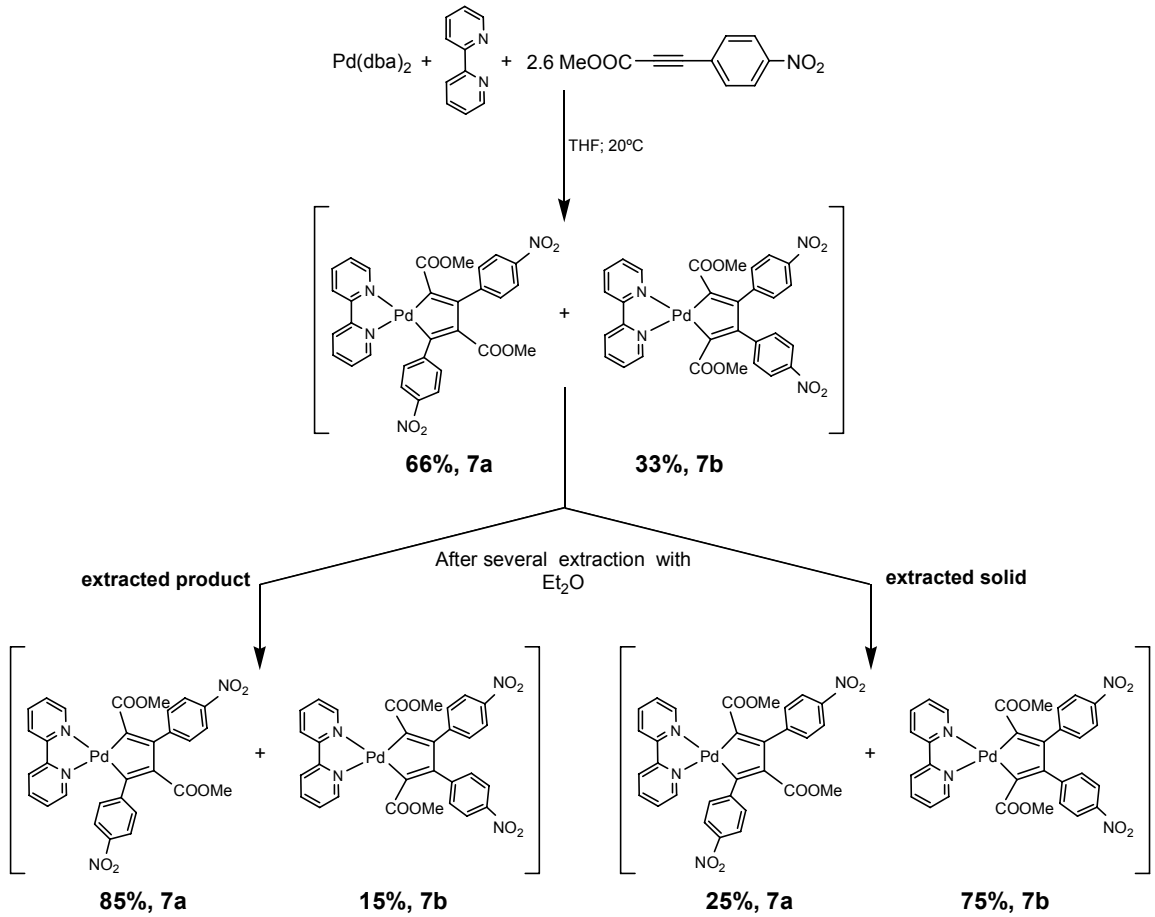


Chart 2-1. Regioisomers proposed by Shirakawa *et al*.

Unfortunately, our two regioisomers cannot be separated by chromatography, crystallization or other classical methods. In some cases they present a difference of solubility in diethyl ether, which allow us to increase the percentage of one or of the other regioisomer (Scheme 2-5).

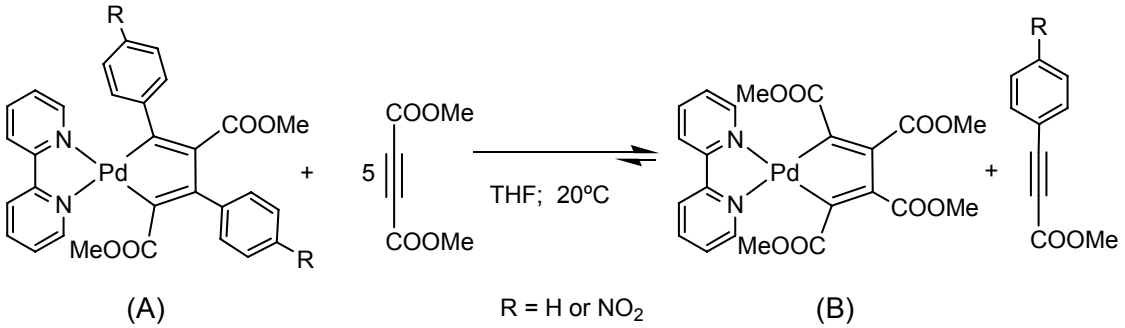


Scheme 2-5. Enhancement of the percentage of one regioisomer by Et_2O extraction.

We posed ourselves the question whether it would be possible to return to the initial ratio of regioisomers from these isolated mixtures of regioisomers? The idea was then to influence the equilibrium **7a**↔**7b** and several experiments were carried out on the various mixtures of regioisomers. We monitored the equilibrium at temperatures varying between 20ºC and 70ºC in THF. In neither of the cases did we observe a change of the ratio of regioisomers. Further experiments were done by reacting 1.0 to 5.0 equivalents of methyl (4-nitrophenyl)propynoate with the mixtures of regioisomers but these experiments still did not lead to a change of the regioisomers ratio. From these results it seems that, if an equilibrium between the two regioisomers is involved, the barrier to interconversion must be very high, which means that both regioisomers, once formed, are relatively stable.

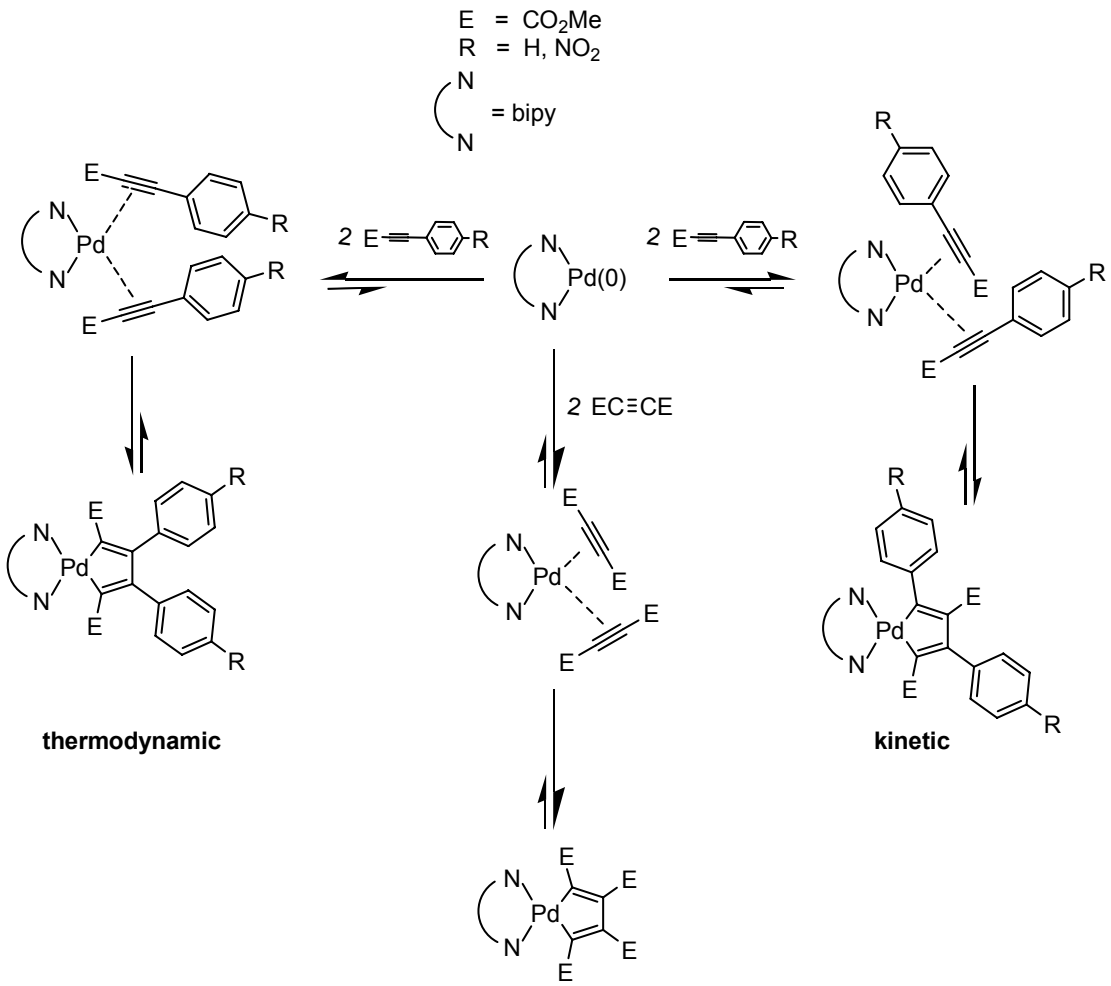
2.3.2.2 Exchange reaction

Despite the fact that there is no equilibrium between the two regioisomers, as evocated above, an alkyne substitution reaction seems to confirm the reversibility of the palladacyclopentadiene formation *via* [Pd(NN)(η^2-alkyne)] intermediate (Scheme 2-6). From complexes formed with methyl (4-nitrophenyl)propynoate or methyl phenylpropynoate, the formation of the classical palladacyclopentadiene with dmbd was obtained by the concomitant release of methyl (4-nitrophenyl)propynoate or methyl phenylpropynoate.



Scheme 2-6. Palladacyclopentadiene's alkyne substitution.

The driving force is the formation of the tetrakis(methoxycarbonyl)palladacyclopentadiene analogue which is thermodynamically favoured (Scheme 2-7). Meanwhile, this exchange reaction is a slow process, after 40 hours the extent of the exchange (A → B) reaches 66%.

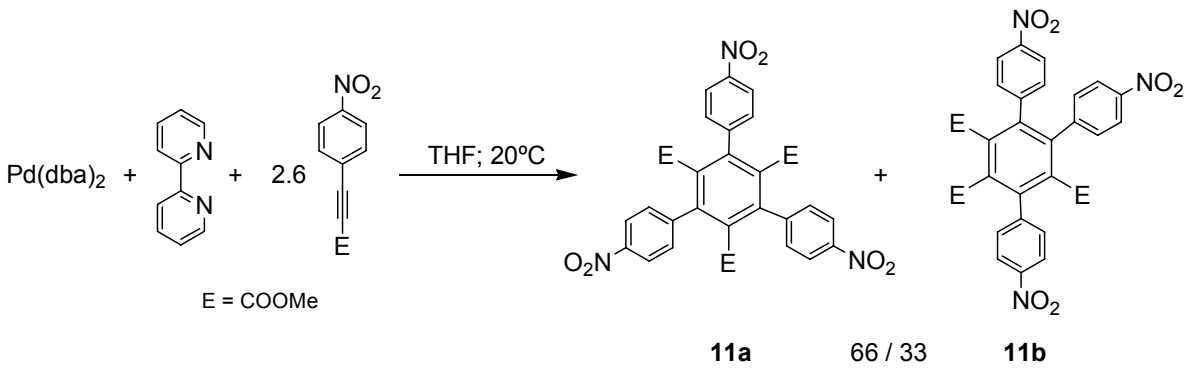


Scheme 2-7. Proposed mechanism for the [Pd(bipy)(CCOOMe)$_4$] formation from the regioisomers mixture.

2.3.2.3 Cyclotrimerization reaction of methyl (4-nitrophenyl)propynoate

Under the employed conditions, the formation of the palladacyclopentadiene is the major reaction, but we observed also the formation of one organic product. Surprisingly, this side reaction is the cyclotrimerization of the alkyne (Scheme 2-8) but irrespective of the reaction time or the excess of acetylene, the formation of the benzene derivatives was never a catalytic process. Indeed, the palladium mediated synthesis of benzenic derivatives *via* cyclotrimerization of alkynes usually requires longer time, high temperature and high alkyne excess.[11,14] However, the formation of hexamethyl mellitate, the cyclotrimer of dmbd, has been also observed under mild conditions.[25] Interestingly, the stable palladacyclopentadiene (**7a**/**7b**) substrate does not react with one further alkyne molecule to give the mellitate under mild conditions but the observed ratio of cyclotrimers (**11a**/**11b**) is the same as the observed ratio of

the regioisomers (**7a**/**7b**). The structure of the cyclotrimer **11a** was confirmed by X-ray diffraction analysis (Figure 2-5).



Scheme 2-8. Cyclotrimerization of methyl (4-nitrophenyl)propynoate, side reaction of the formation of **7a**, **7b**.

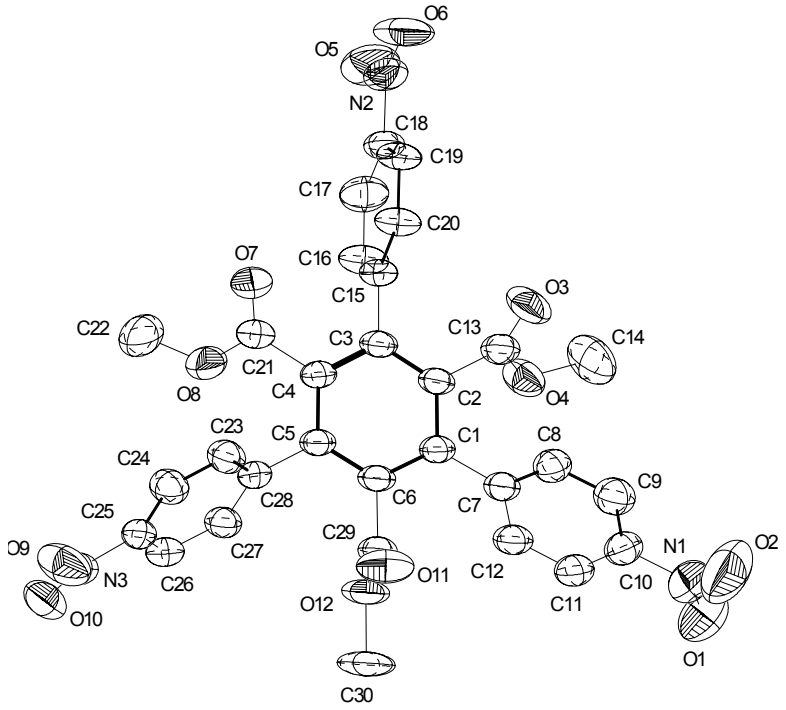


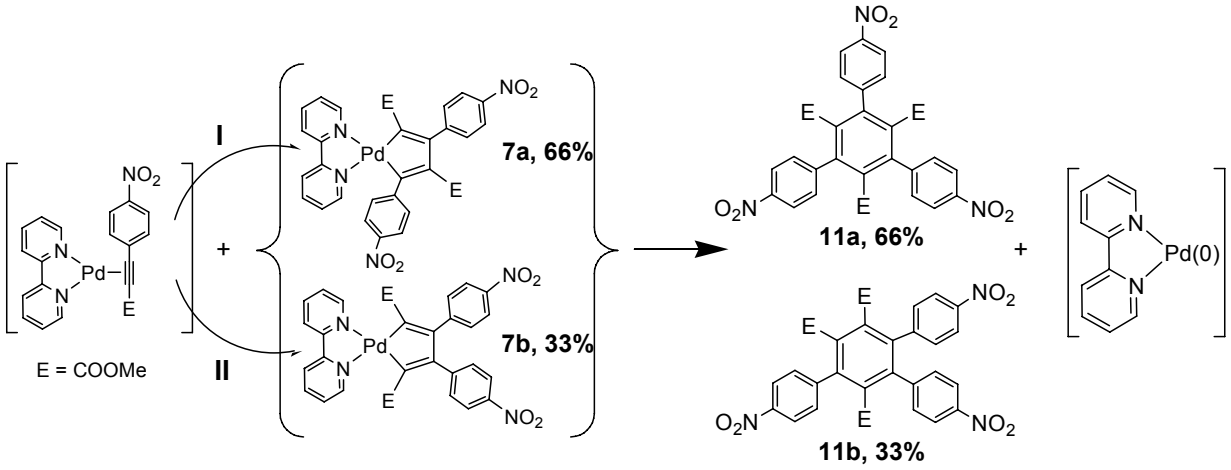
Figure 2-5. Crystal structure of **11a**. Ellipsoids are at the 50% probability level; hydrogen atoms are omitted for clarity.

The adopted numbering schemes of the molecular structures of **11a** is depicted in Figures 2-5, selected bond distances and bond angles have been compiled in Table 2-4. The X-ray shows that the phenyl groups occupy perpendicular positions to the plane of the benzene ring. The bond distances and bond angles are somewhat similar than those in the 1,3,5-trimethyl-2,4,6-triphenyl benzene.[36]

Table 2-4. Selected distances [Å] and angles (º) of **11a** with esd's in parenthesis.

atoms	distance	atoms	bond angle
C1-C2	1.413(9)	C1-C2-C3	121.50(48)
C2-C3	1.380(11)	C2-C3-C4	119.71(52)
C3-C4	1.408(25)	C3-C4-C5	119.79(43)
C4-C5	1.406(9)	C4-C5-C6	119.24(48)
C5-C6	1.381(11)	C5-C6-C1	122.25(52)
C6-C1	1.400(24)		
C1-C7	1.495(11)		
C3-C15	1.523(11)		
C2-C13	1.498(26)		
C6-C24	1.540(11)		

Importantly, Canovese *et al*.,[25a] as a result of their kinetic study of the formation of palladacyclopentadiene, figured out that the formation of hexamethyl mellitate as a by-product under mild conditions was not the product of the reaction between the corresponding palladacyclopentadiene and the dmbd, but rather results from the reaction of palladacyclopentadiene and the palladium π-acetylenic intermediate. We could assume that in the present case, the mellitates (**11a**/**11b**) are also arising from the reaction of **7a**/**7b** with [Pd(bipy)(η^2-alkyne)] (Scheme 2-9).



Scheme 2-9. Proposed reaction path for the formation of **11a**/**11b**.

The conservation of the observed ratio of regioisomers could imply that the insertion of the third molecule of methyl (4-nitrophenyl)propynoate in the palladium–carbon bond of **7a** is regioselective.

2.4 Conclusion

The formation of palladacyclopentadienes starting from dissymmetric alkynes has been explored. The palladacyclic complexes were successfully synthesized from $Pd(dba)_2$, NN ligands, *i.e.*, bipy, phen and tmeda and dissymmetric alkynes. Employing methyl phenylpropynoate or methyl (4-methoxyphenyl)propynoate as the substrate provided complete regioselectivity in the alkyne coupling with the formation of only 'head-to-tail' coupled palladacyclopentadiene products. However, reaction with methyl (4-nitrophenyl)propynoate lead to the formation of both the 'head-to-tail' coupled product and the 'tail-to-tail' coupled product. The lower regioselectivity observed in the formation of palladacyclopentadiene using methyl (4-nitrophenyl)propynoate is most probably due to the relatively high positive charge on carbon-1 of this alkyne compared to the other alkynes. For all other alkynes studied, complete regioselectivity was obtained by increasing the steric encumbrance generated by the NN ligand, *i.e.*, *p*-tolyl-bian. It has become clear from our experiments that a subtle interplay between steric and electronic factors is responsible for the overall selectivity (or non-selectivity) of the oxidative cyclization of a second molecule of alkyne with the [Pd(NN)(η^2-alkyne)] intermediate formed.

The relative constant ratio between the two regioisomers **7a** and **7b** in the mixture renders an equilibrium between 'head-to-tail' (**a**) and 'tail-to-tail' (**b**) coupled products rather unlikely. On the other hand, an exchange reaction together with the release of the initial coordinated alkyne confirmed the reversibility of this palladacyclopentadiene formation process. Hence, we cannot completely disprove the existence of a dynamic equilibrium between the regioisomers, but one may safely assume that the energy barrier to interconversion from one regioisomer to the other is very high. Finally, the overall results have enabled us to obtain a better understanding of the reaction mechanism for the formation of palladacyclopentadienes from dissymmetric alkynes, which is crucial when considering these species as key intermediates in oligomerization, cyclooligomerization or cyclocooligomerization of various alkynes.

2.5 Experimental Section

2.5.1 General considerations

All reactions were carried out by using standard Schlenk techniques under an atmosphere of dry nitrogen unless otherwise specified. The solvents were dried according to standard procedures[37] and distilled before use. Elemental analyses were carried out by Kolbe, Mikroanalytisches Laboratorium, Mülheim a.d. Ruhr, Germany and by the Service d'analyses, Institut de Chimie, Université Louis Pasteur, Strasbourg, France. ^{1}H and ^{13}C NMR spectra were recorded at 298K on a Bruker AMX 300 spectrometer (300.13 and 75.48 MHz respectively) and on a Varian Inova 500 spectrometer (499.86 and 125.70 MHz respectively). The chemical shift values are referenced to external TMS with high frequency shifts signed positive. Chemical shifts (δ) and coupling constants (J) are expressed in ppm and in Hertz (Hz) respectively and the multiplicity as s = singulet, d = doublet, dd = double doublet, t = triplet, pst = pseudo triplet, m = multiplet, br = broad; data in parenthesis are given in the following order: multiplicity, number of protons, labelling of the proton and coupling constants in Hz.

2,2-Bipyridine (Merck), 1,10-phenanthroline (Acros), methyl phenylpropynoate (Aldrich) and dimethyl-2-butynedioate (Acros) were used as received. N,N-tetramethylethylenediamine (Aldrich) was distilled prior to use. $[Pd(dba)_2]$[38], *p*-Me-C_6H_4-bian,[39] methyl (4-nitrophenyl)propynoate,[40] methyl (4-trifluoromethylphenyl)propynoate,[40] methyl (4-methoxyphenyl)propynoate,[41] were prepared according to literature procedures.

2.5.2 Synthesis

Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-diphenylcyclopentadiene-bipyridine (1a)

A suspension of $[Pd(dba)_2]$ (200 mg, 0.35 mmol), 2,2'-bipyridine (55 mg, 0.35 mmol) was stirred at room temperature for 10 minutes in THF (20 mL). Then methyl phenylpropynoate (134 µL, 0.90 mmol) was added to the solution. After 2 hours, the solvent of the resulting orange solution was removed in vacuo and the product was washed with diethyl ether (4 × 50mL). The orange product was dissolved in

dichloromethane and filtered over celite filter aid in order to remove the metallic palladium. The solvent was again removed in vacuo, yielding 145 mg (0.25 mmol, 72%) of yellow orange product.

Anal. Calcd for $C_{30}H_{24}N_2O_4Pd$: C, 61.81; H, 4.15; N, 4.81. Found C, 61.64; H, 4.22; N, 4.88.

^{1}H NMR ($CDCl_3$, 499.86 MHz): δ 8.80 (d, 1H, H6, ^3J = 5.5), 7.99 (m, 2H, H4 and H6'), 7.95 (d, 1H, H3, ^3J = 8.0), 7.82 (dd, 1H, H5', ^3J = 7.6, ^3J = 7.5), 7.50 (dd, 1H, H5, ^3J = 5.3), 7.41 (dd, 2H, $H_{o'}$, ^3J = 7.0), 7.35 (dd, 2H, H_o, ^3J = 7.0), 7.27-7.16 (m, 6H, $H_{m,m'}$ and $H_{p,p'}$), 7.02 (dd, 1H, H4', ^3J = 6.5), 6.98 (d, 1H, H3', ^3J = 5.0), 3.42 (s, 3H, OC*H*$_3$), 3.17 (s, 3H, OC*H*$_3$).

^{13}C NMR ($CDCl_3$, 75.48 MHz): δ 177.1 (*C*O), 175.5 (*C*O'), 166.5 (C_β), 156.9 ($C_{\alpha'}$), 155.4 and 155.2 (2C, C2 and C2'), 151.9 (C3), 151.6 (C6'), 149.0 ($C_{\beta'}$), 147.5 ($C_{i'}$), 146.9 (C_α), 140.1 (C_i), 139.3 (C6), 138.8 (C5), 128.2, 128.0, 127.8 and 127.6 (4×2C, 2 C_o, 2 $C_{o'}$, 2 C_m and 2 $C_{m'}$), 126.5 and 126.4 (2C, C_p and $C_{p'}$), 126.0 (C5'), 125.6 (C4), 122.4 and 122.0 (2C, C3' and C4'), 51.0 and 50.8 (2C, O*C*H$_3$ and O*C*H$_3$').

Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-diphenylcyclopentadiene-*N*,*N*-tetramethylethylenediamine (2a)

The procedure was the same as for **1a**: [Pd(dba)$_2$] (200 mg, 0.35 mmol), tmeda (60 µL, 0.40 mmol) and methyl phenylpropynoate (140 µL, 0.95 mmol) in 20 mL of THF gave **2a** after 3h reaction and washing with diethyl ether (2 × 50 mL) 85mg (0.16 mmol, 45%) of yellow product.

Anal. Calcd for $C_{26}H_{32}N_2O_4Pd$, ½ CH_2Cl_2: C, 54.38; H, 5.68; N, 4.79. Found C, 54.79; H, 5.62; N, 5.19.

^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 7.17 (m, 10H, ar), 3.32 (s, 3H, OC*H*$_3$), 2.98 (s, 3H, OC*H*$_3$), 2.59 (s, 6H, 2 × C*H*$_3$), 2.43 (s, 4H, 2 × C*H*$_2$), 1.95 (s, 6H, 2 × C*H*$_3$).

^{13}C NMR ($CDCl_3$, 75.48 MHz): δ 176.2 (*C*O), 173.0 (*C*O'), 166.5 (C_β), 155.8 ($C_{\alpha'}$), 148.5 (C_α), 148.3 ($C_{\beta'}$), 148.0 ($C_{i'}$), 140.4 (C_i), 127.7 (8C, 2 C_o, 2 $C_{o'}$, 2 C_m and 2 $C_{m'}$), 126.3 and 125.6 (2C, C_p and $C_{p'}$), 62.0 and 61.3 (2C, *C*H$_2$ and *C*H$_2$'), 51.0 and 50.5 (2C, O*C*H$_3$ and O*C*H$_3$'), 48.8 and 48.7 (4C, 2 × *C*H$_3$ and 2 × *C*H$_3$').

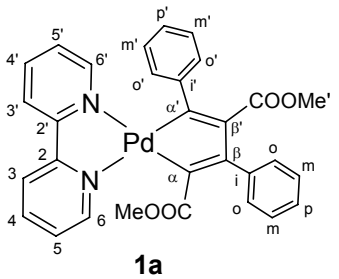
Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-diphenylcyclopentadiene-phenanthroline (3a)

The procedure was the same as for **1a**: $[Pd(dba)_2]$ (307 mg, 0.53 mmol), 1,10-phenanthroline 96 mg, 0.53 mmol) and phenyl methylpropynoate (200 µL, 1.36 mmol) in 25 mL of THF gave **3a** after 1.5 h reaction and washing with diethyl ether (2 × 50 mL) 195 mg (0.32 mmol, 61%) of yellow product.

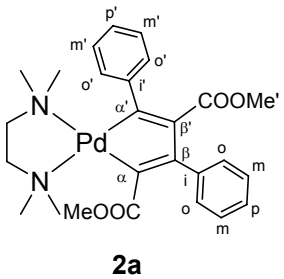
Anal. Calcd for $C_{32}H_{24}N_2O_4Pd$: C, 63.32; H, 3.99; N, 4.62. Found C, 63.26; H, 4.08; N, 4.55.

^{1}H NMR ($CDCl_3$, 499.86 MHz): δ 9.10 (d, 1H, H6, ^3J = 5.0), 8.45 (d, 1H, H4, ^3J = 8.0), 8.29 (d, 1H, H6', ^3J = 8.0), 7.88 (s, 2H, H7 and H7'), 7.80 (dd, 1H, H5, ^3J = 7.8, ^3J = 5.3), 7.41 (d, 2H, $H_{o'}$, ^3J = 6.5), 7.39 (d, 2H, H_o, ^3J = 7.0), 7.30 (dd, 1H, H5', ^3J = 7.8, ^3J = 5.3), 7.27-7.15 (m, 6H, $H_{m,m'}$ and $H_{p,p'}$), 7.08 (d, 1H, H4', ^3J = 5.0), 3.46 (s, 3H, OCH_3), 3.18 (s, 3H, OCH_3).

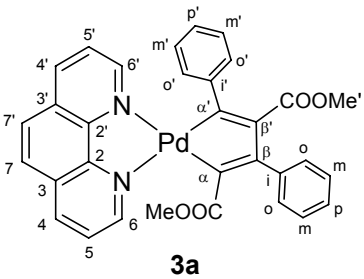
^{13}C NMR ($CDCl_3$, 75.48 MHz): δ 177.0 (*C*O), 175.2 (*C*O'), 166.4 (C_β), 156.7 ($C_{\alpha'}$), 152.0 (C4'), 151.6 (C6), 149.0 ($C_{\beta'}$), 147.8 ($C_{i'}$), 147.1 (C_α), 146.2 (2C, C2 and C2'), 140.2 (C_i), 138.4 (C4), 137.9 (C6'), 130.0 and 129.7 (2C, C3 and C3'), 130.9-125.9 (14C, 2 C_o, 2 $C_{o'}$, 2 C_m, 2 $C_{m'}$, C_p, $C_{p'}$, C5, C5', C7, and C7'), 51.0 and 50.8 (2C, O*C*H_3 and O*C*H_3').



1a



2a



3a

Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-bis(4-methoxyphenyl)-cyclopentadiene-bipyridine (4a)

A suspension of $[Pd(dba)_2]$ (101 mg, 0.18 mmol), 2,2'-bipyridine (28 mg, 0.18 mmol) was stirred at room temperature for 10 minutes in THF (15 mL). Then methyl (4-methoxyphenyl)propynoate (86 mg, 0.45 mmol) was added to the solution. After 2 hours, the solvent of the resulting dark orange solution was removed in vacuo and the product was washed with diethyl ether (4 × 10 mL). The dark orange product was dissolved in dichloromethane and filtered over celite filter aid in order to remove the

metallic palladium. The solvent was again removed in vacuo, yielding 70 mg (0.11 mmol, 63%) of dark orange product **4a**.

MS (FAB+) *m*/*z*: found 642.1000 (M): calcd ($C_{32}H_{28}N_2O_6Pd$) 642.0995.

^{1}H NMR ($CDCl_3$, 499.86 MHz): *δ* 8.80 (d, 1H, H6, ^3J = 5.0), 8.00 (m, 2H, H4 and H6'), 7.95 (d, 1H, H3, ^3J = 8.0), 7.82 (t, 1H, H5', ^3J = 7.5), 7.50 (dd, 1H, H5, ^3J = 5.5), 7.36 (d, 2H, $H_{o'}$, ^3J = 7.0), 7.28 (d, 2H, H_o, ^3J = 7.0), 7.12 (d, 1H, H3', ^3J = 5.0), 7.08 (dd, 1H, H4', ^3J = 7.5, ^3J = 5.0), 6.80-6.76 (m, 4H, $H_{m,m'}$), 3.79 and 3.78 (s, 6H, OC*H*$_3$), 3.43 (s, 3H, COOC*H*$_3$), 3.21 (s, 3H, COOC*H*$_3$).

^{13}C NMR ($CDCl_3$, 125.70 MHz): *δ* 176.1 (*C*O), 175.3 (*C*O'), 166.6 (C_β), 157.9 and 157.7 (2C, C_p and $C_{p'}$), 156.2 ($C_{\alpha'}$), 155.1 and 154.9 (2C, C2 and C2'), 151.7 (C3), 151.4 (C6'), 148.4 ($C_{\beta'}$), 146.9 (C_α), 139.5 (C_i), 138.9 (C6), 138.4 (C5), 132.5 ($C_{i'}$), 128.9 and 128.7 (2×2C, 2 C_o, 2 $C_{o'}$), 126.1 (C5'), 125.4 (C4), 122.0 and 121.6 (2C, C3' and C4'), 113.2 and 112.8 (2×2C, 2 C_m and 2 $C_{m'}$), 55.4 and 55.2 (2C, O*C*H$_3$ and O*C*H$_3$'), 50.7 and 50.6 (2C, OO*C*H$_3$ and OO*C*H$_3$').

Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-bis(4-methoxyphenyl)-cyclopentadiene-*N*,*N*-tetramethylethylenediamine (5a)

The procedure was the same as for **4a**: [Pd(dba)$_2$] (40 mg, 0.07 mmol), tmeda (14 µL, 0.07 mmol) and methyl (4-methoxyphenyl)propynoate (34 mg, 0.18 mmol) in 15 mL of THF gave **5a** after 2.5 hours reaction and washing with diethyl ether (3 × 10 mL) 15mg (0.03 mmol, 37%) of yellow product.

MS (FAB+) *m*/*z*: found 602.1619 (M): calcd ($C_{28}H_{36}N_2O_6Pd$) 602.1620.

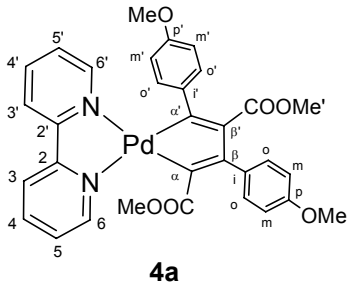
^{1}H NMR ($CDCl_3$, 300MHz): *δ* 7.15 (d, 2H, H_o or $H_{o'}$, ^3J = 8.4), 7.10 (d, 2H, $H_{o'}$ or H_o, ^3J = 8.1), 6.76 (d, 2H, H_m or $H_{m'}$, ^3J = 8.7), 6.71 (d, 2H, $H_{m'}$ or H_m, ^3J = 8.4), 3.76 and 3.74 (s, 6H, OC*H*$_3$), 3.35 (s, 3H, COOC*H*$_3$), 3.03 (s, 3H, COOC*H*$_3$), 2.57 (s, 6H, 2 × C*H*$_3$), 2.42 (br, 4H, 2 × C*H*$_2$), 1.97 (s, 6H, 2 × C*H*$_3$).

^{13}C NMR ($CDCl_3$, 125.70 MHz): *δ* 176.1 (*C*O), 171.6 (*C*O'), 166.6 (C_β), 157.7 and 157.3 (2C, C_p and $C_{p'}$), 154.8 ($C_{\alpha'}$), 148.9 ($C_{\beta'}$), 148.0 (C_α), 140.1 (C_i), 132.9 ($C_{i'}$), 128.6 (4C, 2 C_o and 2 $C_{o'}$), 112.9 and 112.8 (2×2C, 2 C_m and 2 $C_{m'}$), 61.7 and 61.0 (2C, *C*H$_2$ and *C*H$_2$'), 55.2 and 55.1 (2C, O*C*H$_3$ and O*C*H$_3$'), 50.7 and 50.3 (2C, OO*C*H$_3$ and OO*C*H$_3$'), 48.6 and 48.4 (4C, 2 × *C*H$_3$ and 2 × *C*H$_3$').

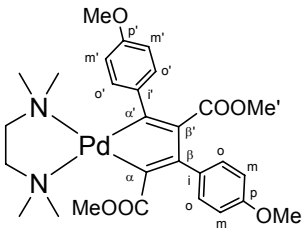
Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-bis(4-methoxyphenyl)-cyclopentadiene-phenanthroline (6a)

The procedure was the same as for **4a**: [Pd(dba)$_2$] (100 mg, 0.17 mmol), 1,10-phenanthroline 32 mg, 0.18 mmol) and methyl (4-methoxyphenyl)propynoate (86 mg, 0.45 mmol) in 13 mL of THF. After 2 hours of reaction no conversion was observed, the solution was then heated at 40 ºC for 22 hours. We could only deduce from ^{1}H NMR that **6a** was formed. The purification and further treatment did not permit us to isolate the product for more characterization.

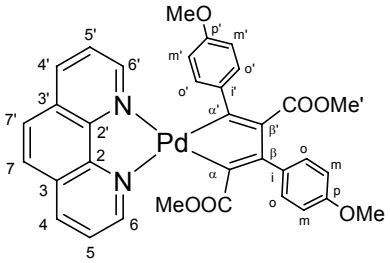
Partial ^{1}H NMR ($CDCl_3$, 300MHz): δ 3.82 and 3.79 (s, 6H, OCH_3), 3.47 (s, 3H, COOCH_3), 3.23 (s, 3H, COOCH_3).



4a



5a



6a

Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-bis(4-nitrophenyl)-cyclopentadiene-bipyridine (7a) and Pallada-2,5-bis(carbomethoxy)-3,4-bis(4-nitrophenyl)-cyclopentadiene-bipyridine (7b)

The procedure was the same as for **1a**: [Pd(dba)$_2$] (200 mg, 0.35 mmol), 2,2'-bipyridine (55 mg, 0.35 mmol) and methyl (4-nitrophenyl)propynoate (187 mg, 0.91 mmol) gave **7a/b** after 2 hours reaction and washing with diethyl ether (4 × 15 mL) 127 mg (0.03 mmol, 54%) of brown orange product **7a/b** in a ratio 25/75.

MS (FAB+) *m*/*z*: found 673.0568 (M + H): calcd ($C_{30}H_{23}N_4O_8Pd$) 673.0563.

7a: ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 8.79 (d, 1H, H6), 8.15 (d, 2H, H_m or $H_{m'}$, ^3J = 9.0), 8.13 (d, 2H, $H_{m'}$ or H_m, ^3J = 8.7), 8.15-8.12 (m, 2H, H4 and H6'), 8.08-7.95 (m, 2H, H3 and H5'), 7.60 (br, 1H, H5), 7.58 (d, 2H, H_o or $H_{o'}$, ^3J = 9.0), 8.13 (d, 2H, $H_{o'}$ or H_o, ^3J = 8.7), 7.16 (m, 2H, H3' and H4'), 3.44 (s, 3H, COOCH_3), 3.18 (s, 3H, COOCH_3).

7b: ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 8.79 (d, 2H, H6, ^3J = 5.4), 8.09 (m, 4H, H3 and H4), 7.97 (d, 4H, H_m, ^3J = 8.1), 7.60 (pst, 2H, H5), 7.17 (d, 4H, H_o, ^3J = 8.1), 3.46 (s, 6H, 2 × OCH_3).

^{13}C NMR ($CDCl_3$, 125.70 MHz): δ 174.1 (*C*O), 156.4 (C_β), 155.5 (C2), 155.2 (C_p), 151.6 (C6), 146.3 (C_α), 146.2 (C_i), 139.6 (C4), 129.7 (C_o), 126.8 (C5), 123.2 (C_m), 122.4 (C3), 51.2 (O*C*H_3).

Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-bis(4-nitrophenyl)-cyclopentadiene-*N,N*-tetramethylethylenediamine (8a) and Pallada-2,5-bis(carbomethoxy)-3,4-bis(4-nitrophenyl)-cyclopentadiene-*N,N*-tetramethylethylenediamine (8b)

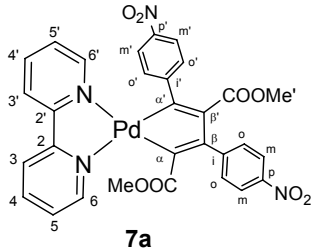
The procedure was the same as for **1a**: [Pd(dba)$_2$] (100 mg, 0.17 mmol), tmeda (28 µL, 0.18 mmol) and methyl (4-nitrophenyl)propynoate (93 mg, 0.45 mmol) gave **8a/b** after 2 hours reaction and washing with diethyl ether (2 × 15 mL) 75mg (0.12 mmol, 68%) of yellow product **8a/b** in the ratio 95/5.

MS (FAB+) *m*/*z*: found 632.1111 (M): calcd ($C_{26}H_{30}N_4O_8Pd$) 632.1109.

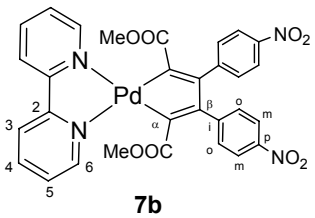
8a: ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 8.14 (d, 2H, 2 H_m, ^3J = 8.4), 8.09 (d, 2H, 2 $H_{m'}$, ^3J = 8.7), 7.34 (d, 2H, 2 H_o, ^3J = 8.4), 7.33 (d, 2H, 2 $H_{o'}$, ^3J = 8.7), 3.36 (s, 3H, OCH_3), 3.01 (s, 3H, OCH_3'), 2.61 (s, 6H, 2 × CH_3), 2.49 (br, 4H, CH_2 and CH_2'), 2.0 (s, 6H, 2 × CH_3').

^{13}C NMR ($CDCl_3$, 75.48 MHz): δ 175.1(*C*O), 173.0 (*C*O'), 165.3 (C_β), 156.3 ($C_{\alpha'}$), 153.4 and 151.1 (2C, C_p and $C_{p'}$), 147.5 (C_α), 147.2 ($C_{\beta'}$), 146.5 ($C_{i'}$), 145.7 (C_i), 128.5 and 128.1 (2 × 2C, 2 C_o and 2 $C_{o'}$), 123.5 and 123.4 (2 × 2C, 2 C_m and 2 $C_{m'}$), 62.1 and 61.6 (2C, *C*H_2 and *C*H_2'), 51.4 and 50.8 (2C, O*C*H_3 and O*C*H_3'), 49.1 and 48.9 (2 × 2C, 2 *C*H_3 and 2 *C*H_3').

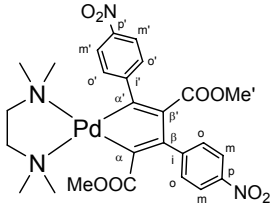
8b: ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 7.91 (d, 4H, H_m, ^3J = 8.7), 7.03 (d, 4H, H_o, ^3J = 8.4), 3.31 (s, 6H, 2 × OCH_3), 2.65 (s, 12H, 4 × CH_3), 2.54 (br, 4H, 2 × CH_2).



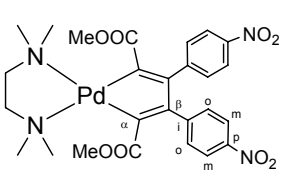
7a



7b



8a



8b

Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-bis(4-nitrophenyl)-cyclopentadiene-phenanthroline (9a) and Pallada-2,5-bis(carbomethoxy)-3,4-bis(4-nitrophenyl)-cyclopentadiene-phenanthroline (9b)

The procedure was the same as for **1a**: [$Pd(dba)_2$] (130 mg, 0.23 mmol), 1,10-phenanthroline 41 mg, 0.23 mmol) and methyl (4-nitrophenyl)propynoate (116 mg, 0.57 mmol) in 14 mL of THF. In few minutes a red suspension in an orange solution is observed. After 2 hours of reaction, the red solid is filtrated off; the rest of the procedure remains the same. After the washing with diethyl ether (4 × 15 mL), 43 mg (0.12 mmol, 27%) of yellow product **9a/b** in the ratio 66/33 were obtained.

Anal. Calcd for $C_{32}H_{22}N_4O_8Pd$: C, 55.15; H, 3.18; N, 8.04. Found C, 54.93; H, 3.16; N, 7.89.

9a: ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 9.11 (d, 1H, H6), 8.54 (d, 1H, H4), 8.38 (d, 1H, H6'), 8.17 (d, 2H, 2 $H_{m'}$, ^3J = 9.0), 8.16 (d, 2H, 2 H_m, ^3J = 9.0), 8.01 (s, 2H, H7 and H7'), 7.90 (m, 1H, H5), 7.60 (d, 2H, 2 H_o, ^3J = 9.0), 7.53 (d, 2H, 2 $H_{o'}$, ^3J = 8.7), 7.40 (pst, 1H, H5'), 7.32 (psd, 1H, H4'), 3.46 (s, 3H, OCH_3), 3.19 (s, 3H, OCH_3')

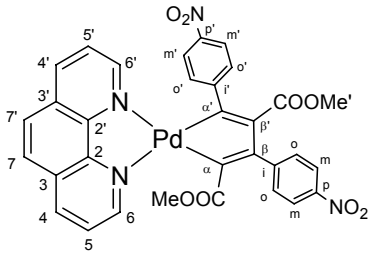
9b: ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 9.11 (d, 2H, H6, ^3J = 5.4, ^4J = 1.8), 8.56 (d, 2H, H4, ^3J = 8.1, ^4J = 1.4), 7.99 (d, 4H, H_m, ^3J = 8.7), 7.95 (s, 2H, H7), 7.90 (dd, 2H, H5, ^3J = 8.1, ^3J = 5.1), 7.21 (d, 4H, H_o, ^3J = 8.7), 3.48 (s, 6H, 2 × OCH_3).

Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-bis(4-nitrophenyl)-cyclopentadiene-*p*-tolyl-bian (10a)

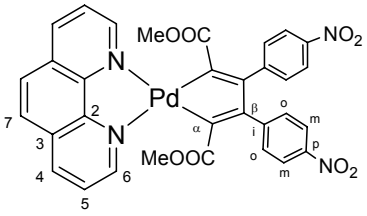
The procedure was the same as for **1a**: [$Pd(dba)_2$] (150 mg, 0.27 mmol), *p*-tolyl-bian 102 mg, 0.28 mmol) and methyl (4-nitrophenyl)propynoate (148 mg, 0.72 mmol) in 20 mL of THF, gave **10a** after 1 hour reaction and washing with diethyl ether (4 × 20 mL) 125 mg (0.14 mmol, 53%) of brownish product.

^{1}H NMR ($CDCl_3$, 499.86 MHz, 233K): δ 8.06 (d, 2H, 2 H_m, ^3J = 8.8), 8.03 (d, 1H, H6, ^3J = 8.3), 8.01 (d, 1H, H6', ^3J = 8.5), 7.67 (d, 2H, 2 $H_{m'}$, ^3J = 8.5), 7.45 (pst, 1H, H5, ^3J = 8.3 and ^3J = 7.3), 7.38 (d, 2H, 2 H11, ^3J = 8.1), 7.36 (pst, 1H, H5', ^3J = 8.1), 7.30 (d, 2H, 2 H_o, ^3J = 8.5), 7.19 (d, 2H, 2 H10, ^3J = 8.1), 6.92 (d, 2H, 2 H11', ^3J = 7.8), 6.91 (d, 2H, 2 $H_{o'}$, ^3J = 8.3), 6.50 (d, 2H, 2 H10', ^3J = 8.1), 6.47 (d, 1H, H4, ^3J = 7.6), 6.04 (d, 1H, H4', ^3J = 7.3), 3.00 (s, 3H, OCH_3 or OCH_3'), 2.74 (s, 3H, OCH_3' or OCH_3), 2.49 (s, 3H, CH_3), 2.42 (s, 3H, CH_3').

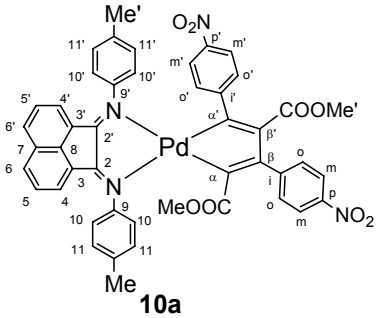
^{13}C NMR ($CDCl_3$, 125.70 MHz, 233K): δ 179.6 (C), 172.0 (C), 171.9 (C), 171.5 (C), 164.3 (C), 154.4 (C), 153.0 (C), 152.5 (C), 146.4 (C). 145.2 (C), 145.1 (C), 144.7 (C), 144.3 (C), 144.0 (C), 143.8 (C), 137.4 (1C, C12 or C12'), 136.8 (1C, C12' or C12), 131.5 (2C, C6 and C6'), 130.6 (1C, C7), 130.2 (2C, 2 C11), 130.1 (2C, 2 C11'), 128.4 (2C, C5 and C5'), 127.9 (2C, 2 C_o), 126.0 (1C, C4'), 125.8 (1C, C4), 125.6 (2C, 2 $C_{o'}$), 125.5 (1C, C3 or C3'), 125.4 (1C, C3' or C3), 122.9 (2C, 2 C_m), 122.6 (2C, 2 $C_{m'}$), 120.7 (2C, 2 C10), 119.3 (2C, 2 C10'), 51.1 and 50.7 (2C, O*C*H_3 and O*C*H_3'), 21.5 and 21.1 (2C, *C*H_3 and *C*H_3').



9a



9b



10a

Synthesis of 1,3,5-tris(carbomethoxy)-2,4,6-tris(4-nitrophenyl)benzene (11a) and 1,2,4-tris(carbomethoxy)-3,5,6-tris(4-nitrophenyl)benzene (11b)

The procedure was the same as for **1a**: [Pd(dba)$_2$] (65 mg, 0.11 mmol), bipy (18 mg, 0.12 mmol) and methyl (4-nitrophenyl)propynoate (60 mg, 0.29 mmol) were stirred for 2 hours. The solvent was removed in vacuo and the residue was chromatographied on silica gel with CH_2Cl_2 as eluent yielding to 18 mg of white product **11a/11b** (0.03 mmol, 10%) in a ratio of 66/33.

MS (FAB+) *m*/*z*: found 616.1237 (M + H): calcd ($C_{30}H_{22}N_3O_{12}$) 616.1203.

11a: ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 8.32-8.05 (m, 6H, H_{ar}), 7.57-7.19 (m, 6H, H_{ar}), 3.26 (s, 9H, OC*H$_3$*).

^{13}C NMR ($CDCl_3$, 75.48 MHz): δ 166.57 (CO), 148.24 (C_p), 142.97 (C_i), 137.1 (C), 137.0 (C), 130.8 (CH), 123.7 (CH), 52.82 (OCH_3).

11b: ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 8.32-8.05 (m, 6H, H_{ar}), 7.57-7.19 (m, 6H, H_{ar}), 3.58 (s, 3H, OC*H$_3$*), 3.55 (s, 3H, OC*H$_3$*), 3.21 (s, 3H, OC*H$_3$*).

^{13}C NMR ($CDCl_3$, 75.48 MHz): δ 166.74 (CO), 166.64 (CO), 166.46 (CO), 148.15 (C_p), 147.70 (C_p), 147.62 (C_p), 143.33 (2 $\times$ C_i), 142.97 (C_i), 139.2 (C), 138.3 (C),

137.1 (C), 135.1 (C), 134.6 (C), 133.0 (C), 130.1 (4 × CH), 129.9 (2 × CH), 124.0 (2 × CH), 123.5 (4 × CH), 53.26 (2 × OCH_3), 52.42 (OCH_3).

Synthesis of Pallada-2,4-bis(carbomethoxy)-3,5-bis(4-trifluoromethylphenyl)-cyclopentadiene-phenanthroline (12a) and Pallada-2,5-bis(carbomethoxy)-3,4-bis(4-trifluoromethylphenyl)-cyclopentadiene-bipyridine (12b)

The procedure was the same as for **1a**: [$Pd(dba)_2$] (150 mg, 0.26 mmol), bipy (40 mg, 0.26 mmol) and methyl (4-trifluoromethylphenyl)propynoate (156 mg, 0.68 mmol) gave **12a/b** after 2 hours reaction and washing with diethyl ether (4 × 20 mL) 117 mg (0.16 mmol, 63%) of brown yellow product **12a/b** in a ratio 89/11.
MS (FAB+) *m*/*z*: found 718.0526 (M): calcd ($C_{32}H_{22}F_6N_2O_4Pd$) 718.0531.
12a: ^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 8.79 (br, 1H), 8.05 (m, 3H), 7.87 (br, 1H), 7.52-7.43 (m, 7H), 7.33 (br, 2H), 7.18 (br, 1H), 6.95 (d, 1H), 3.43 (s, 3H, COOCH_3), 3.17 (s, 3H, COOCH_3).

2.5.3 Probing of interconversion and alkyne exchange concerning the mixtures of regioisomers

Modification of the ratio 7a/7b

The procedure started by the synthesis of **7a/7b**: [$Pd(dba)_2$] (100 mg, 0.17 mmol), bipy (28 mg, 0.18 mmol) and methyl (4-nitrophenyl)propynoate (93 mg, 0.45 mmol). After 2.0 hours reaction the solvent was removed in vacuo, the residue was dissolved in CH_2Cl_2 and filtered over celite. The solvent was again removed in vacuo and the red orange product was washed with diethyl ether (4 × 25 mL). The washed product was then dried in vacuo and characterized by ^{1}H NMR, the 23mg (0.03 mmol, 20%) of red orange solid is a mixture of **7a/7b** with a ratio of 25/75. The 4 portions of ether from the washing were then evaporated together, the obtained residue was then dissolved in a minimum of CH_2Cl_2 and Et_2O was added dropwise until a precipitation was initiated. The red orange solid was filtered off, washed with 5 mL of cold ether, dried in vacuo and characterized by ^{1}H NMR. The 15 mg (0.02 mmol, 13%) red orange solid is this time a mixture of **7a/7b** with a ratio of 85/15.

Experiments with the mixtures of regioisomers 7a and 7b

Procedure A: Attempts to influence the equilibrium **7a**↔**7b** were carried out by stirring 10 mg of **7a/7b** (0.01 mmol, ratio 85/15) in 7 mL of THF during 20 hours at room temperature. The solvent was then removed in vacuo, the product has been dried and analyzed by ^{1}H NMR. A similar experiment has been done at 50ºC, the remainder of the procedure remaining the same.

Procedure B: To a solution of 10 mg of **7a/7b** (0.01 mmol, ratio 85/15) in 8 mL of THF, 10 mg (0.05 mmol) of methyl (4-nitrophenyl)propynoate were added. After 3 hours of reaction, the solvent was removed in vacuo and the residue was dried and analyzed by ^{1}H NMR.

Procedure C: A solution of 10 mg of **7a/7b** (0.01 mmol, ratio 25/75) in 9 mL of THF during 20 hours at room temperature. The solvent was then removed in vacuo, the product has been dried and analyzed by ^{1}H NMR.

Procedure D: To a solution of 10 mg of **7a/7b** (0.01 mmol, ratio 25/75) in 6 mL of THF, 8 mg (0.04 mmol) of methyl (4-nitrophenyl)propynoate were added. After 3 hours of reaction at room temperature, the solvent was removed in vacuo and the residue was dried and analyzed by ^{1}H NMR. The same reaction mixture was redissolved in 7 mL of THF and heated up at 70ºC overnight, the solvent was then removed in vacuo and the residue was analyzed by ^{1}H NMR.

Exchange reaction

Exchange concerning methyl phenylpropynoate complex **1a**: To a solution of **1a** (10 mg, 0.02 mmol) in 7 mL of THF, dmbd (15 mg, 0.11 mmol) was added at room temperature. The reaction was monitored by ^{1}H NMR. After 40 hours of reaction, the solvent was removed in vacuo and the residue was analyzed by ^{1}H NMR.

Exchange concerning methyl (4-nitrophenyl)propynoate complexes **7a/7b**: The procedure was the same as for the previous case, 10 mg of **7a/7b** (0.01 mmol) in 5 mL of THF, 13 mg (0.09 mmol) of dmbd was then added.

2.5.4 X-ray crystal structure analyses

Pertinent data for the structure determinations are given in Table 2-5. Data were collected at different temperature on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Cu K*α* radiation (λ(Cu K*α*) = 1.5418 Å) and ω-2θ scan. Unit-cell parameters were refined by a least-squares fitting procedure. Corrections for Lorentz and polarisation effects were applied. Absorption correction was performed with the program PLATON,[42] following the method of North et al.[43] using Ψ-scans of five reflections. The structure of **3a**, **4a**, **7a**, and **8b** were solved by the PATTY option of the DIRDIF-99 program system.[44] The structure of **11a** was solved by the program package CRUNCH.[45]

The hydrogen atoms were calculated. Full-matrix least-squares refinement on F, anisotropic for the non-hydrogen atoms and isotropic for the hydrogen atoms, restraining the latter in such a way that the distance to their carrier remained constant at approximately 1.0 Å. Scattering factors were taken from Cromer et al.[46] and from International Tables for X-ray Crystallography.[47] All calculations were performed with XTAL,[48] unless stated otherwise.

Table 2-5. Crystallographic data for crystal structure determinations of **3a**, **4a**, **7a**, **8b and 11a**.

Compound	**3a**	**4a**	**7a**
Empirical formula	$C_{32}H_{24}N_2O_4Pd$	$C_{32}H_{28}N_2O_6Pd$	$C_{30}H_{22}N_4O_8Pd$
Formula weight (g mol^{-1})	606.96	642.98	672.94
Temperature (K)	295	293	250
Crystal size (nm)	0.35 × 0.30 × 0.15	0.75 × 0.25 × 0.05	0.40 × 0.20 × 0.05
Wavelength (Å)	1.54180	1.5418	1.5418
Crystal system	monoclinic	monoclinic	triclinic
Space group	$P2_1/n$	$C2/c$	$P\bar{1}$
a (Å)	11.3922(8)	31.654(3)	7.490(2)
b (Å)	12.4860(6)	8.7108(10)	13.725(4)
c (Å)	18.318(4)	22.155(3)	14.651(5)
β (˚)	90.57(2)	111.279(6)	84.87(3)
α (˚);*γ* (˚)	90; 90	90; 90	79.58(3); 78.14(3)
Volume (Å^3)	2605.5(6)	2605.5(6)	1447.5(8)
Z	4	8	2
Number of data meas.	5350	5646	5472
Number of data	4605 with F > 4σ(F)	5214 with F > 4σ(F)	4568 with F > 4σ(F)
Number of variables	353	471	476
Goodness-of-fit on *F*	1.04	1.026	1.033
R	0.080	0.039	0.062
wR_2	0.091	0.041	0.066

Compound	**8b**	**11a**
Empirical formula	$C_{26}H_{30}N_4O_8Pd$	$C_{30}H_{21}N_3O_{12}$
Formula weight (g mol^{-1})	633.02	615.54
Temperature (K)	293	293
Crystal size (nm)	0.30 × 0.25 × 0.25	0.60 × 0.30 × 0.20
Wavelength (Å)	1.5418	1.5418
Crystal system	monoclinic	monoclinic
Space group	$P2_1/a$	$P2_1/c$
a (Å)	10.927(2)	18.070(6)
b (Å)	22.0530(10)	10.495(2)
c (Å)	11.691(2)	15.885(3)
β (°)	94.646(8)	103.49(3)
Volume (Å^3)	2808.0(7)	2929.4(13)
Z	4	4
Number of data meas.	5761	5776
Number of data	4910 with F > 4σ(F)	3433 with I > 2.5σ(I)
Number of variables	1241	470
Goodness-of-fit on *F*	1.146	1.095
R	0.037	0.077
wR_2	0.038	0.077

2.5.5 Acknowledgement

We thank Prof. Luciano Canovese and Dr. Fabiano Visentin for their studies concerning the kinetics of the palladacycle formation and for the discussions of the obtained results.

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Chapter 3

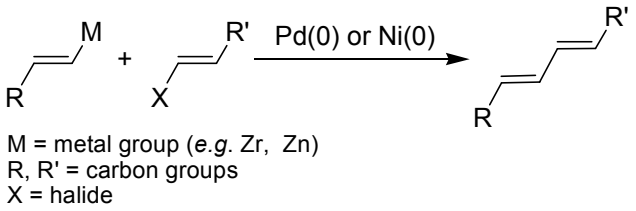
Mechanistic and Kinetic Investigation of the Conversion of Dimethyl-2-butynedioate to Conjugated (*Z*,*Z*)-Dienes Catalyzed by [Pd(4-CH_3-C_6H_4-bian)$(CCOOMe)_4$]

Abstract

The palladacyclopentadiene [Pd(p-tolyl-bian)$(CCOOMe)_4$] was employed as pre-catalyst in the catalytic three-component synthesis of the conjugated diene, dimethyl-(2Z,4Z)-2-benzyl-3,4-bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate, from dimethyl-2-butynedioate, benzyl bromide and tetramethyltin in DMF. The mechanism of the catalytic reaction has been explored by studying the formation and the reactivity of several intermediates and by investigating the kinetics of the formation of the palladacyclopentadiene [Pd(bipy)$(CCOOMe)_4$] from [Pd(bipy)(η^2-DMF)] and [Pd(bipy)(η^2-dmbd)]. In this manner, the formation of secondary products observed in the catalytic synthesis of diene such as (dimethyl-(Z)-2-dimethylamino-but-2-en-1,4-dioate), dimethyl-(Z)-2-benzyl-3-methyl-but-2-en-1,4-dioate or dimethyl-(2Z,4Z)-3,4-bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate was revisited. The "true catalyst" is hypothesized to be a homogeneous "naked palladium" species [Pd^0(bipy)] that may enter into several competing catalytic cycles that occur at different rates.

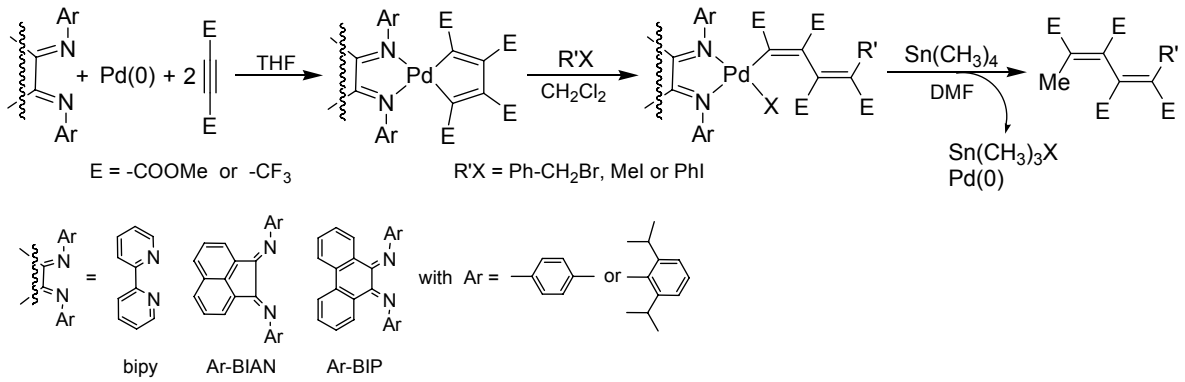
3.1 Introduction

The stereospecific synthesis of conjugated dienes is of considerable importance, since many natural products and bioactive compounds contain the 1,3-diene unit or even multiple unsaturations with higher degrees of conjugation. For these reasons, transition-metal-mediated conversion of alkynes into polyenes and more precisely, the development of selective methods for the synthesis of 1,3-dienes has been a research area of interest for many years now. This had led to the development of catalysts based on cobalt,[1] ruthenium,[2] nickel[3] and palladium[3b,4] for double addition of diazo compounds to alkynes or direct coupling of a stereo-defined alkenyl-metallic compound with a stereo-defined vinyl electrophile, such as a vinyl halide (Scheme 3-1). Other stereoselective methods of dienes synthesis based on diyne reduction with a zinc/copper reagent or a sodium-mercury amalgam were also described.[5]



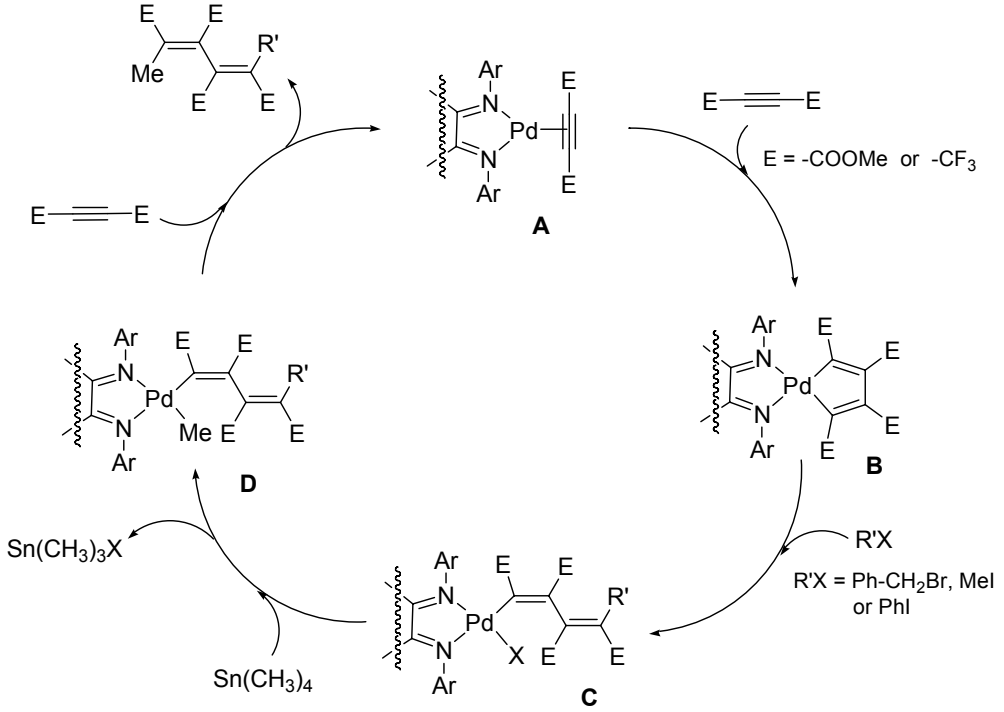
Scheme 3-1. Palladium- or nickel-catalyzed reactions of alkenylmetals with unsaturated organic halides as selective route to conjugated dienes.

In addition to these approaches, some catalytic processes involving metallacyclopentadiene species as intermediate, as reported in chapter 2, have been published.[6-9] However, to the best of our knowledge, the synthesis of conjugated dienes from two molecules of an alkyne *via* a metallacyclopentadiene is limited to only few transition metals, such as titanium,[6] zirconium,[7] iridium[8] and palladium.[9] Van Belzen *et al*.[9c,d] reported the stoichiometric synthesis of conjugated diene reacting palladacyclopentadienes, containing chelating bidentate nitrogen ligands, with organic halide and a transmetallation reagent (Scheme 3-2). Competition experiments involving a [Pd(NN)(η^2-alkene)] complex, 2 equiv of dimethyl-2-butynedioate (dmbd) and alkyl halide revealed that the palladacyclopentadiene is formed much more rapidly than the concurrent oxidative addition of alkyl halide.



Scheme 3-2. Stoichiometric conversion of alkynes to conjugated (Z,Z)-dienes *via* palladacyclopentadienes.

Moreover, the insertion of a third molecule of acetylene in **B** is slower than reaction of the organic halide with **B** to give **C**. From the observations made above, a catalytic cycle, involving the single steps in the stoichiometric process, was then developed (Scheme 3-3).[9c,d] These complexes (**B**), in combination with an organic halogen compound and an organotin compound, were able to convert dimethyl-2-butynedioate into the desired dienes in 75-82% isolated yield, depending on the organic halide used.

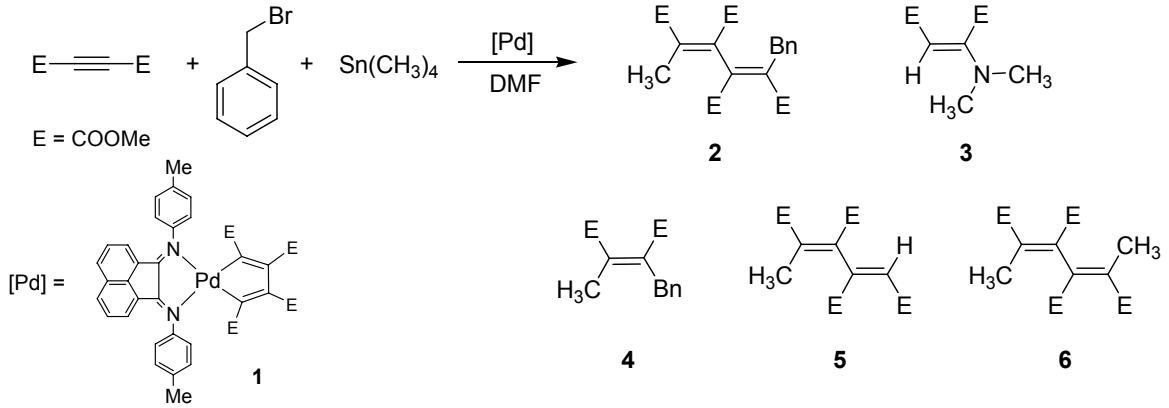


Scheme 3-3. Proposed cycle for the three-component synthesis of conjugated dienes from alkynes, organic halide and tetramethyltin.

Recently, kinetic studies on the mechanism of formation of palladacyclopentadiene from alkene palladium(0) derivatives of pyridylthioethers and dmbd have been done by Canovese and co-workers.[10] Their results are comparable in terms of kinetics: formation of the palladacyclopentadiene (**B**) is a fast process; and in terms of reactivity: palladacyclopentadiene (**B**) does not react with an other molecule of alkyne under mild condition even in case of a large excess of the latter.
Van Belzen and co-workers have, furthermore, reported significant formation of by-products during the catalytic process, such as the cyclotrimerization product hexamethylmellitate, a product originating from decarbonylative addition of DMF to the dmbd and 1-phenyl-1,2-di(methoxycarbonyl)-1-propene that is probably formed by transmetalation of the adduct resulting from phenylpalladation of **A**. So, after our investigations on the reactions between dissymmetrically substituted alkynes and palladium(0) derivatives to give the corresponding pallacyclopentadienyl complexes,[11,Chapter2] we decided to re-investigate the catalytic process exhaustively, in order to find an eventual extension to include dissymmetrically substituted alkynes in the range of possible substrates.

3.2 Results and Discussion

3.2.1 Catalytic three-component synthesis of conjugated dienes from alkynes



Scheme 3-4. Catalytic three-component synthesis of the conjugated diene with dmbd, benzyl bromide and tetramethyltin.

The palladacyclopentadiene **1** was employed as pre-catalyst in the catalytic three-component synthesis of the conjugated diene, dimethyl-(2*Z*,4*Z*)-2-benzyl-3,4-

bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate (**2**), from dimethyl-2-butynedioate (dmbd), benzyl bromide and tetramethyltin in DMF (Scheme 3-4).

It appears that the formation of the diene is accompanied by the sometimes extensive decarbonylation process of DMF, after which the arising amido-palladium species amine adds to the alkyne, yielding product **3** (dimethyl-(*Z*)-2-dimethylamino-but-2-en-1,4-dioate). Furthermore, the compound dimethyl-(*Z*)-2-benzyl-3-methyl-but-2-en-1,4-dioate (**4**), which has not been described by Van Belzen *et al*.[9d] is also formed. The formation of dimethyl-(2*Z*,4*Z*)-3,4-bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate (**5**) was observed before as well. The reported[9d] dimethyl-(2*Z*,4*Z*)-3,4-bis(carbomethoxy)-2,5-dimethyl-2,4-hexadien-1,6-dioate (**6**) was observed by GC-MS as by-product but could not be successfully isolated and characterized. The results have been compiled in Table 3-1.

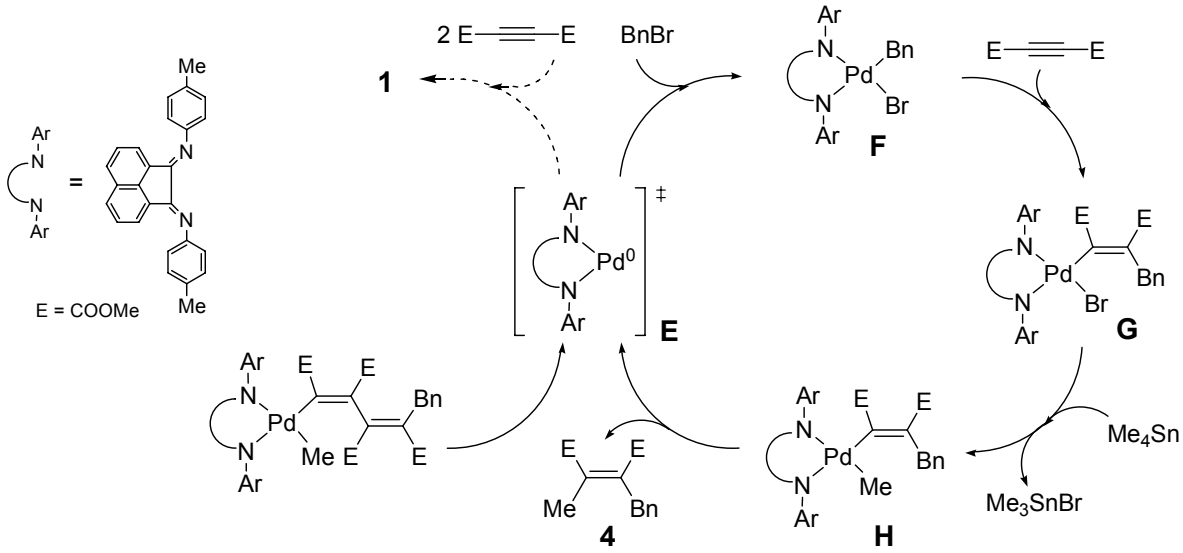
Table 3-1. Synthesis of dimethyl-(2*Z*,4*Z*)-2-benzyl-3,4-bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate (**2**) from dmbd, benzyl bromide and tetramethyltin catalyzed by palladacyclopentadiene complex (**1**).[a]

Entry	dmbd / benzyl bromide (mmol)	Temperature (ºC)	Selectivity (%)[b] **2** : **3** : **4** : **5**
1	2/1	85	27.2 : 40.9 : 10.1 : 21.8
2	2/1	65	19.1 : 45.9 : 10.9 : 24.1
3	2/10	65	17.0 : 21.7 : 37.6 : 23.7
4	5/1	85	49.5 : 21.4 : 11.4 : 17.7
5	5/1	100	42.1 : 16.8 : 15.5 : 25.6
6[c]	5/1	85	61.6 : 21.4 : 7.2 : 9.8
7[c]	10/1	85	52.4 : 12.9 : t : 34.7
8[d]	2/1	85	t : 18 : t : 82
9[c,e]	10/1	85	9.4 : 46.9 : t : 43.7

[a] Pre-catalyst **1** (0.02 mmol), tetramethyltin (1 mmol), DMF (10 mL). [b] determined by ^{1}H-NMR; t = trace. [c] DMF (5 mL). [d] DMAC (5 mL) was used as solvent. [e] 2% (V/V) of water was added.

Initially, we applied the conditions described by Van Belzen *et al*.[9d] (Table 3-1, entry 1), but a very low selectivity for the formation of **2** (27.2%) was observed with an important degree of decarbonylation of DMF (**3**) (40.9%). This tendency is even

higher by decreasing the temperature to 65ºC (entry 2), 45.9% of **3** versus 19.1% of **2**. Apparently, a lower dmbd/benzyl bromide ratio (ratio = 0.2) leads, importantly, to the formation of by-products **3**, **4** and **5** (entry 3). As expected, the major difference is the increase of the amount of **4** (37.6%), relative to previous cases (10% when ratio = 2). Probably, benzyl bromide acts as an inhibitor, thereby blocking the oxidative coupling of dmbd to form **1**. A plausible cycle for the formation of **4** could be that, after a reductive elimination of diene, the oxidative addition of benzyl bromide occurs on the Pd^0 species (**E**) forming **F**, that is followed by a insertion step of dmbd into the palladium carbon bond with the formation of *σ*-enylpalladium compound **G**. In the envisaged cycle, the formation of *σ*-enylpalladium compound is followed by a transmetalation step with the formation of a diorganopalladium species **H** which then follows a similar catalytic cycle as for the diene (Scheme 3-5).



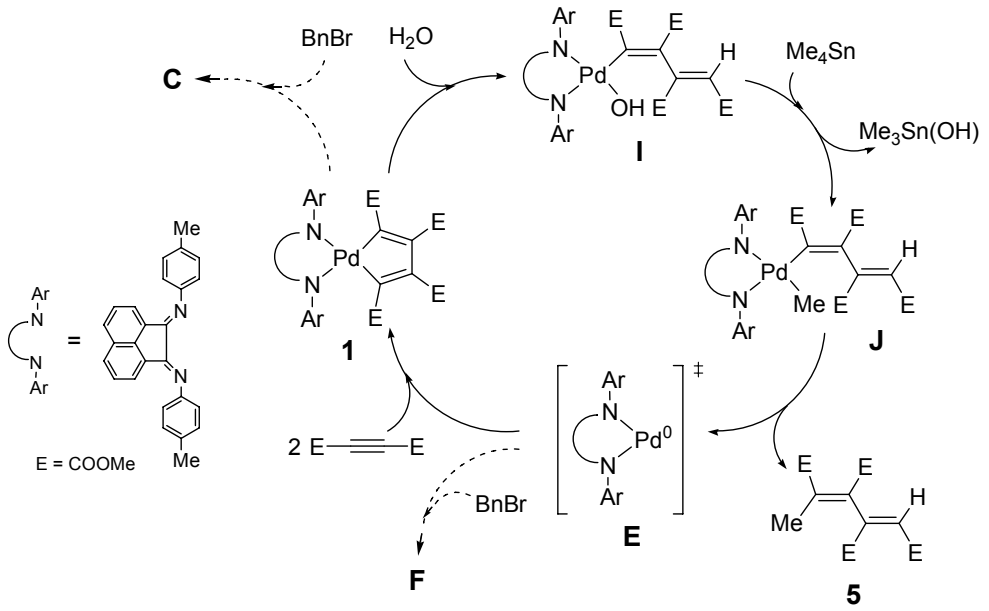
Scheme 3-5. Proposed mechanism for the formation of dimethyl-(*Z*)-2-benzyl-3-methyl-but-2-en-1,4-dioate (**4**).

This catalytic cycle closely resembles the one proposed for the cross-coupling reaction of organic halides with organotin compounds, except for the additional insertion of alkyne. When a higher dmbd/benzyl bromide ratio of 5 was applied (entry 4), indeed a higher selectivity for the synthesis of **2** was obtained (about two times higher than for dmbd/benzyl = 2; entry 1), although the formation of by-products was still relevant. Further increasing of dmbd/benzyl bromide ratio, from 5 to 10 (entry 7), did not lead to a best selectivity. When we increased the reaction temperature, selectivity for the formation of desired diene **2** slightly decreased (entries 4 and 5)

contrary to the formation of the diene **5**. The highest and best selectivity to diene **2** (61.6%) was obtained when we increased the concentration of reactants; an almost 20% higher quantity of **2** was observed when the solution was two times more concentrated (entries 4 and 6).

It was shown by Van Belzen *et al*.[9c] that DMF was essential, because in other common solvents the substitution of the halide by the methyl group to deliver dienes failed. We have attempted to use DMAC to prevent the formation of the product arising from the decarbonylation process, but this was unsuccessful and only traces of **2** were observed. Significantly, but completely unexpectedly, formation of the diene **5** considerably increased in DMAC as solvent and the amino product was still formed (entry 8).

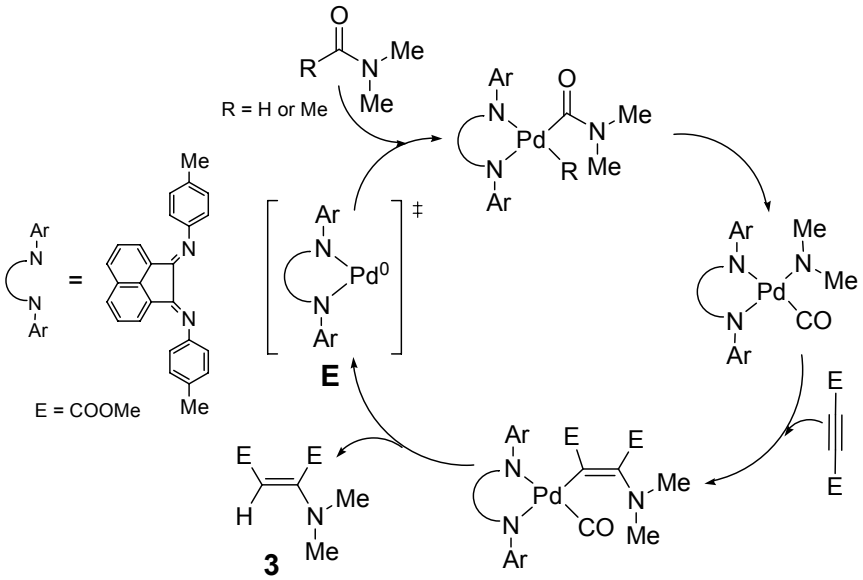
In order to determine the origin of the added hydrogen in **3** and **5**, we added 2% of water to the reaction mixture (entry 9), which resulted in an increase of both **3** and **5**. When the same experiment was executed with 2% of deuterated water, it became clear that the added hydrogen in **5** originates directly from water, suggesting that there might be an oxidative addition of the water on **1** which after reductive elimination might give a *σ*-dienylpalladium compound **I** (Scheme 3-6). The formation of this *σ*-dienylpalladium is also followed by a transmetalation step to give a diorganopalladium species **J**.



Scheme 3-6. Proposed mechanism for the formation of dimethyl-(2*Z*,4*Z*)-3,4-bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate (**5**).

Dimethyl-(2*Z*,4*Z*)-3,4-bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate (**5**) would be formed together with a zerovalent palladium intermediate (**E**) that could react with dmbd to form **1**, more or less like in the proposed mechanism for the formation of the conjugated diene **2** (Scheme 3-3), or with benzyl bromide to form **F** (Scheme 3-5).

The formation of the product **3** (dimethyl-(*Z*)-2-dimethylamino-but-2-en-1,4-dioate) arises from the decarbonylation process of DMF is more difficult to explain. The formation of the product is accounted for by assuming oxidative addition of the DMF[12] to palladium, involving the cleavage of the formyl C–H bond followed by decarbonylation. We can then assume an insertion step of dmbd into the palladium nitrogen bond with the formation of *σ*-enylpalladium compound. However, using DMAC as solvent, the formation of **3** is also observed although the origin of the olefinic hydrogen of **3** was initially attributed to the DMF. Since this decarbonylation process is promoted by water (entry 9) we assumed that the water provides the proton, but this hypothesis has to be rejected based on the experiment with deuterated water. A possible mechanism for the formation of **3** is given in Scheme 3-7.



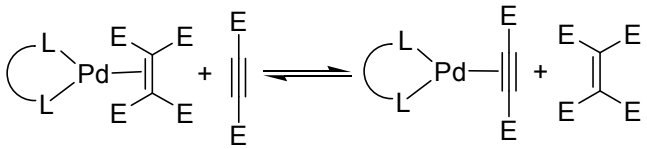
Scheme 3-7. Proposed mechanism for the formation of dimethyl-(*Z*)-2-dimethylamino-but-2-en-1,4-dioate (**3**).

3.2.2 Kinetic aspects of the catalytic three-component synthesis of conjugated dienes from alkynes

3.2.2.1 [Pd(NN)(η^2-DMF)] and [Pd(NN)(η^2-alkyne)] complexes involved in the catalysis

In order to shed light on the intimate mechanism governing the three-component catalytic cycle leading to conjugate dienes from alkynes we decided to study the reaction between [Pd(NN)(η^2-alkene)] derivatives and alkynes in more detail. It is well known that the reaction of [Pd(NN)(η^2-alkene)] derivatives and electron poor alkynes in excess leads to the palladacyclopentadiene species which represent the pre-catalyst of the catalytic cycle.

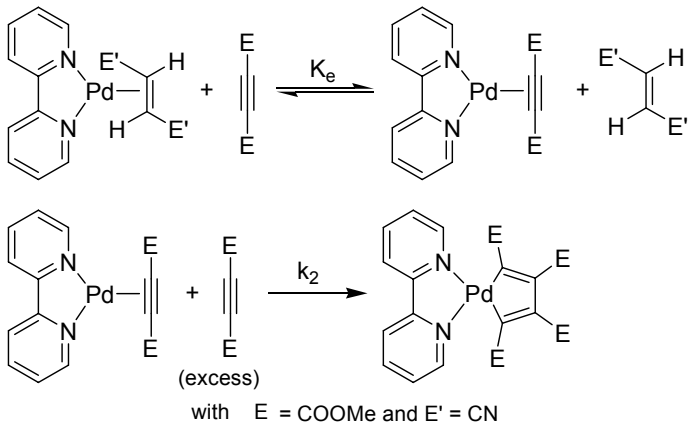
To perform this kind of study stoichiometric and mild conditions are necessary. We chose the complex [Pd(bipy)(η^2-DMF)][13] and the alkyne dmbd as the model for the catalyst and the reacting alkyne, respectively. The reactivity of the species involved indeed allows mild conditions and reasonable rates of reaction. The reaction between [Pd(LL)(η^2-alkene)] derivatives and alkynes is well describes as a two step reaction. The first step is represented by the fast equilibrium reaction in which the alkene is substituted by one alkyne (Scheme 3-8).



Scheme 3-8. Fast equilibrium reaction of alkene/alkyne exchange.

Then the [Pd(NN)(η^2-alkyne)] complex can react with a further alkyne molecule or, depending on its electronic and steric characteristics, accumulate as an unreactive species.[10a and refs therein] When, to a solution in CD_2Cl_2 of the complex [Pd(bipy)(η^2-DMF)], a slight excess of the alkyne dmbd is added, the starting complex [Pd(bipy)(η^2-DMF)] instantaneously disappears and the formation of the relevant palladacyclopentadiene **B** (see Scheme 3-3) is observed by ^{1}H NMR. The second order reaction rate k_2 (k_2 = 0.42 ± 0.03 mol^{-1} dm^3 s^{-1}) was obtained for the reaction in

Scheme 3-9 by measuring the k_{obs} that was determined under various pseudo-first order conditions by UV-Vis spectroscopy in $CHCl_3$.

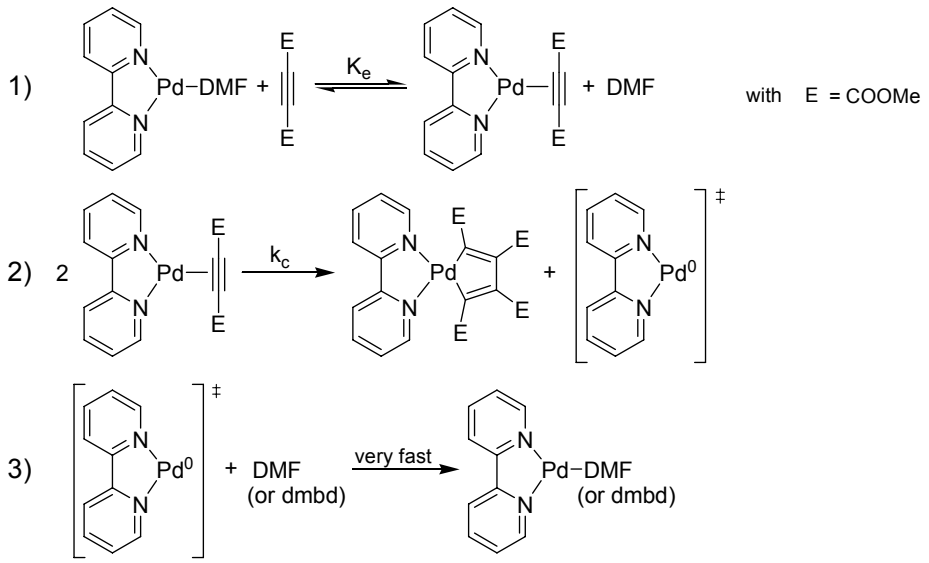


Scheme 3-9. Multistep reaction for the formation of palladacyclopentadiene.

In order to disentangle the overall reaction network, the value of the $Ke_{DMF/dmbd}$ which concerns the equilibrium of displacement of DMF by dmbd was firstly estimated (Scheme 3-10, equation 1). The ^1H NMR titration of the complex [Pd(bipy)(η^2-DMF)] with dmbd is quantitative (high $Ke_{DMF/dmbd}$ value) at any dmbd concentration at , furthermore the equilibrium itself is complicated by the subsequent cyclization reaction, so that no significant measures of $Ke_{DMF/dmbd}$ could safely be done. This fact is the consequence of the weak coordinating capability of DMF to Pd^0 complexes. It appeared previously that the K_e for alkenes like maleic anhydride and fumaronitrile are, 7900 and 4400, respectively, times larger than for DMF.[14]

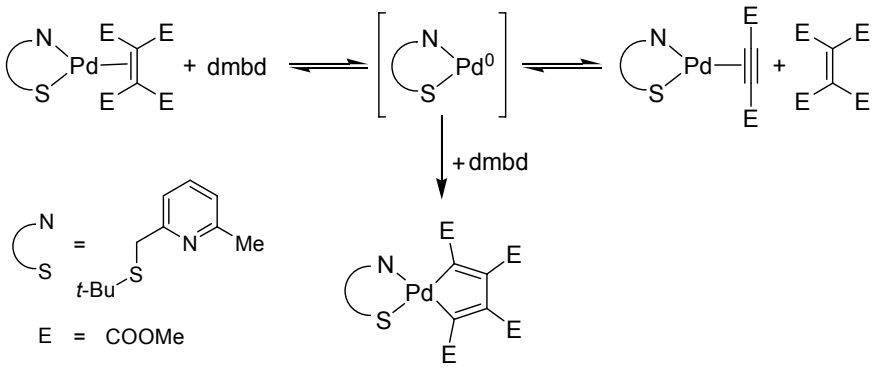
Thus, taking advantage of the stability of the complex [Pd(bipy)(η^2-fn)], the ^1H NMR titration of the latter by dmbd at low temperature (-60°C) was carried out in order to freeze the subsequent reactions. The determined $Ke_{fn/dmbd}$ value was 0.16 ± 0.01. When assumed that $Ke_{fn/dmbd}$ is not much affected by increasing the temperature, the equilibrium constant $Ke_{DMF/dmbd}$ could be obtain by multiplying the values of $Ke_{DMF/fn}$ and $Ke_{fn/dmbd}$ obtained at different temperatures: $Ke_{DMF/dmbd}$ = $Ke_{DMF/fn}$ * $Ke_{fn/dmbd}$ = 4400 * 0.16 = 700). In view of numerical value of $Ke_{DMF/dmbd}$ (hereafter K_e) obtained, one can justify the peculiar reactivity observed upon addition of slight excess of dmbd to [Pd(bipy)(η^2-DMF)]. This value, even though approximate, tells us that in the presence of an equimolecular amount of dmbd the complex [Pd(bipy)(η^2-DMF)] completely disappears giving rise to the quantitative formation of [Pd(bipy)(η^2-dmbd)]. Of course, this compound is not stable in the presence of

excess of alkyne; when obtained by equimolecular addition of dmbd to [Pd(bipy)(η^2-DMF)], it undergoes palladacyclopentadiene formation leading to a 1:1 mixture of [Pd(bipy)(η^2-DMF)] and [Pd(bipy)(CCOOMe)$_4$] complexes. Overall, the relevant equations have been summarized in Scheme 3-10.



Scheme 3-10. Oxidative coupling of dmbd promoted by [Pd(bipy)(η^2-DMF)] complex.

The constant k_c was determinated from the reactions illustrated in Scheme 3-10 (equation 2, k_c = 44 mol^{-1} dm^3 s^{-1}). This result suggests an alternative route for the formation of the palladacyclopentadiene based on the reaction between two molecules of the complex [Pd(bipy)(η^2-dmbd)]. The reactive 14-electrons species [Pd^0(bipy)] (**E**) also produced in that reaction promptly reacts with the free DMF to give the starting complex [Pd(bipy)(η^2-DMF)] when the reaction is carried out under equimolecular conditions between [Pd(bipy)(η^2-DMF)] and dmbd or the complex [Pd(bipy)(η^2-dmbd)] with dmbd in excess. It is noteworthy that the presence of the 14-electrons species was already suggested by other authors as a reactive by-product in the formation of hexamethylmellitate in analogous reactions of palladacyclopentadiene formation from pyridylthioethers Pd^0 derivatives (Scheme 3-11).[10]



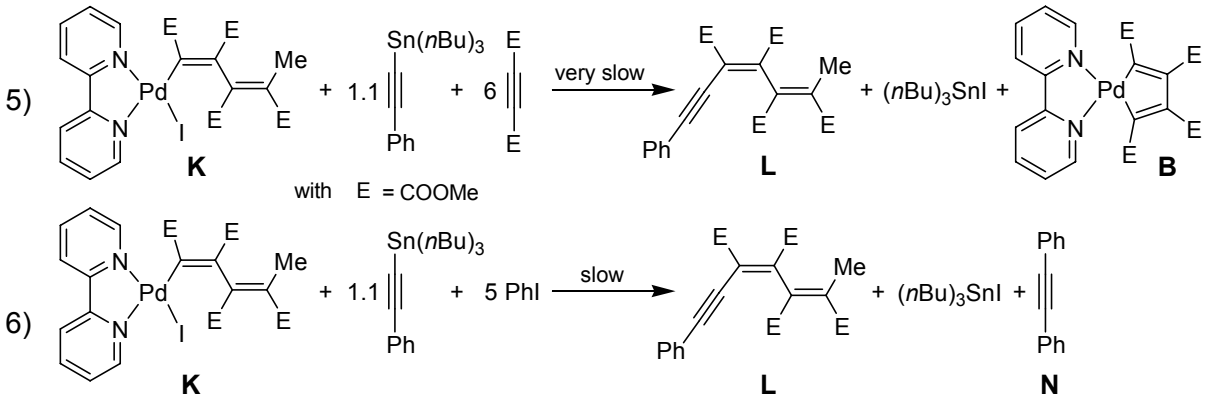
Scheme 3-11. Multistep mechanism for the formation of cyclopalladate complex.[10a]

3.2.2.2 Reactivity of organic halide with [Pd(bipy)(η^2-DMF)], [Pd(bipy)(η^2-dmbd)] and palladacyclopentadiene complexes

In order to explain the formation of **4** (Scheme 3-5), we assume that after a reductive elimination of diene, the oxidative addition of benzyl bromide occurs on the zerovalent palladium intermediate **E** (Scheme 3-5). The reactions of phenyl iodide with [Pd(bipy)(η^2-DMF)], [Pd(bipy)(η^2-dmbd)] (**A**) and [Pd(bipy)(CCOOMe)$_4$] (**B**) were carried out in dichloromethane at room temperature at a Pd^0/phenyl iodide ratio of 3 and were followed by ^{1}H NMR. In none of these cases, oxidative addition was observed. The [Pd(bipy)(η^2-DMF)] complex does not react with phenyl iodide, even in the presence of dmbd. The lack of reactivity of phenyl iodide with [Pd(bipy)(CCOOMe)$_4$] (**B**), under mild conditions, to form a *σ*-dienylpalladium compound (as **C** in Scheme 3-3), is conform to the literature.[9c-d,16]

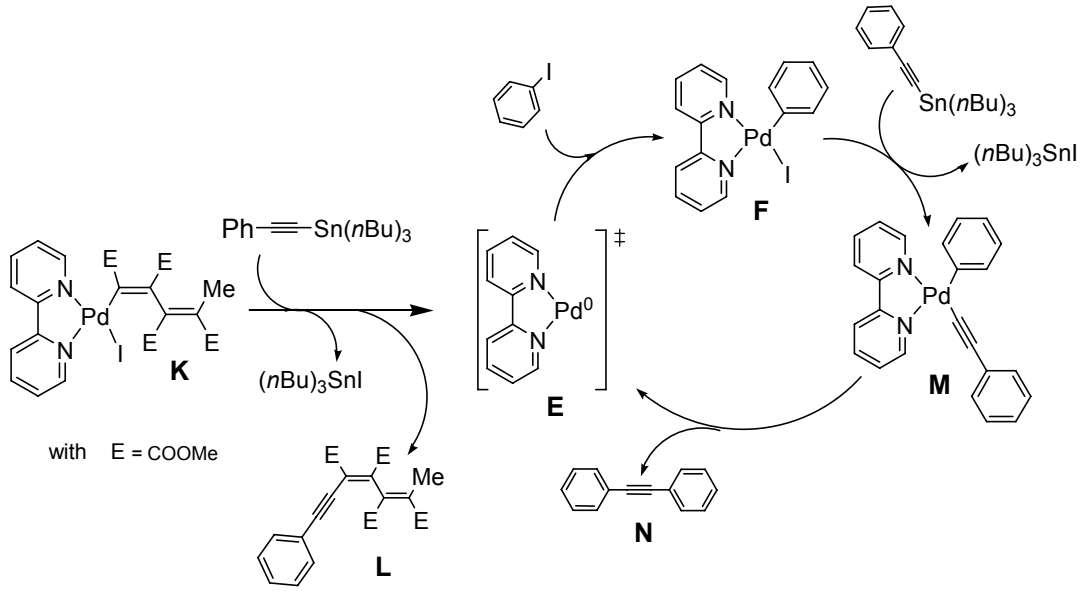
3.2.2.3 Reaction involving the σ-dienylpalladium complex

Despite the fact that the formation of the *σ*-dienylpalladium species is not observed under mild conditions and in order to consider all the species involved in the catalysis, the reactions of [Pd(bipy)I((EC=CE)$_2$Me)] (**K**) with an organotin reagent and dmbd or phenyl iodide have been studied and followed by ^{1}H NMR under almost the same experimental conditions as before (Scheme 3-12).



Scheme 3-12. Reactions of [Pd(bipy)I((EC=CE)$_2$Me)] (**K**), an organotin reagent and an excess of dmbd or phenyl iodide.

In both cases, the formation of the diene **L** was observed, the transmetalation step followed by the reductive elimination proceeds slowly under mild experimental conditions. Obviously, in the reaction 5, the diene **L** is produced in very small quantity. More significantly, in reaction 4, the formation of the palladacyclopentadiene **B** is noticed and may be explained by the reaction of the excess of dmbd with **E**, the intermediate [Pd^0(bipy)] (Scheme 3-9, reaction 2), arising from the reductive elimination of the diene. The predominant formation of diphenylacetylene **N** in reaction 5 is even more relevant and this observation indicates that the oxidative addition of phenyl iodide on intermediate **E** is operative. A catalytic cycle for the formation of diphenylacetylene is proposed (Scheme 3-13), which is similar to that generally proposed for the cross-coupling reaction of organic halides with organotin compounds and closely resembles the one proposed for the formation of 1-benzyl-1,2-di(carbomethoxy)-1-propene (**4**) in Scheme 3-5. Indeed, we assumed that, after the oxidative addition of the organic halide, insertion of the acetylene in the palladium–aryl/alkyl bond may occur in the presence of dmbd. In this case (absence of dmbd), the oxidative addition is followed directly by the transmetalation step and then the reductive elimination leading to diphenylacetylene **N**.

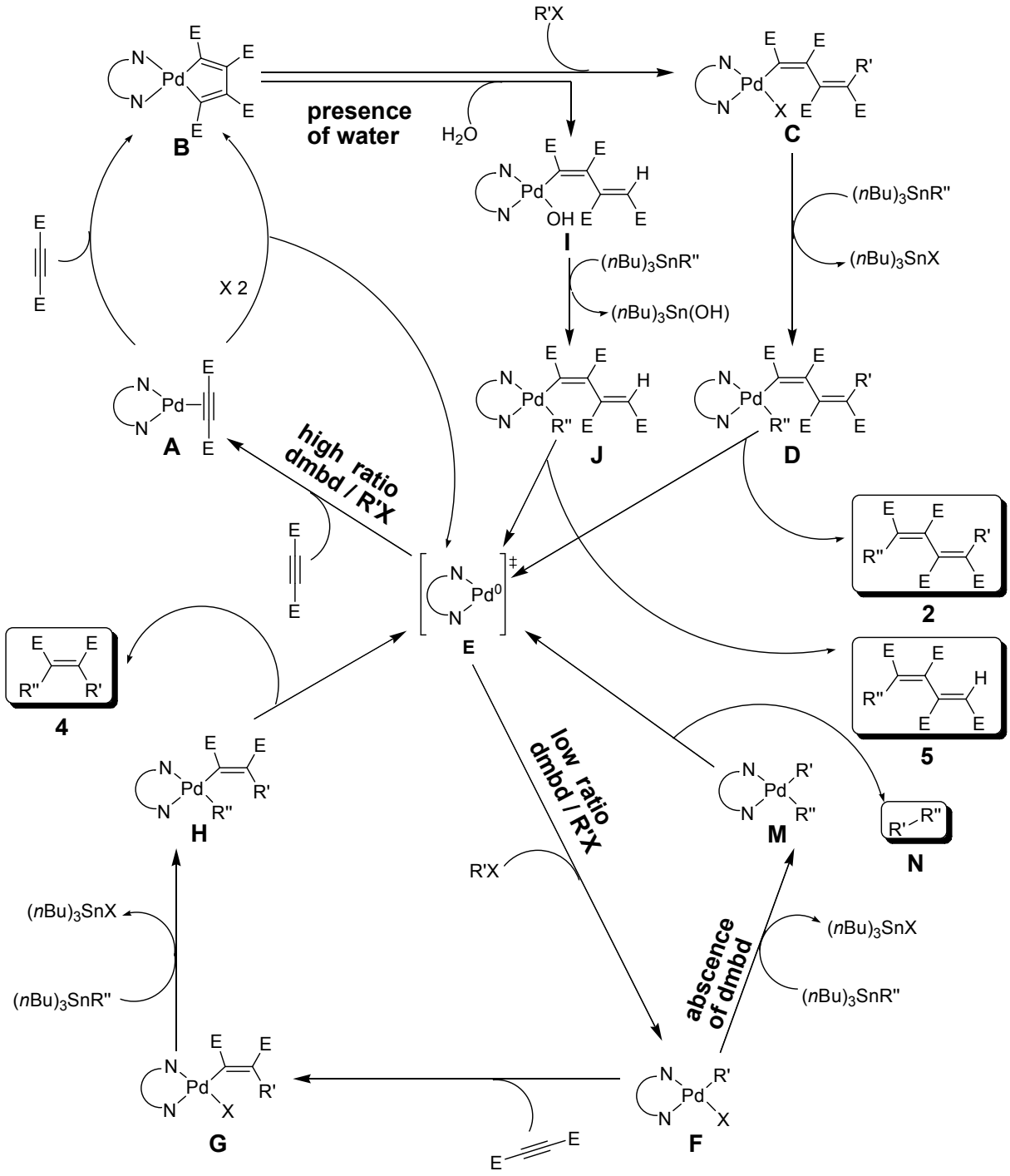


Scheme 3-13. Proposed mechanism for the formation of diphenylacetylene (**N**).

3.2.3 Mechanism of the reaction of dmbd, organic halide and organotin reagent catalyzed by [Pd(NN)(CCOOMe)$_4$]

Based on the combined results of the catalysis, of the kinetic investigation described in this chapter and on the contemporary presence of the three components, the coexistence of two catalytic cycles for the reaction is proposed to account for all observed products (Scheme 3-14).

Although the reaction between the palladacyclopentadiene and the organic halide was not observed during the kinetic investigation, we did consider the ring opening as part of the mechanism since a higher temperature and a considerable excess of organic halide was employed.



Scheme 3-14. Proposed general mechanism for the catalytic three components reaction catalyzed by [Pd(NN)(CCOOMe)$_4$].

The undetected reactive intermediate (**E**) is the active species linking the two catalytic cycles and is at the origin of all products. Regarding the synthesis of the alkene (**4**) and the diene (**2**), it seems obvious that a high dmbd/organic halide ratio leads to the upper part of the catalytic cycle. However, the reaction of the traces of

water on the palladacyclopentadiene leading to diene (**5**) and the oxidative addition of the organic halide on the “naked palladium” intermediate cannot be ignored.

3.3 Conclusion

The catalytic three component synthesis of diene starting from dimethyl-2-butynedioate has been explored by studying the formation and the reactivity of some intermediates.

The present kinetic and mechanistic investigation of the formation of the palladacyclopentadiene [Pd(bipy)(CCOOMe)$_4$] from [Pd(bipy)(η^2-DMF)] and [Pd(bipy)(η^2-dmbd)] shows that this reaction with the NN ligand is similar to the one described by Canovese *et al*., with pyridylthioether derivative as ligand.

The results, that have been obtained during the study of the reactivity of the zerovalent palladium compounds and the *σ*-dienylpalladium compound with organic halide in presence of organotin reagent, are in agreement with the observation made during the catalytic conversion of dimethyl-2-butynedioate to conjugated (*Z*,*Z*)-dienes.

The low selectivity observed in the catalytic synthesis of diene is due to the high reactivity of the zerovalent intermediate (**E**), which arises from the reductive elimination of the diene product. It can react with dmbd, DMF but also with the organic halide leading to the alkene product. This formation of the alkene derivative *via* an insertion of the dmbd into the palladium–aryl/alkyl bond is supported by the formation of diphenylacetylene (**N**) observed in absence of dmbd. However it is possible to direct the catalysis in such a way to obtain predominantly the diene by increasing the dmbd/organic halide ratio. The decarbonylation of DMF proceeds easily during our catalysis, leading to the formation of the dimethyl-(*Z*)-2-dimethylamino-but-2-en-1,4-dioate (**3**) and unfortunately the use of other solvents was unsuccessful to complete the catalysis. However, by performing the catalysis at high concentration ([dmbd] = 1M) we succeeded to significantly reduce the amount of this side reaction. The aqueous origin of the proton from the secondary diene (dimethyl-(2*Z*,4*Z*)-3,4-bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate (**5**)) is supported by experiments with deuterated water.

Finally, the overall results have enabled us to provide a viable reaction mechanism for the three component synthesis of dienes starting from dimethyl-2-

butynedioate, catalyzed by a palladacyclopentadiene complex such as [Pd(NN)(CCOOMe)$_4$]. However, the extension of this catalytic process to dissymmetrically substituted alkynes seems compromised since it proved difficult to limit the side reactions even with this very reactive acetylenic substrate. Also, as it was shown in chapter 2, the asymmetric alkynes that we studied are less reactive than dmbd, which will probably promote the side reactions such as the formation of the alkene product even more.

3.4 Experimental Section

3.4.1 General considerations

All reactions were carried out by using standard Schlenk techniques under an atmosphere of dry nitrogen unless otherwise specified. The solvents were dried according to standard procedures[17] and distilled before use. ^{1}H and ^{13}C NMR spectra were recorded at 298K on a Bruker AMX 300 spectrometer (300.13 and 75.48 MHz respectively) and on a Varian Inova 500 spectrometer (499.86 and 125.70 MHz respectively). The chemical shift values are referenced to external TMS with high frequency shifts signed positive. Chemical shifts (δ) and coupling constants (J) are expressed in ppm and in Hertz (Hz) respectively and the multiplicity as s = singulet, d = doublet, dd = double doublet, t = triplet, pst = pseudo triplet, m = multiplet, br = broad; data in parenthesis are given in the following order: multiplicity, number of protons, labelling of the proton and coupling constants in Hz.
2,2-Bipyridine (Merck), benzyl bromide (Acros), tetramethyltin (Acros), dimethyl-2-butynedioate (Acros) were used as received. *p*-Me-C$_6$H$_4$-bian[18] and pallada-2,3,4,5-tetrakis(carbomethoxy)cyclopentadiene-*p*-Me-C$_6$H$_4$-bian were prepared according to literature procedures.

3.4.2 Catalytic synthesis of conjugated diene

General procedure for the catalytic synthesis of conjugated diene
A solution of 15 mg of **1** (0.02 mmol), 245 μL of dmbd (2 mmol), 140 μL of tetramethyltin (1 mmol) and 120 μL of benzyl bromide (1 mmol) in DMF (10 mL) was stirred for 16h at 85ºC. The reaction mixture was dissolved in 100 mL, washed with

water (3 × 150 mL), dried and the solvent was removed to yield a brown liquid. Ether (75 mL) was added to the residue and the mixture was stirred for 0.5 hour. The mixture was then filtered over celite and the solvent was removed to give light brown oil. This oil was then chromatographied over silica with ether/hexane (1:1) as eluent.

Dimethyl-(2*Z*,4*Z*)-2-benzyl-3,4-bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate (2)

^{1}H NMR ($CDCl_3$, 499.86 MHz): δ 7.27-7.13 (m, 5H, H_{ar}), 3.83 (s, 3H, OC*H*$_3$), 3.72 (s, 3H, OC*H*$_3$), 3.71 (s, 2H, C*H*$_2$), 3.67 (s, 3H, OC*H*$_3$), 3.65 (s, 3H, OC*H*$_3$), 1.93 (s, 3H, C*H*$_3$).

^{13}C NMR ($CDCl_3$, 125.70 MHz): δ 169.5 (*C*O), 168.6 (*C*O), 165.3 (*C*O), 165.11 (*C*O), 146.0 (*C*=C), 144.2 (*C*=C), 135.7 (C_i), 129.3 ($2C_o$ or $2C_m$), 128.6 ($2C_m$ or $2C_o$), 128.0 (*C*=C), 127.1 (C_p and *C*=C), 52.9 (O*C*H$_3$), 52.8 (O*C*H$_3$), 52.7 (O*C*H$_3$), 52.5 (O*C*H$_3$), 37.7 (*C*H$_2$), 18.3 (*C*H$_3$).

Dimethyl-(*Z*)-2-dimethylamino-but-2-en-1,4-dioate (3)

^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 4.57 (s, 1H, C*H*), 3.92 (s, 3H, OC*H*$_3$), 3.62 (s, 3H, OC*H*$_3$), 2.86 and 2.85 (s, 6H, N(C*H*$_3$)$_2$).

^{13}C NMR ($CDCl_3$, 75.48 MHz): δ 168.3 (*C*O), 166.3 (*C*O), 155.3 (C=*C*N), 84.6 (*C*H), 53.1 (O*C*H$_3$), 51.0 (O*C*H$_3$), 39.9 (N*C*H$_3$)$_2$).

Dimethyl-(*Z*)-2-benzyl-3-methyl-but-2-en-1,4-dioate (4)

^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 7.31-7.16 (m, 5H, H_{ar}), 3.78 (s, 3H, OC*H*$_3$), 3.73 (s, 2H, C*H*$_2$), 3.66 (s, 3H, OC*H*$_3$), 2.04 (s, 3H, C*H*$_3$).

^{13}C NMR ($CDCl_3$, 75.48 MHz): δ 169.8 (*C*O), 168.8 (*C*O), 137.4 (*C*=C), 136.0 (*C*=C), 135.6 (C_i), 128.8 ($2C_o$ or $2C_m$), 128.5 ($2C_m$ or $2C_o$), 126.8 (C_p), 52.6 (O*C*H$_3$), 52.4 (O*C*H$_3$), 35.3 (*C*H$_2$), 16.4 (*C*H$_3$).

MS (FAB+) *m*/*z*: found 249.1124 [MH^+]: calcd ($C_{14}H_{17}O_4$) 249.1127.

Dimethyl-(2*Z*,4*Z*)-3,4-bis(carbomethoxy)-5-methyl-2,4-hexadien-1,6-dioate (5)

^{1}H NMR ($CDCl_3$, 300.13 MHz): δ 6.13 (s, 1H, C*H*), 3.81 (s, 3H, OC*H*$_3$), 3.79 (s, 6H, 2 × OC*H*$_3$), 3.74 (s, 3H, OC*H*$_3$), 2.07 (s, 3H, C*H*$_3$).

3.4.3 Kinetic and mechanistic study[19]

Synthesis of the complexes

The complexes [Pd(bipy)(η^2-DMF)][13] was synthesized by adding the appropriate olefin (0.4 mmol) to a solution of $Pd_2dba_3 \cdot CHCl_3$ (0.2 mmol) and bipy (0.4 mmol) in 15 ml of anhydrous acetone. The complex [Pd(bipy)I((EC=CE)$_2$Me)] was synthesized by ligand exchange by adding the bipy ligand to the complex [Pd(MeNSPh)Cl((EC=CE)$_2$Me)][10a]. The chloride was eventually replaced by metathetic exchange with NaI.

Reaction involving the [Pd(bipy)I((EC=CE)$_2$Me)] complex

The reactivity of the *σ*-dienylpalladium compound [Pd(bipy)I((EC=CE)$_2$Me)] (**K**) (reactions 4 and 5, Scheme 3-12) was studied by ^{1}H NMR (CD_2Cl_2 at 25ºC, and [Pd(bipy)I((EC=CE)$_2$Me)]$_0$ = 10^{-2} M).

NMR Studies

All reactions were studied by ^{1}H NMR technique. The cyclometallation reactions were investigated by dissolving the olefin complex under study [Pd(bipy)(η^2-DMF)] and [Pd (bipy)(η^2-fn)] in 0.8 ml of CD_2Cl_2 ([complex]$_0$ ≈ 1x10^{-2} mol dm^{-3}) into a NMR tube (concentration ratios [Pd(bipy)(η^2-DMF)]/[dmbd], 1/1 and 1/2). An appropriate aliquot of mother solution (0.4 mol dm^{-3}) of dmbd was then added at -60°C, and the reaction was followed to half or total completion by monitoring the disappearance of the signals of the starting complex and the contemporary appearance of the signals of the palladacyclopentadiene complex at different temperatures (-20, 20, 25°C).

Determination of equilibrium constant

In the case of the complex [Pd(bipy)(η^2-fn)] the equilibrium constant at T = -60°C was determined by adding microaliquots of dmbd (concentration range 0<[dmbd]<0.06 mol dm^{-3}) to a CD_2Cl_2 solution of the complex ([Pd(bipy)(η^2-fn)] = 1x10^{-2} mol dm^{-3}). The equilibrium constant was determined from the titration curve ([Pd(bipy)(η^2-dmbd)]$_{formed}$ vs. [dmbd]$_{add}$) using the model:

$$[Pd(bipy)(\eta^2\text{-fn})] + dmbd \leftrightarrow [Pd(bipy)(\eta^2\text{-dmbd})] + fn \qquad (1)$$

$Ke_{fn/dmbd}$ = 0.16 ± 0.01

Thus, at low temperature (-60°C) the reaction between two molecules of the complex [Pd(bipy)(η^2-dmbd)] to give the palladacyclopentadiene and the substrate

[Pd(bipy)(η^2-DMF)] (see discussion) does not take place and only the displacement of the DMF by dmbd is observed. Under these experimental conditions the ensuing equilibrium constant for the equilibrium reaction (1) is 0.16.

$$[Pd(bipy)(\eta^2\text{-DMF})] + dmbd \leftrightarrow [Pd(bipy)(\eta^2\text{-dmbd})] + DMF \qquad (2)$$

The $Ke_{DMF/dmbd}$ value (≈ 700) for the reaction (2) was calculated by taking into account the order of coordinative strength between fn and DMF (fn/DMF ≈ 4400/1) which was previously determined.[14] On the basis of the calculated value one can state that an equimolar addition of dmbd at -60°C to a solution of [Pd(bipy)(η^2-DMF)] ≈ $1x10^{-2}$ mol dm^{-3} leads to the complete formation of [Pd(bipy)(η^2-dmbd)]. We suppose that the $Ke_{DMF/dmbd}$ value does not change significantly between -60°C and 25°C.

Kinetic Studies

In order to determine the best absorbance interval a preliminary spectrophotometric investigation was carried out. To 3 ml of $CHCl_3$ (stored on silver foil) solution of the complex [Pd(bipy)(η^2-DMF)] ($[complex]_0$ ≈ $1x10^{-4}$ mol dm^{-3}) placed in the thermostated (25°C) cell compartment of a UV-Vis spectrophotometer (Perkin-Elmer Lambda 40) a micro-aliquot of a concentrated solution of dmbd ([dmbd] = 20 x [complex]) was added. The absorbance change was monitored in the 300-530 nm wavelength interval at different times (A_t).

Determination of k_c

The starting complex [Pd(bipy)(η^2-DMF)] when reacted with an equimolar amount of dmbd undergoes the DMF displacement (≥ 95%); the [Pd(bipy)(η^2-dmbd)] complex formed reacts according to reactions 7-8 to give the complexes [Pd(bipy)$(CCOOMe)_4$] and [Pd(bipy)(η^2-DMF)].

The k_c value was calculated from three independent determinations at three different concentrations of [Pd(bipy)(η^2-DMF)] and dmbd (ratio 1:1; $[Pd(bipy)(\eta^2\text{-DMF})]_0$ = $[dmbd]_0$ = $4x10^{-4}$, $2x10^{-4}$, $1x10^{-4}$ mol dm^{-3}) at λ = 420 nm.

Determination of k_2

The k_2 value was determined by UV-Vis experiments under pseudo-first order conditions ($[dmbd]_0$ ≥ 10 x $[Pd(bipy)(\eta^2\text{-DMF})]_0$). Under these conditions the reaction leads to the formation of [Pd(bipy)$(CCOOMe)_4$] only.

[Pd(bipy)(η^2-dmbd)] + dmbd → [Pd(bipy)$(CCOOMe)_4$] $\qquad k_2 = 0.8$ mol^{-1} dm^3 s^{-1}

3.4.4 Acknowledgement

We thank Prof. Luciano Canovese and Dr. Fabiano Visentin (Università di Venezia) for the kinetic measurements and the discussions of the obtained results. Ginger Lutteke is acknowledged for his aid in this study concerning the catalytic three-component synthesis of conjugated dienes from alkynes.

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Chapter 4

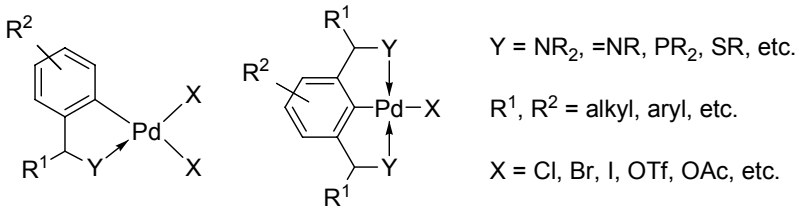
Synthesis of Cyclopalladated and Cycloplatinated Complexes and their Application as Sonogashira Coupling Catalysts

Abstract

The dimeric species $[M(C^{\wedge}N)(\mu\text{-}X)]_2$ (M = Pt, Pd; C^N = N,N-dimethylbenzylamine (dmba), benzo[h]quinoline (bzq), X = Cl, I) react with a series of chelating NN or PP ligand such as (4,4'-bis(tert-butyl)-2,2'-bipyridine), bis(diphenylphosphino)ethane and bis(diphenylphosphino)propane, to give the cationic mononuclear complexes $[M(C^{\wedge}N)(LL)]^+$. Whereas, in the case of the chelating 2,2'-biphosphinines ligand, the formation of the complexes was not observed. X-ray crystal structure of $[Pt(bzq)(dppe)]^+$ and $[Pd(bzq)(dppe)]^+$ have been obtained. The complexes have been employed as pre-catalysts in the cross-coupling reaction of phenylacetylene and 4-bromobenzonitrile. The cyclopalladated complexes are likely to operate in a common phosphine-free Pd(0)-Pd(II) catalytic cycle, while the differences between various types of cyclopalladated precursors are accounted for by the kinetics of the catalyst preactivation step.

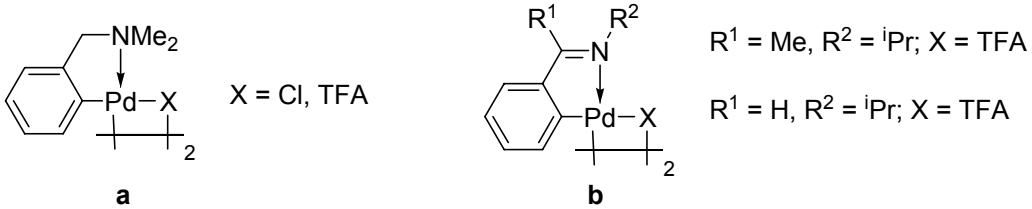
4.1 Introduction

Cyclopalladated compounds or palladacycles are one of the most popular and thoroughly investigated classes of organopalladium derivatives in particular due to their facile synthesis, thermal stability and possibility to modulate their steric and electronic properties. Cyclopalladated complexes are palladium compounds containing at least one metal-carbon bond intramolecularly stabilized by at least one or two neutral donor atoms (Scheme 4-1). The first examples were reported in the 1960s.[1]



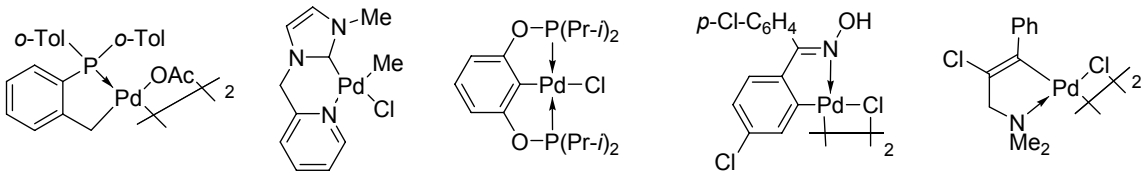
Scheme 4-1. Examples of Palladacycles.[2]

The catalytic properties of cyclopalladated complexes were investigated only two decades later for hydrogenation of alkenes and alkynes.[3] But it is the introduction of the cyclopalladated tri-*o*-tolyl-phosphine by Herrmann et al.[4] to palladium catalyzed Heck and cross-coupling reactions which excited high expectation about this class of palladium catalysts.[5] Catalytic activity is by no means limited to phosphorus-containing palladacycles. The orthopalladated N,N-dimethylbenzylamine[6] (**a**) and imine containing catalysts[7] (**b**). (Scheme 4-2) were the first nitrogen-containing palladacycles to be used in the Heck type reactions. Since then by far the most investigated applications of palladacyclic catalysts has been C–C coupling and, to a lesser extent, C-heteroatom coupling reactions.[8]



Scheme 4-2. First nitrogen-containing palladacycles as catalysts.

More recently, palladacycles received more attention for other promising properties in medicinal and biological chemistry,[9] nonlinear optic, photoluminescence and liquid crystals properties.[2a,10] However, regarding the cyclopalladated complexes and comparatively to the Heck and Suzuki coupling, the investigation of Pd-catalyzed alkynylations of aryl halides (the Sonogashira reaction) is, to the best of our knowledge, still limited (Scheme 4-3) to Herrmann's phosphapalladacycle (**c**),[5,11] carbene-derived palladacycle (**d**),[12] palladium P^C^P pincer complex (**e**),[13] oxime-derived palladacycles[14] (**f**) and the palladacycle derived from the chloropalladation of 3-(dimethylamino)-1-phenyl-1-propyne (**g**).[15] Generally, low catalyst loadings of pre-catalysts like **c** suffice, 0.1 to 0.0001 mol % to perform the Heck reaction of aryl bromides with *n*-butyl acrylate[5] or 0.00005 mol % of **g** to promote the arylation of alkynes.[15]

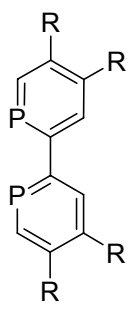


c **d** **e** **f** **g**

Scheme 4-3. Palladacycles in Sonogashira reaction.

The high cost of palladium catalysts, together with the fact that the classical catalysts apparently require loads of 1-5 mol % to induce effective coupling make those cyclopalladated complexes clearly attractive in C–C bond formation processes due to their high TONs.

In this chapter the synthesis and characterization of cationic divalent cyclopalladated and cycloplatinated complexes of the type $[Pd(C^{\wedge}N)(LL)]^{+}$ (LL = nitrogen or phosphorus donor ligand) is described. The catalytic activity of this class of palladacycles for the Sonogashira reaction and the attempts to improve this type of pre-catalyst by using biphosphinine as chelating PP ligand (Scheme 4-4) are reported.



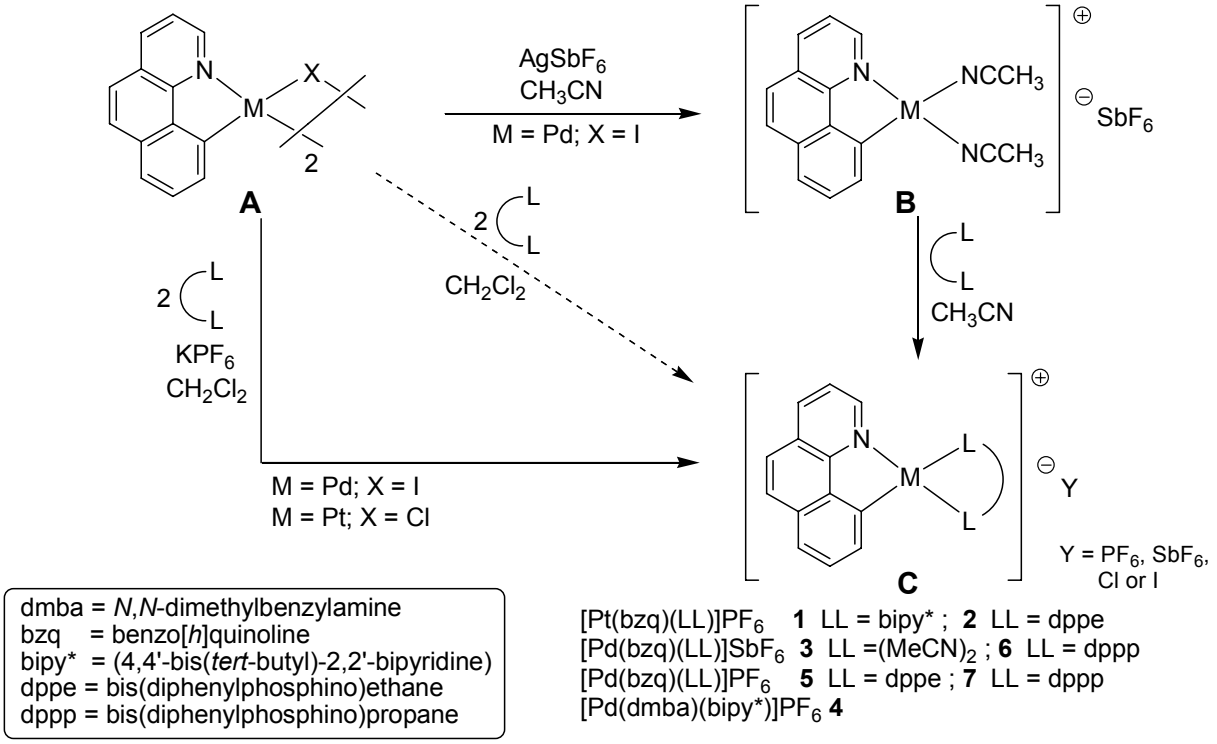
R = H or Me

Scheme 4-4. 2,2'-Biphosphinines ligands

4.2 Results and Discussion

4.2.1 Synthesis of the cyclometalated complexes

Preparations of derivatives like **B** and **C** from halogeno-bridged dinuclear cyclopalladated complexes **A** *via* halogeno-bridge cleavage has been reported in several instances.[16] The direct method, which consists to react the dimeric species with monodentate L or bidentate LL ligand, was used but was limited by the strength of the anion's coordination. Cockburn *et al.*[17] reported one of the classical procedure which consisted of treatment of the halogeno-bridged complex with the NN or PP ligand in a 1:2 molar ratio in the presence of salts such as NH_4PF_6, KPF_6 or $NaClO_4$ to substitute the bridging anion by a non-bridging one. Deeming and co-workers[18] described a slightly modified procedure, that consisted in the formation of $[M(C^{\wedge}N)(solv)_2]^+$ by reacting stoichiometric amounts of silver salt on the dimeric species in a coordinating solvent followed by the reaction of this isolated intermediate on the desired ligands.

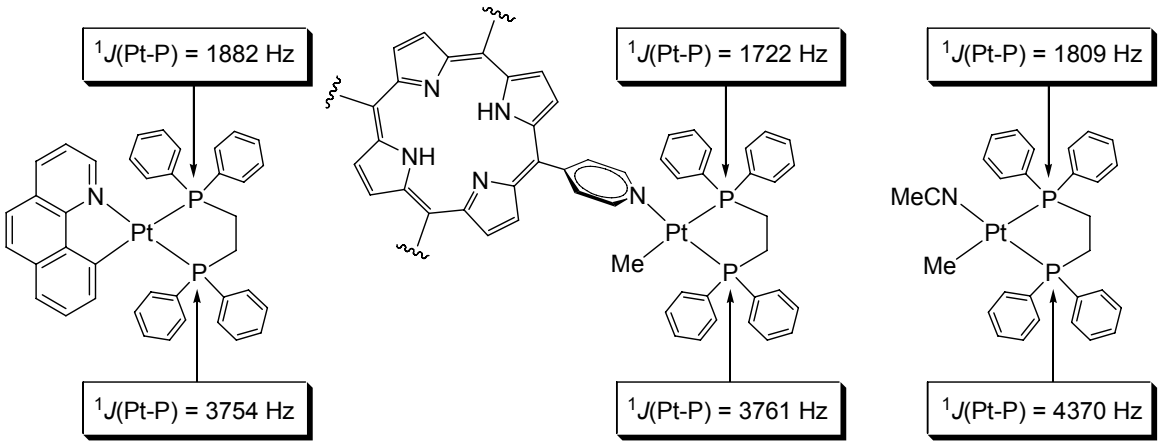


Scheme 4-5. Synthesis of cationic cyclometalated complexes $[M(C^{\wedge}N)(LL)]^+$ (**1**-**7**).

The synthesis of the target platinum and palladium complexes **B** and **C** is shown in Scheme 4-5. Bridge cleavage of $[M(C^{\wedge}N)(\mu\text{-}X)]_2$ (M = Pt, Pd; C^N = *N,N*-dimethylbenzylamine (dmba), benzo[*h*]quinoline (bzq), X = Cl, I) with 2 equiv of chelating NN or PP ligand affords the cationic mononuclear complexes $[M(C^{\wedge}N)(LL)]^+$ (LL = NN (4,4'-bis(*tert*-butyl)-2,2'-bipyridine) (bipy*) and PP bis(diphenylphosphino)ethane (dppe) or bis(diphenylphosphino)propane (dppp).

The complexes **1**-**7** were obtained as yellow-orange (**1**-**2**) or white solids (**3**-**7**) in 60-80% yield. All complexes are air stable at room temperature and also reasonably stable in solution. It was also attempted to synthesize complexes with the 2,2'-bipyridine ligand, but the solids obtained during reaction were almost insoluble in all the common solvents. The problem of solubility was however solved by using the (4,4'-bis(*tert*-butyl)-2,2'-bipyridine). It is important to note that **2**[19] and **5**[17] are reported in literature but these products were obtained *via* different method of synthesis, they were partially characterized and the reported yields were low.

The presence of the chelating dppe bound in an asymmetrical square planar complexes **2** and **5** is clearly illustrated by the $^{31}P\{^1H\}$ NMR spectrum. The $^{31}P\{^1H\}$ NMR spectra of **2** shows 2 singlets with their platinum satellites. The phosphorus–platinum coupling constants recorded for the two singlet resonance signals within the same complex are significantly different from each other revealing the presence, in *trans* position, of groups having a very different *trans*-influence (Scheme 4-6).



Scheme 4-6. ^1J(Pt–P) coupling constants of cationic platinum(II) complexes such as **2**, $[PtMe(dppe)]_4TpyP\cdot(BF_4)_4$[20d] and $[PtMe(NCCH_3)(dppe)]\cdot(BF_4)$.[20c]

The lower frequency signal at δ 43.44 is associated with the larger ^{195}Pt–P coupling constant of 3754 Hz, this singlet is assigned to the PPh_2 group that is coordinated *trans* to the σ-donating nitrogen atom. The signal at δ 53.13 is assigned to the PPh_2 group *trans* to the carbon, since it shows a ^{195}Pt–P coupling constant of 1882 Hz characteristic of P *trans* to large *trans*-influence σ-donor ligands such as the orthometalated carbon atom.[20]

The $^{31}P\{^1H\}$ NMR spectra of **5** and **7** shows two doublets in the wide range δ 6 to 65 ppm. Contrary to the previous complex (**2**), the phosphorus–phosphorus coupling is visible and the coupling constants recorded for the two complexes **5** and **7** are $^2J_{P\text{-}P}$ = 26.7 and $^2J_{P\text{-}P}$ = 57.8 Hz respectively.

The structures of complexes with a chelated diphosphine were ascertained by X-ray analysis of **2** and **5** (see paragraph 4.2.2).

4.2.2 X-ray structure determinations of [Pt(bzq)(dppe)]PF_6 (2) and [Pd(bzq)(dppe)]PF_6 (5)

The molecular structures of [Pt(bzq)(dppe)]PF_6 (**2**) and [Pd(bzq)(dppe)]PF_6 (**5**) have been confirmed by X-ray crystallography. The adopted numbering diamond drawing of the cationic parts are shown in Figure 4-1 (**2**), Figure 4-2 (**5**) and selected bond distances, bond angles, torsion angles have been compiled in Table 4-1. The metals adopt an approximately square planar configuration, the cyclometalated part itself is essentially planar, similar to the situation found in almost all known orthometalated complexes. In both complexes, it is noteworthy that the M–P1 bonds *trans* to M–C bonds are longer than M–P2 bonds *trans* to M–N bonds. M–P1 2.335(2) Å (**2**) and 2.3684(19) Å (**5**) versus M–P2 2.235(2) Å (**2**) and 2.2594(19) Å (**5**), which could be attributed to the greater *trans* influence of an anionic carbon centre over that of a neutral iminic nitrogen atom. The Pt–C (2.075(9) Å) and the Pd–C (2.077(5) Å) metalated bond distances are found to be in accordance with the *trans*-influence of the dppe's phosphorus atom type observed in other cycloplatinated and cyclopalladated complexes such as [Pt(bzq)($PPh_2C(Ph)$=$C(H)PPh_2$)]ClO_4[20b] (2.084(5) and 2.099(5) Å), [Pd(dmba)(dppp)]PF_6[21] (2.07(2) and 2.18(1) Å). Their bite angles (N1–Pt–C12 (80.6(3)º) and N1–Pd–C12 (81.18(18)º) are comparable to those found for this type of five-membered ring complexes,[20b-22] somewhat small due to the requirements of the five-membered ring formation.

Table 4-1. Selected distances [Å] and angles (º) of **2** and **5** with Esd's in parenthesis.

	2 (M = Pt)	**5** (M = Pd)
atoms	**distance**	
M–N1	2.070(7)	2.112(5)
M–C12	2.075(9)	2.077(5)
M–P1	2.335(2)	2.3684(19)
M–P2	2.235(2)	2.2594(19)
atoms	**bond angle**	
N1–M–C12	80.6(3)	81.18(18)
P1–M–P2	84.73(8)	84.41(5)
N1–M–P1	98.67(19)	99.45(13)
C12–M–P2	96.6(3)	95.63(14)
N1–M–P2	173.1(2)	172.17(15)
C12–Pd–P1	175.0(3)	174.6(2)
atoms	**torsion angle**	
C12–C13–C14–N1	-4.6(13)	-2.0(8)
P1–C15–C16–P2	-51.4(6)	-52.7(6)

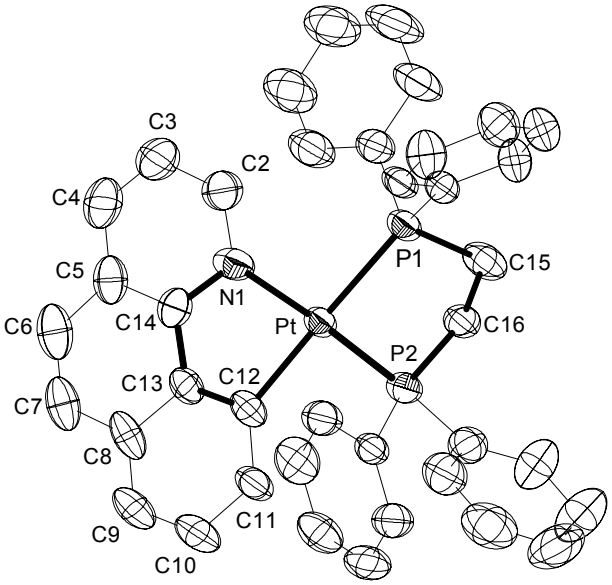


Figure 4-1. Thermal ellipsoid plot of the $[Pt(bzq)(dppe)]^+$ cation drawn at 50% probability level. All hydrogen atoms were omitted for clarity.

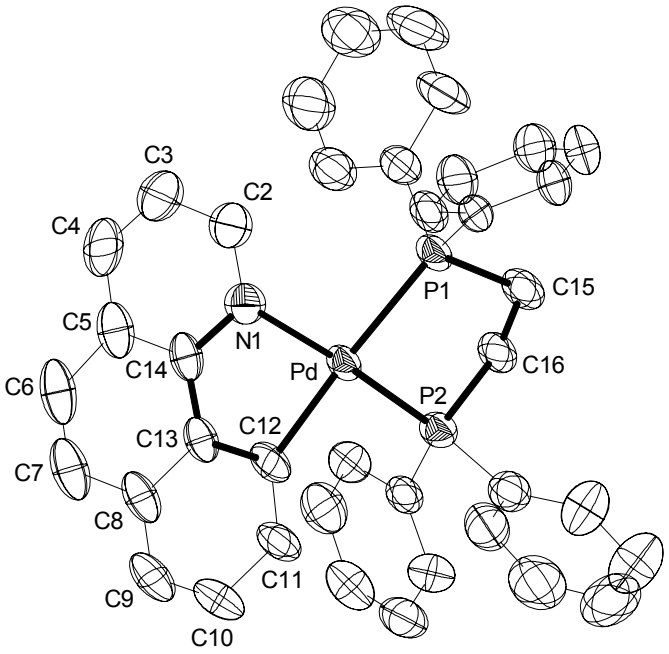
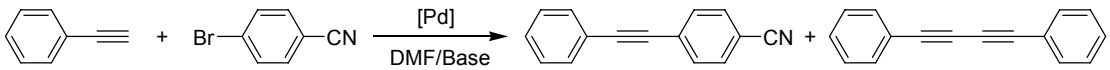


Figure 4-2. Thermal ellipsoid plot of the $[Pd(bzq)(dppe)]^+$ cation drawn at 50% probability level. All hydrogen atoms were omitted for clarity.

4.2.3 Sonogashira reaction catalyzed by cyclopalladated complexes



I **II**

Scheme 4-7. Sonogashira reaction of phenylacetylene and 4-bromobenzonitrile with palladacycles as catalysts.

The cross-coupling reaction of phenylacetylene and 4-bromobenzonitrile yielding to 4-(2-phenylethynyl)benzonitrile (**I**) and 1,4-diphenylbuta-1,3-diyne (**II**) was monitored at 100˚C to study the stability and the activity of the palladacycle complexes (Scheme 4-7). In a typical reaction, 1.5 equiv of phenylacetylene and 1 equiv of 4-bromobenzonitrile were mixed in the presence of 1.5 equiv base, 9 mol % CuI and 1.2 mol % palladacycles at 100˚C. Reaction progress was monitored by GC. Table 4-2 shows the conversion and yield obtained for the catalytic Csp^2–Csp coupling reaction using the cyclopalladated complexes. The cross-coupling product accounted for 100% of the 4-bromobenzonitrile (the limiting reagent). The use of an excess of phenylacetylene and copper salt as co-catalyst lead to the formation of small amounts (2-5%) of homo-coupled product **II**.

Table 4-2. Coupling of 4-bromobenzonitrile with phenylacetylene promoted by palladacycles [Pd(bzq)(μ-I)]$_2$, **3** and **5**.[a]

Entry	Catalyst	t (h)	Conversion (%)[b]	Yield (%)[b]	Selectivity **I**/**II** (%)
1	[Pd(bzq)(μ-I)]$_2$	1.5	98	95	99/1
2	**5**	1.5	38	37	99/1
3	**5**	17	>99	97	98/2
4	**3**	0.75	98	96	98/2
5[c]	**3**	0.5	>99	95	95/5

[a] *Reaction conditions:* DMF (6 mL), 100ºC, 4-bromobenzonitrile (0.17 mmol), phenylacetylene (0.25 mmol), tetra-*n*-butylammonium acetate (TBAA, 0.25 mmol), CuI (9 mol %), palladacycles (1.2 mol %). [b] Conversions of 4-bromobenzonitrile and yield of **I** obtained by GC (using pentadecane as internal standard). [c] Reaction without CuI.

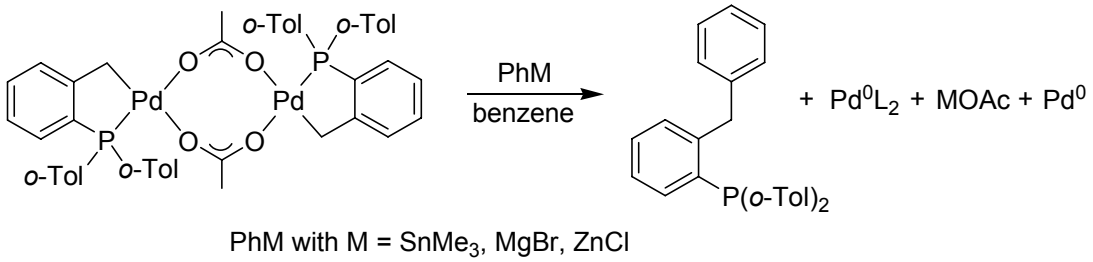
These phosphine free palladacycles can perform this alkynylation of a bromoarene substituted with electron-withdrawing group (entries 1,4 and 5) and show good activities. The results are slightly comparable to the ones obtained with **g** by Dupont and co-workers[15] and **f** from Nájera *et al.*,[14] the palladium loading can be low and, contrary to the P^C^P pincer type palladacycle **e** of Jensen *et al.,* the reaction does not need copper salts as co-catalyst (entry 5).[13] The presence of a diphosphine such as dppe has a detrimental effect on the conversion and the yield (compare entries 1,2 and 4); the same effect was observed with the electron-rich phosphine adduct of **g**.[15] Probably, dppe stabilizes the palladacycle which acts as reservoir of catalytically active Pd^0 species, making the activation period longer and the activity lower compared to [Pd(bzq)(μ-I)]$_2$ and **3**.

4.2.4 Research of a cyclopalladated complex more catalyst than pre-catalyst

4.2.4.1 How do the palladacycles act in catalytic reactions?

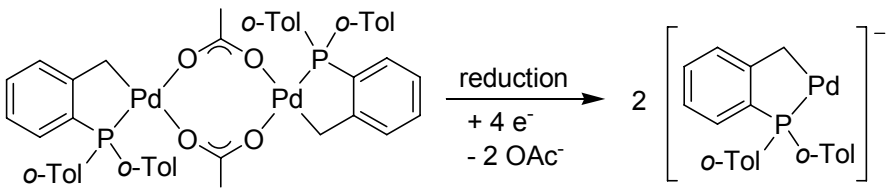
The available variety of C^N-palladacycles is remarkable, and their activities in catalysis are considerable. It was initially assumed, since the palladacyclic unit was found not modified after the catalytic reaction, that the reactions occurred through Pd(II)/Pd(IV) oxidation states.[5] In the cases of the Stille, Grignard, Negishi and Suzuki-Miyaura cross coupling reactions, the reduction mechanism of the Herrmann's

palladacycle into a catalytically active Pd^0 species has been elucidated (Scheme 4-8).[23] However, all attempts made to prove the role of the palladacyclic unit in these catalytic reactions were so far unsuccessful for most of the reactions studied.



Scheme 4-8. Reduction of the Herrmann's cyclopalladated catalyst to Pd^0 species.

In the case of the Heck reaction, contrary to other C–C coupling reactions catalyzed by palladacycles, a Pd(0)/Pd(II) mechanism has only been hypothesized in the 2000's,[24] since almost all prior studies led to the conclusion that the preliminary step is the reduction of Pd(II) to Pd(0), affording palladium colloids that very likely provide the active species[25] or a cyclometallated anionic palladium(0) (Scheme 4-9).[26]

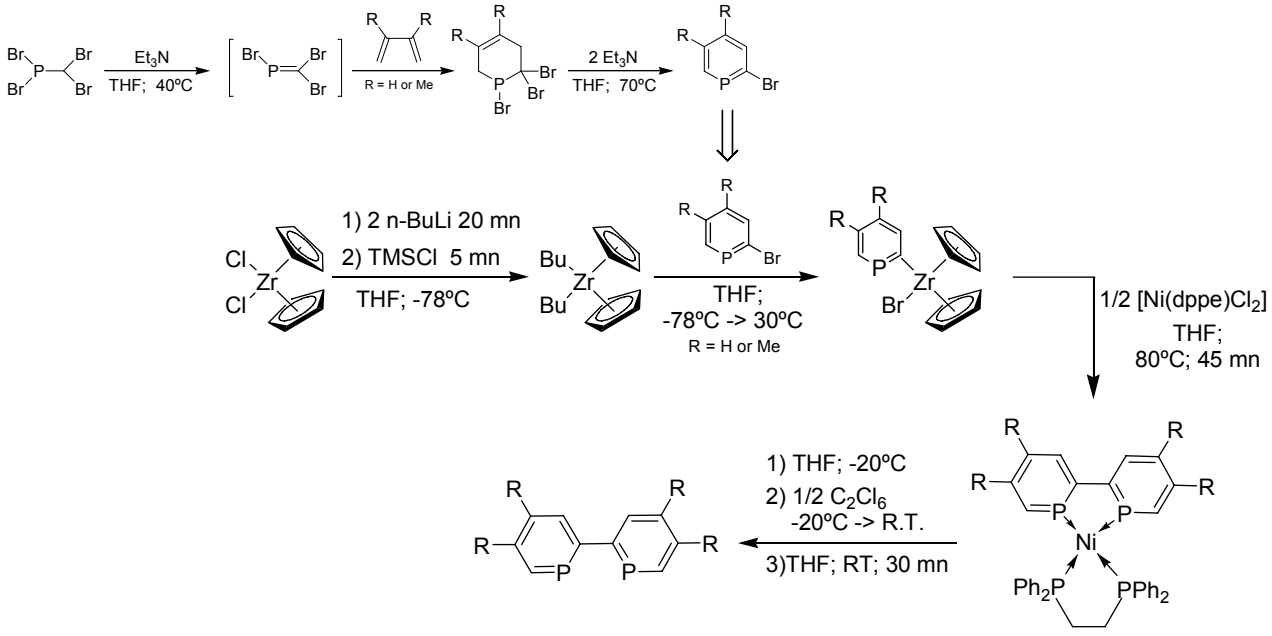


Scheme 4-9. Reduction of the Herrmann's pre-catalyst without rupture of the carbon–palladium bond.

4.2.4.2 Stabilization of zerovalent C^N-palladacycles

Based on these observations, the synthesis of a zerovalent C^N-palladacycles of the type $[Pd(C^N)L_n)]^-$ (similar to the $[Pd(C^P)L_n)]^-$ suggested by Herrmann) was hypothesized. The question was which type of ligand might have the potential for the stabilization of electron-rich and/or reduced (low valent) palladium complexes? Phosphinines and more precisely the 2,2'-biphosphinines (bp), with its 4,4'-5,5'-tetramethyl derivative (tmbp) (Scheme 4-10), show specific electronic properties

which markedly differ from those of classical tertiary mono or diphosphines and pyridines or 2,2'-bipyridines, their nitrogen analogues.[27,28] Their strong π-accepting ability can in principle be exploited for the stabilization of an electron rich palladium center.[29] Indeed, an electrochemical study of [Ni(bipy)$_2$] and [Ni(tmbp)$_2$] revealed that, whereas [Ni(bipy)$_2$] decomposes upon reduction to Ni^0 and bipy anion radical, the [Ni(tmbp)$_2$]$^{\cdot-}$ anion radical (19e$^-$) and [Ni(tmbp)$_2$]$^{2-}$ (20e$^-$) dianion complexes could be electrogenerated. These results underline the exceptional ability of 2,2'-biphosphinines to stabilize low-valent highly reduced transition metal centers.[27] Based on these observations, we try to accommodate the charge of the negatively charged [Pd(C^N)L$_n$]$^-$ species by employing a good π-acceptor ligand such as 4,4'-5,5'-tetramethyl-2,2'-biphosphinine.

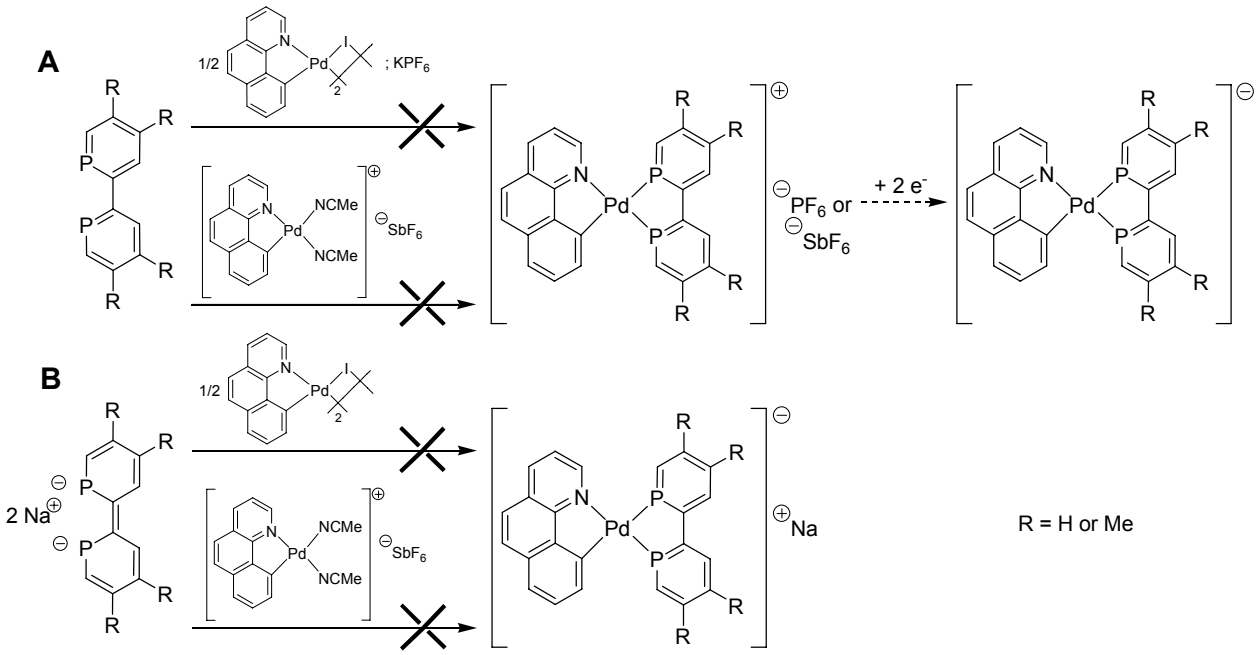


Scheme 4-10. Synthesis of the 2-bromophosphinine intermediates,[30,31] following by it Ni(II)-promoted homo-coupling to form 2,2'-Biphosphinine.[32]

Several approaches to coordinate the 2,2'-biphosphinine to the C^N-cyclopalladated compounds, in order to obtain a zerovalent [Pd(C^N)(PP)]$^-$, were investigated. The first method (**A**, see Scheme 4-11) would consist of two steps: (i) coordination of the 2,2'-biphosphine to the C^N-palladacycles and (ii) electrochemical or chemical reduction of the complex obtained. We used both methods of coordination described in paragraph 4.2.1, the treatment of the halogeno-bridged

complex with the 2,2'-biphosphines ligand in a 1:2 molar ratio in the presence of KPF_6 to substitute the bridging anion by a non-bridging one or by reacting the 2,2'-biphosphines ligand on the isolated intermediate $[Pd(C^{\wedge}N)(solv)_2]^+$ specie. Whatever the method, in none of them the divalent palladium complex $[Pd(C^{\wedge}N)(LL)]^+$ was obtained. Unfortunately, no information could be extracted from the reaction mixtures, since ^1H or ^{31}P NMR spectroscopy or mass spectrometry measurements were meaningless. Despite many efforts, the desired zerovalent $[Pd(C^{\wedge}N)(PP)]^-$ complexes were not obtained by this method. Meanwhile, the formation of a divalent palladium complex with 2,2'-biphosphinine was very challenging since the 2,2'-biphosphinine's coordination generates a highly reactive P=C double bond of the phosphinine ring trans to the less electron donating ligand.[33]

The second method (**B**, see Scheme 4-11) consists of the reaction of the divalent palladacycle precursor complexes at -80°C in a THF solution of the 2,2'-biphosphinine dianion. The doubly reduced ligand was obtained by stirring a solution of 2,2'-biphosphinine on sodium mirror, according to the method described by Rosa *et al*..[34] Once the solution of the dianion ready, the reaction with the palladium reactant was executed. One more time, despite the multiplication of the attempts and our efforts, no results and informations were extracted from the reaction mixtures.



Scheme 4-11. Attempted synthesis of stabilized monoanionic Pd^0 complexes.

4.3 Conclusion

In conclusion, several cyclometallic platinum and palladium compounds of the type $[M(C^N)(LL)]^+$ with chelating ligand such as diphosphine or bipyridine have been obtained. These complexes are air-, moisture- and thermally stable for months in the solid state and are reasonably stable in solution. Two routes have been used for the synthesis of these complexes: the method consisting of the substitution of the bridging anion by a non-bridging one is the more direct one and provides the target complexes in good yields.

The cyclopalladated complexes are good catalysts for the copper- and phosphine-free Sonogashira reaction. The observed stability and activity obtained with these complexes are relatively good but are rather similar compared to reported catalysts such as oxime-derived palladacycles or the palladacycle derived from the chloropalladation of 3-(dimethylamino)-1-phenyl-1-propyne.

In contrast, we could not isolate the desired zerovalent palladacycle $[Pd(C^N)(PP)]^-$ that we wanted to explore as a catalyst in this process. Unfortunately, when using biphosphinine as chelating ligand, we were not able to synthesize those cyclopalladated complexes. Biphosphinine appeared to be a good choice to synthesize a monoanionic zerovalent palladium but whatever the procedure, either using the neutral ligand or the doubly reduced ligand, we did not observe the formation of the desired complex.

4.4 Experimental Section

4.4.1 General considerations

All reactions were carried out by using standard Schlenk techniques under an atmosphere of dry nitrogen unless otherwise specified. The solvents were dried according to standard procedures[35] and distilled before use. Elemental analyses were carried out by Kolbe, Mikroanalytisches Laboratorium, Mülheim a.d. Ruhr, Germany and by the Service d'analyses, Institut de Chimie, Université Louis Pasteur, Strasbourg, France. ^1H and ^{13}C NMR spectra were recorded at 298K on a Bruker AMX 300 spectrometer (300.13 and 75.48 MHz respectively) and on a Varian Inova

500 spectrometer (499.86 and 125.68 MHz respectively). The chemical shift values are referenced to external TMS with high frequency shifts signed positive. Chemical shifts (δ) and coupling constants (J) are expressed in ppm and in Hertz (Hz) respectively and the multiplicity as s = singlet, d = doublet, dd = double doublet, t = triplet, pst = pseudo triplet, m = multiplet, br = broad; data in parenthesis are given in the following order: multiplicity, number of protons, labelling of the proton and coupling constants in Hz.

Materials: KPF_6 (Acros), $AgSbF_6$ (Acros), dppe (Acros), dppp (Johnson Matthey), 4-bromobenzonitrile (Acros), phenylacetylene (Aldrich), tetra-*n*-butylammonium acetate (TBAA) (Aldrich), CuI (Acros). $[Pt(bzq)(\mu\text{-}Cl)]_2$,[36] $[Pd(bzq)(\mu\text{-}I)]_2$[37] and $[Pd(dmba)(\mu\text{-}Cl)]_2$[38] were synthesized according to the literature. 4,4'-Bis(*tert*-butyl)-2,2'-bipyridine was provided by L. Barloy from Université Louis Pasteur, Strasbourg.

4.4.2 Synthesis

Synthesis of $[Pt(bzq)(bipy^*)]PF_6$ (1)

To a suspension of $[Pt(bzq)(\mu\text{-}Cl)]_2$ (25 mg, 0.031 mmol) in CH_2Cl_2 (10 mL), 4,4'-bis(*tert*-butyl)-2,2'-bipyridine (16.4 mg, 0.061 mmol) and KPF_6 (30 mg, 0.16 mmol) were added. The solution was stirred at room temperature for 10 hours. After a quick filtration over celite, the solvent of the resulting orange solution was removed in vacuum. The product was crystallized from a mixture of acetonitrile, hexane and diethyl ether. The orange product **1** was filtered off and dried under vacuum, yielding 30 mg (0.047 mmol, 76%).

MS (FAB+) *m*/*z*: found 641.2241 (M – PF_6): calcd ($C_{31}H_{32}N_3Pt$) 641.2247.

^{1}H NMR (CD_3CN, 300.13 MHz): δ 9.20 (d, 1H, H2, ^3J = 6.2), 8.86 (d, 1H, H9, ^3J = 5.5), 8.70 (d, 1H, H15 or H20, ^3J = 5.9), 8.41 (d, 1H, H7, ^3J = 8.0), 8.21 (d, 1H, H17 or H18, ^4J = 2.0), 8.14 (d, 1H, H18 or H17, ^4J = 2.2), 7.78 (d, 1H, H5 or H6, ^3J = 8.0), 7.65 (d, 1H, H6 or H5, ^3J = 8.0), 7.63-7.42 (m, 6H), 1.51 (s, 9H, 3 $\times$ Me), 1.50 (s, 9H, 3 $\times$ Me).

No ^{13}C NMR spectrum was recorded due to the low solubility of the complex.

Synthesis of [Pt(bzq)(dppe)]PF_6 (2)

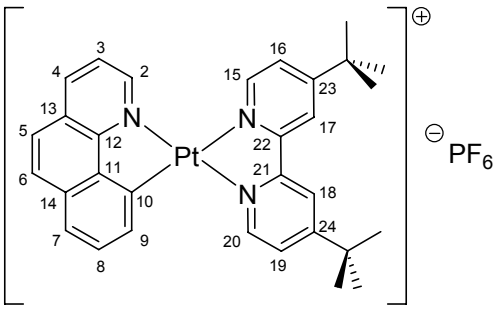
To a suspension of $[Pt(bzq)(\mu\text{-}Cl)]_2$ (20 mg, 0.024 mmol) in CH_2Cl_2 (8 mL), diphenylphosphinoethane (20 mg, 0.50 mmol) and KPF_6 (30 mg, 0.16 mmol) were added. The solution was stirred at room temperature for 10 hours. After a quick filtration over celite, the solvent of the resulting yellow solution was removed in vacuum. The product was crystallized from a mixture of acetonitrile, hexane and diethyl ether. The yellow product **2** was filtered off and dried under vacuum, yielding 34 mg (0.037 mmol, 77%).

Anal. Calc. for $C_{39}H_{32}N_1F_6P_3Pt$: C, 51.10; H, 3.52; N, 1.53. Found: C, 51.05; H, 3.47; N, 1.17.

^{1}H NMR (CD_3COCD_3, 499.86 MHz): δ 8.77 (d, 1H, H2, ^3J = 8.0), 8.74 (pst, 1H, H4), 8.21-8.12 (m, 8H, H_o and $H_{o'}$), 8.04 (d, 1H, H5 or H6, ^3J = 8.5), 7.91 (d, 1H, H6 or H5, ^3J = 8.5), 7.78 (d, 1H, H9, ^3J = 8.0), 7.76-7.62 (m, 12H, H_m, $H_{m'}$, H_p and $H_{p'}$), 7.56 (pst, 1H, H3, ^3J = 8.5, ^3J = 8.0), 7.34 (pst, 1H, H7), 7.28 (pst, 1H, H8, ^3J = 8.0, ^3J = 7.5), 2.89-2.69 (m, 4H, 2 × CH_2).

^{13}C NMR (CD_3COCD_3, 75.48 MHz): δ 159.8 (m, C10), 156.9 (C), 152.6 (C4), 143.7 (C13/14), 141.1 (C2), 137.2 (C7), 135.0 (C), 134.9 (d, $C_{o,o'}$), 134.7 (d, $C_{o,o'}$, $^2J_{C\text{-}P}$ = 12.8), 133.1 ($C_{p,p'}$), 133.0 ($C_{p,p'}$), 130.8 (C5 or C6), 130.3 (d, $C_{m,m'}$, ^3J = 11.1), 129.8 (d, $C_{m,m'}$, ^3J = 11.0), 130.7-129.7 signal overlapped (C8), 128.5 (C), 127.9 (d, $C_{i,i'}$, $^1J_{C\text{-}P}$ = 46.0), 126.5 (d, $C_{i,i'}$, $^1J_{C\text{-}P}$ = 61.6), 125.1 (C9), 124.5 (C6 or C5), 123.8 (C3), 32.2 (m, CH_2), 27.2 (m, CH_2).

^{31}P{^{1}H} NMR (CD_3COCD_3, 121.50 MHz): δ 257.91 (sept, PF_6^-, $^1J_{P\text{-}F}$ = 705.2), 53.13 (s, dppe, P trans to C, $^1J_{P\text{-}Pt}$ = 1882), 43.44 (d, dppe, P trans to N, $^1J_{P\text{-}Pt}$ = 3754).



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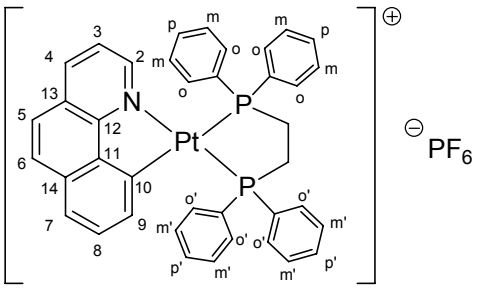


2

Synthesis of $[Pd(bzq)(CH_3CN)_2]SbF_6$ (3)

To a suspension of $[Pd(bzq)(\mu\text{-}I)]_2$ (221.5 mg, 0.269 mmol) in CH_3CN (20 mL), $AgSbF_6$ (185 mg, 0.538 mmol) was added. The solution was stirred at room temperature for 2 hours, and then, the white precipitate was filtered off by filtration over celite. The solvent of the solution was removed in vacuum, yielding 219 mg (0.363 mmol, 68%) of a white product **3**.

Anal. Calc. for $C_{17}H_{14}F_6N_3PdSb$: C, 33.89; H, 2.34; N, 6.97. Found: C, 34.14; H, 2.45; N, 6.32.

^{1}H NMR (CD_3CN, 300.13 MHz): δ 8.43 (m, 2H, H2 and H4), 7.76 (d, 1H, H5 or H6, ^3J = 8.4), 7.67 (d, 1H, H6 or H5, ^3J = 9.0), 7.65 (d, 1H, H9, ^3J = 8.1), 7.50 (dd, 1H, H3. ^3J = 8.2, ^3J = 5.3), 7.36 (dd, 1H, H8, ^3J = 8.1, ^3J = 7.2), 7.24 (d, 1H, H7, ^3J = 7.5), 1.95 (s, 6H, 2 × NC(CH_3)).

^{13}C NMR (CD_3CN, 75.48 MHz): δ 154.9 (C10), 150.5 (C4), 147.3 (C), 141.5 (C), 139.9 (C2), 134.9 (C7), 132.4 (C), 129.7 and 129.8 (C5 or C6 and C8), 128.2 (C), 125.4 (C9), 125.1 (C6 or C5), 123.3 (C3).

Synthesis of $[Pd(dmba)(bipy^*)]PF_6$ (4)

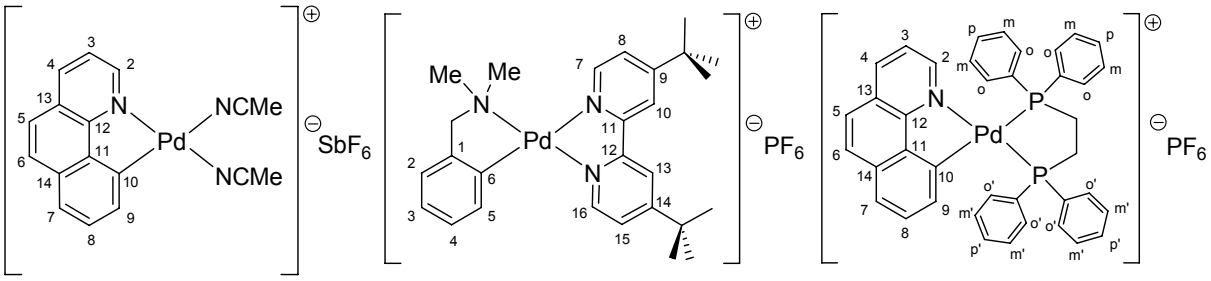
To a suspension of $[Pd(dmba)(\mu\text{-}Cl)]_2$ (25 mg, 0.045 mmol) in CH_2Cl_2 (6 mL), 4,4'-bis(*tert*-butyl)-2,2'-bipyridine (24.5 mg, 0.091 mmol) and KPF_6 (45 mg, 0.24 mmol) were added. The solution was stirred at room temperature for 2 hours, and then, the white precipitate was removed by filtration. The solvent of the resulting colourless solution was removed in vacuum and the product was crystallized from a mixture of acetonitrile, hexane and diethyl ether. The white product **4** was filtered off and dried under vacuum, yielding 46 mg (0.070 mmol, 78%).

Anal. Calc. for $C_{27}F_6H_{36}N_3PPd$: C, 49.59; H, 5.55; N, 6.43. Found: C, 49.99; H, 5.18; N, 6.15.

^{1}H NMR (CD_3CN, 300 MHz): δ 8.68 (d, 2H, H7 and H16, ^3J = 5.9), 8.35 (d, 2H, H10 and H13, ^4J = 2.0), 7.73 (dd, 2H, H8 and H15, ^3J = 5.9, ^4J = 1.7), 7.12 (m, 4H, H2, H3, H4 and H5), 4.21 (s, 2H, CH_2), 2.90 (s, 6H, 2 × NCH_3), 1.47 (s, 18H, 2 × C(CH_3)$_3$).

^{13}C NMR (CD_3CN, 75.48 MHz): δ 176.6 (C, dmba), 166.2 (2 × C, bipy*), 156.4 (C, bipy*), 152.4 (C, bipy*), 152.3 and 152.2 (C7 and C16, bipy*), 148.6 (C, dmba), 134.6 (CH, dmba), 127.4 (CH, dmba), 126.4 (CH, dmba), 125.3 (C8 and C15, bipy*), 123.0

(CH, dmba), 122.3 and 122.0 (C10 and C13, bipy*), 75.8 (CH_2, dmba), 52.2 (2 × CH_3, dmba), 36.6 (2 × C, bipy*), 30.6, 30.4 and 30.2 (6 × CH_3, bipy*).



3 **4** **5**

Synthesis of [Pd(bzq)(dppe)]PF_6 (5)

Method A: To a suspension of [Pd(bzq)(*μ*-I)]$_2$ (101 mg, 0.123 mmol) in MeOH (35 mL), diphenylphosphinoethane (110 mg, 0.276 mmol) was added. The solution was stirred at room temperature for 2 hours, and then, aqueous solution of KPF_6 (15%) was added dropwise until no further precipitation was observed. The white product was filtered off, washed with H_2O, MeOH and Et_2O and dried under vacuum yielding 40 mg (0.048 mmol, 20%) of **5**.

Method B: To a suspension of [Pd(bzq)(*μ*-I)]$_2$ (75 mg, 0.09 mmol) in a mixture of CH_2Cl_2 (8 mL) and $(CH_3)_2CO$ (5 mL), diphenylphosphinoethane (80 mg, 0.2 mmol) was added. After the complete homogenization of the solution, KPF_6 (120 mg, 0.65 mmol) was added. The solution was stirred at room temperature for 3 hours. Then the solvent was removed under vacuum and the white residue was washed with H_20 and Et_2O (2 × 20 mL) and dried under vacuum yielding 98 mg (0.12 mmol, 66%) of **5**.

Anal. Calc. for $C_{39}F_6H_{32}NP_3Pd$: C, 56.57; H, 3.90; N, 1.69. Found: C, 56.41; H, 3.84; N, 1.74.

^{1}H NMR (CD_3COCD_3, 499.86 MHz): *δ* 8.71 (d, 1H, H2, ^3J = 8.0), 8.48 (br, 1H, H4), 8.19 (d, 2H, $H_{o'}$, ^3J = 8.5), 8.16 (dd, 2H, H_o, ^3J = 8.5, ^4J = 1.0), 8.09 (d, 2H, H_o, ^3J = 8.5), 8.07 (dd, 2H, $H_{o'}$, ^3J = 7.5, ^4J = 1.5), 8.02 (d, 1H, H5 or H6, ^3J = 9.0), 7.93 (d, 1H, H6 or H5, ^3J = 8.5), 7.74 (m, 4H, 2H$_m$ and 2H$_{m'}$), 7.66 (m, 9H, H9, 2H$_m$, 2H$_{m'}$ and 4H$_{p,p'}$), 7.55 (dd, 1H, H3, ^3J = 7.8, ^3J = 6.0), 7.20 (t, 1H, H8, ^3J = 7.5), 7.13 (dd, 1H, H7, ^3J = 8.0, ^3J = 6.0), 2.94-2.73 (m, 4H, 2 × CH_2).

^{13}C NMR (CD_3COCD_3, 125.68 MHz): *δ* 161.8 (m, C10), 156.0 (C), 151.8 (C4, $^5J_{C\text{-}P}$ = 6.4), 143.4 (C13/14), 140.1 (C2), 136.9 (br, C7), 134.9 (d, C$_{o,o'}$, $^2J_{C\text{-}P}$ = 12.7), 134.87 (C), 134.3 (d, C$_{o,o'}$, $^2J_{C\text{-}P}$ = 12.7), 132.97 (d, C$_{p,p'}$, ^4J = 2.3), 132.74 (d, C$_{p,p'}$, $^4J_{C\text{-}P}$ =

2.9), 130.27 (C5 or C6), 130.22 (d, $C_{m,m'}$, ^3J = 10.4), 129.78 (d, $C_{m,m'}$, ^3J = 11.6), 129.6 (C8), 128.4 (C), 128.0 (d, $C_{i,i'}$, $^1J_{C\text{-}P}$ = 37.5), 127.1 (d, $C_{i,i'}$, $^1J_{C\text{-}P}$ = 52.0), 125.2 (C9), 124.3 (C6 or C5), 123.2 (C3), 32.2 (m, CH_2), 27.2 (m, CH_2).

^{31}P NMR (CD_3COCD_3, 121.50 MHz): δ 257.89 (sept, PF_6^-, $^1J_{P\text{-}F}$ = 705.2), 64.29(d, dppe, P trans to C, $^2J_{P\text{-}P}$ = 26.7), 46.74 (d, dppe, P trans to N, $^2J_{P\text{-}P}$ = 26.7).

Synthesis of [Pd(bzq)(dppp)]SbF_6 (6)

To a solution of [Pd(bzq)$(CH_3CN)_2$]SbF_6 (51 mg, 0.085 mmol) in CH_3CN (10 mL), diphenylphosphinopropane (35 mg, 0.085 mmol) was added. The solution was stirred at room temperature for 1 hour. Then the solvent was removed under vacuum and the residue was washed with Et_2O (2 × 10 mL) and dried under vacuum yielding 50 mg (0.059 mmol, 63%) of white product **6**.

MS (FAB+) *m*/*z*: found 696.1217 (M – SbF_6): calcd ($C_{40}H_{34}NP_2Pd$) 696.1216.

^{1}H NMR (CD_3COCD_3, 300.13 MHz): δ 8.59 (dd, 1H, H2, ^3J = 8.1, ^4J = 1.3), 8.15 (m, 9H, H4, 4H_o and 4$H_{o'}$), 7.94 (d, 1H, H5 or H6, ^3J = 8.7), 7.85 (d, 1H, H6 or H5, ^3J = 9.0), 7.62 (m, 13H, H9, 8$H_{m,m'}$ and 4$H_{p,p'}$), 7.32 (dd, 1H, H3, ^3J = 8.1 and ^3J = 5.7), 7.04 (m, 2H, H7 and H8), 2.86 (br, 2H, PCH_β), 2.72 (m, 4H, PCH_α).

No ^{13}C NMR spectrum was recorded due to the low solubility of the complex.

^{31}P{^{1}H} NMR (CD_3COCD_3, 121.50 MHz): δ 33.82 (br, dppp, P trans to C), 6.19 (br, dppp, P trans to N).

Synthesis of [Pd(bzq)(dppp)]PF_6 (7)

To a suspension of [Pd(bzq)(μ-I)]$_2$ (55 mg, 0.067 mmol) in a mixture of CH_2Cl_2 (5 mL) and $(CH_3)_2CO$ (5 mL), diphenylphosphinopropane (62 mg, 0.150 mmol) was added. After the complete homogenization of the solution, KPF_6 (100 mg, 0.54 mmol) was added. The solution was stirred at room temperature for 4 hours. Then the solvent was removed under vacuum and the white residue was washed with H_20 and Et_2O (2 × 10 mL) and dried under vacuum yielding 70 mg (0.083 mmol, 62%) of **7**.

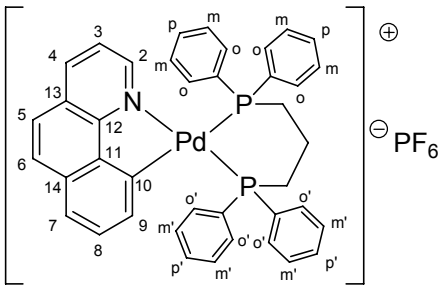
MS (FAB+) *m*/*z*: found 696.1221 (M – PF_6): calcd ($C_{40}H_{34}NP_2Pd$) 696.1216.

^{1}H NMR (CD_3COCD_3, 300.13 MHz): δ 8.59 (dd, 1H, H2, ^3J = 7.8, ^4J = 1.3), 8.20 (m, 5H, H4, 2H_o and 2$H_{o'}$), 8.12 (dd, 2H, 2H_o or 2$H_{o'}$, ^3J = 7.8, ^4J = 1.5), 8.08 (dd, 2H, 2$H_{o'}$ or 2H_o, ^3J = 8.1, ^4J = 1.5), 7.95 (d, 1H, H5 or H6, ^3J = 8.7), 7.85 (d, 1H, H6 or H5, ^3J = 8.7), 7.69-7.62 (m, 9H, H9, 2H_m, 2$H_{m'}$ and 4$H_{p,p'}$), 7.60-7.54 (m, 4H, 2H_m and 2$H_{m'}$),

7.32 (dd, 1H, H3, ^{3}J = 7.1 and ^{3}J = 5.7), 7.05 (m, 2H, H7 and H8), 2.86-2.72 (m, 6H, P(CH_2)$_3$P).

^{13}C NMR (CD_3COCD_3, 75.48 MHz): δ 157.4 (C10), 155.8 (C), 151.1 (C4), 139.8 (C2), 138.2 (C), 137.8 (C), 137.2(br, C7), 134.8 (d, $C_{o,o'}$, $^{2}J_{C\text{-}P}$ = 12.2), 134.2 (d, $C_{o,o'}$, $^{2}J_{C\text{-}P}$ = 12.2), 132.4 ($C_{p,p'}$), 132.3 ($C_{p,p'}$), 130.2 (C5 or C6), 130.0 ($C_{m,m'}$), 129.5 (d, $C_{m,m'}$, ^{3}J = 10.9), 130.2-129.0 signal overlapped (C8), 128.6 (d, $C_{i,i'}$, $^{1}J_{C\text{-}P}$ = 40.3), 128.5 (C), 128.4 (d, $C_{i,i'}$, $^{1}J_{C\text{-}P}$ = 53.0), 124.9 (C9), 124.2 (C6 or C5), 122.3 (C3), 33.2 (m, CH_2), 32.0 (m, CH_2), 30.5-29.8 signal overlapped (CH_2).

^{31}P NMR (CD_3COCD_3, 121.50 MHz): δ 258.73 (sept, PF_6^-, $^{1}J_{P\text{-}F}$ = 705.2), 30.45 (d, dppp, P trans to C, $^{2}J_{P\text{-}P}$ = 57.8), 6.19 (d, dppp, P trans to N, $^{2}J_{P\text{-}P}$ = 57.8).



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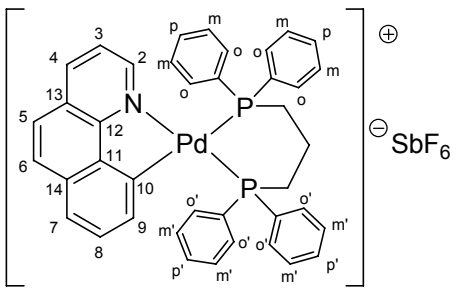

7

4.4.3 Cross-coupling of 4-bromobenzonitrile with phenylacetylene

In a two-necked Schlenk tube with 6 mL of degassed DMF was filled with, 27.5 µL (0.25 mmol) of phenylacetylene, 2.8 mg (0.01 mmol) of CuI, 75 mg (0.25 mmol) of TBAA. Then, 30.2 mg (0.17 mmol) of 4-bromobenzonitrile and 1.2 mol % of "Pd" catalyst were added and the mixture was stirred at 100ºC for 0.5 to 17 h under a slight overpressure of N_2. Samples were taken periodically for GC-analysis.

4.4.4 X-ray crystal structure analyses

X-ray crystal structure determination of [Pt(bzq)(dppe)]PF_6 (2)

$[C_{39}H_{32}NP_2Pt]^+.PF_6^-$, *Mr* = 916.7, monoclinic, $P2_1/c$, *a* = 11.550(2), *b* = 14.141(2), *c* = 21.836(2) Å, β = 92.329(10)˚, *V* = 3563.5(9) Å^3, *Z* = 4, *D*x = 1.71 gcm^{-3}, λ(Cu Kα) = 1.5418 Å, μ(Cu Kα) = 9.2 mm^{-1}, *F*(000) = 1800, room temperature, Final *R* = 0.051 for 6228 observed reflections. A crystal with dimensions 0.05 x 0.40 x 0.75 mm approximately was used for data collection on an Enraf-Nonius CAD-4 diffractometer

with graphite-monochromated Cu Kα radiation and ω-2θ scan. A total of 7309 unique reflections were measured within the range -14 ≤ h ≤ 14, -17 ≤ k ≤ 0, 0 ≤ l ≤ 27. Of these, 6228 were above the significance level of 4$\sigma(F_{obs})$ and were treated as observed. The range of (sin θ)/λ was 0.042 - 0.626 Å (3.7 ≤ θ ≤ 74.8˚). Two reference reflections ([0 3 2], [3 0 2]) were measured hourly and showed no decrease during the 105 h collecting time. Unit-cell parameters were refined by a least-squares fitting procedure using 23 reflections with 40.11 ≤ 2θ ≤ 40.94˚. Corrections for Lorentz and polarisation effects were applied. Absorption correction was performed with the program PLATON,[39] following the method of North et al.[40] using Ψ-scans of five reflections, with coefficients in the range 0.462 - 0.959. The structure was solved by the PATTY option of the DIRDIF-99 program system.[41] The hydrogen atoms were calculated and kept fixed at theirs calculated positions with U = 0.10 Å^2. Full-matrix least-squares refinement on F, anisotropic for the non-hydrogen atoms converged to R = 0.051, Rw = 0.063, (Δ/σ)max = 0.08, S = 1.11. A weighting scheme w = [15. + 0.01*($\sigma(F_{obs})$)^2 + 0.01/($\sigma(F_{obs})$)]$^{-1}$ was used. The secondary isotropic extinction coefficient was refined to g = 188(32). A final difference Fourier map revealed a residual electron density between -1.74 and 1.82 eÅ^{-3} in the vicinity of the heavy atom. Scattering factors were taken from Cromer and Mann;[42] International Tables for X-ray Crystallography.[43] The anomalous scattering of Pd, F and P was taken into account.[44] All calculations were performed with XTAL3.7,[45] unless stated otherwise.

X-ray crystal structure determination of [Pd(bzq)(dppe)]PF_6 (5)

$[C_{39}H_{32}NP_2Pd]^+.PF_6^-$, Mr = 828.0, monoclinic, $P2_1/c$, a = 11.562(1), b = 14.078(8), c = 21.950(3) Å, β = 91.980(9)˚, V = 3571(2) Å^3, Z = 4, Dx = 1.54 gcm^{-3}, λ(Cu Kα) = 1.5418Å, μ(Cu Kα) = 6.0 mm^{-1}, F(000) = 1672, room temperature, Final R = 0.053 for 6063 observed reflections. A crystal with dimensions 0.15 x 0.40 x 0.40 mm approximately was used for data collection on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Cu Kα radiation and ω-2θ scan. A total of 7077 unique reflections were measured within the range -14 ≤ h ≤ 14, 0 ≤ k ≤ 16, 0 ≤ l ≤ 27. Of these, 6063 were above the significance level of 4$\sigma(F_{obs})$ and were treated as observed. The range of (sin θ)/λ was 0.042 - 0.626 Å (3.7 ≤ θ ≤ 74.8˚). Two reference reflections ([$\bar{2}$ 0 2], [1 2 4]) were measured hourly and showed no decrease during

the 95 h collecting time. Unit-cell parameters were refined by a least-squares fitting procedure using 23 reflections with $40.04 \leq 2\theta \leq 41.07^{\circ}$. Corrections for Lorentz and polarisation effects were applied. Absorption correction was performed with the program PLATON,[39] following the method of North et al.[40] using Ψ-scans of five reflections, with coefficients in the range 0.343 - 0.981. The structure was solved by the PATTY option of the DIRDIF-99 program system.[41] The hydrogen atoms were calculated. Full-matrix least-squares refinement on F, anisotropic for the non-hydrogen atoms and isotropic for the hydrogen atoms, restraining the latter in such a way that the distance to their carrier remained constant at approximately 1.0 Å, converged to $R = 0.053$, $Rw = 0.056$, $(\Delta/\sigma)\text{max} = 0.09$, S = 1.05. A weighting scheme $w = [6. + 0.01*(\sigma(F_{obs}))^2 + 0.01/(\sigma(F_{obs}))]^{-1}$ was used. The secondary isotropic extinction coefficient was refined to g = 536(49). A final difference Fourier map revealed a residual electron density between -2.13 and 1.20 eÅ^{-3} in the vicinity of the heavy atom. Scattering factors were taken from Cromer and Mann;[42] International Tables for X-ray Crystallography.[43] The anomalous scattering of Pd, F and P was taken into account.[44] All calculations were performed with XTAL3.7,[45] unless stated otherwise.

Table 4-3. Crystallographic data for crystal structure determinations of **2** and **5**.

Compound	**2**	**5**
Empirical formula	$C_{39}H_{32}F_6NP_3Pt$	$C_{39}H_{32}F_6NP_3Pd$
Formula weight (g mol^{-1})	916.65	827.99
Temperature (K)	293	293
Crystal size (nm)	0.05 × 0.40 × 0.75	0.15 × 0.40 × 0.40
Wavelength (Å)	1.54180	1.54180
Crystal system	monoclinic	monoclinic
Space group	$P2_1/c$	$P2_1/c$
a (Å)	11.550(2)	11.5620(10)
b (Å)	14.141(2)	14.078(8)
c (Å)	21.836(2)	21.950(3)
β (°)	92.329(10)	91.980(9)
α (°);*γ* (°)	90; 90	90; 90
Volume (Å^3)	3563.5(9)	3571.0(2)
Z	4	4
Number of data meas.	7309	7077
Number of data	6228 with F > 4σ(F)	6063 with F > 4σ(F)
Number of variables	452	580
Goodness-of-fit on *F*	1.11	1.05
R	0.0510	0.0530
wR_2	0.0630	0.0560

4.5 References

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Chapter 5

[Pd^0(Ar-bian)(η^2-Alkene)] Complexes Catalyze Chemo- and Stereoselective Partial Hydrogenation of Functional 1,2-Dienes

Abstract

Several zerovalent palladium catalysts bearing bis(arylimino)acenaphtene and alkene ligands were employed in the partial hydrogenation of various functionalized allenes to give the corresponding trisubstituted alkenes. These catalysts provided excellent activities as well as chemo- and positional selectivities but variable stereoselectivities to trisubstituted (Z)-1-alkenyl phosphonates (85-95%) and trisubstituted (Z)-1-alkenyl esters (20-93%). The palladium pre-catalyst bearing the 4-MeO-C_6H_4-bis(arylimino)acenaphtene and dimethylfumarate as ligands showed higher activities, chemo-, positional and stereoselectivities. Some Z-E isomerization was observed after initial stereoselective hydrogenation. However, no over-reduction was observed in the partial hydrogenation of 1,2-dienyl phosphonates and 2,3-dienoates employing this catalytic system.

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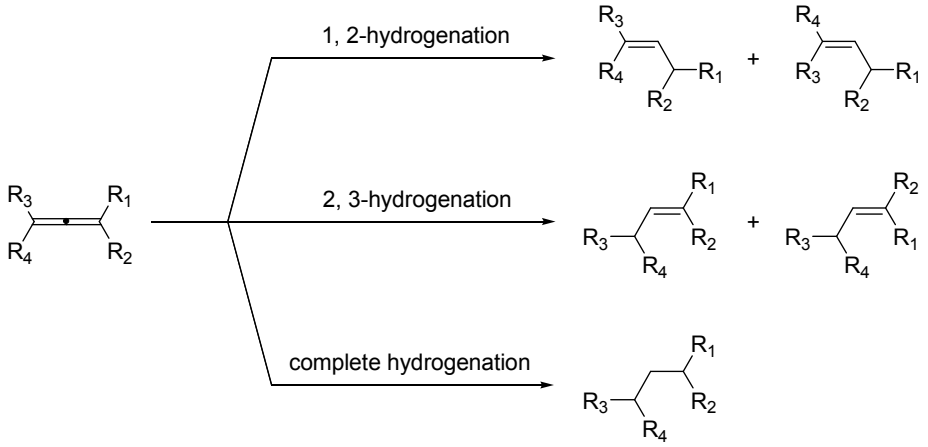
5.1 Introduction

Allenes (n,n+1-dienes) are an important class of compounds with many applications in organic chemistry.[2] In spite of the fact that the catalytic hydrogenation of unsaturated hydrocarbons has been extensively studied,[3] the hydrogenation of allenes has been reported in only a very limited number of studies. Moreover this reaction is very challenging since there are issues of chemo- and stereoselectivity like for alkyne semi-hydrogenation, but also an issue of positional selectivity[4] (Scheme 5-1). The chemoselective hydrogenation is an important method for removing allenes from distillate oil, especially the selective hydrogenation in C_3 streams of methylacetylene and propadiene to propene.[5]

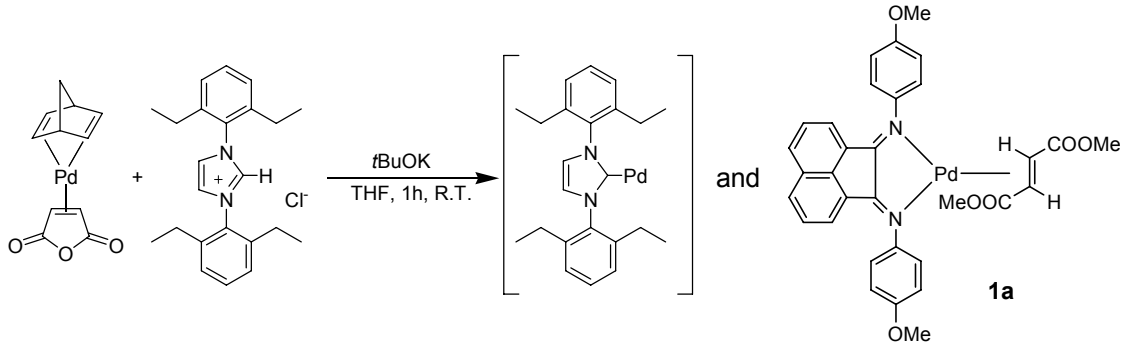


Scheme 5-1. The hydrogenation of allenes.

Several heterogeneous and homogeneous catalysts have been developed or used for this reaction such as the Wilkinson-Osborn catalyst $RhCl(PPh_3)_3$,[6,7] the cationic Rh(I) systems of Schrock and Osborn or of Selke,[7] the MoS_2 catalyst,[8] hydrogenation with diimide.[9] Moreover, palladium catalysts have also been reported such as heterogeneous palladium catalysts[10] and some allylpalladium(II) derivatives.[11] So far the selectivity in the reported cases is low.[12]

In recent years, stereoselective semi-hydrogenation of alkynes by zerovalent palladium catalyst bearing either a Ar-bian ligand (Ar-bian = bis(arylimino)acenaphtene) or a NHC ligand (NHC = nitrogen heterocyclic carbene), that are able to homogeneously hydrogenate a wide variety of alkynes to the corresponding (*Z*)-alkenes have been reported by our group (Scheme 5-2).[13,14] The

observed selectivity towards (*Z*)-alkenes is very high under very mild conditions (25˚C, 1 bar H_2).



Scheme 5-2. Palladium(0)-NHC catalyst generated in situ[14] and [Pd(bis(*p*-methoxyphenylimino)acenaphtene)(η^2-dimethylfumarate)].[13]

The objective of this study was to investigate whether or not [Pd(Ar-bian)(η^2-alkene)] complexes are suitable catalysts for the hydrogenation of allenes, which would be en interesting and valuable extension of the known semi-hydrogenation of isomeric alkynes. If so, we would be particularly interested to see whether any chemo-, positional and/or stereoselectivity would be exhibited by the [Pd(Ar-bian)(η^2-alkene)] complexes in such a hydrogenation. Similarly to the hydrogenation of alkynes, the hydrogenation of 1,2-dienes could lead to an alkene if the reduction of one double bond occurs selectively. In that case the reaction is chemoselective. The stereoselectivity or lack thereof will determine the *Z*/*E* ratio of the obtained alkene. In catalytic hydrogenation of 1,2-dienes, the chemoselectivity and the stereoselectivity are even more interesting if either the 1,2-hydrogenation or the 2,3-hydrogenation reaction is performed preferentially, this positional selectivity is represented in Scheme 5-1. In this chapter, the use of various [Pd^0(Ar-bian)(η^2-alkene)] catalysts in the selective hydrogenation of 1,2-dienyl phosphonates and 2,3-dienyl carboxylates is described.

5.2 Results and Discussion

5.2.1 [Pd^0(Ar-bian)(η^2-alkene)] complexes (1-8)

The complexes that have been used as hydrogenation catalysts (**1**-**8**) have been compiled in Figure 5-1. These complexes contain various Ar-bian and co-ligands, *e.g.* alkenes, and have been selected to study the effects of the various ligands on the activity, stability and selectivity in the hydrogenation reaction.

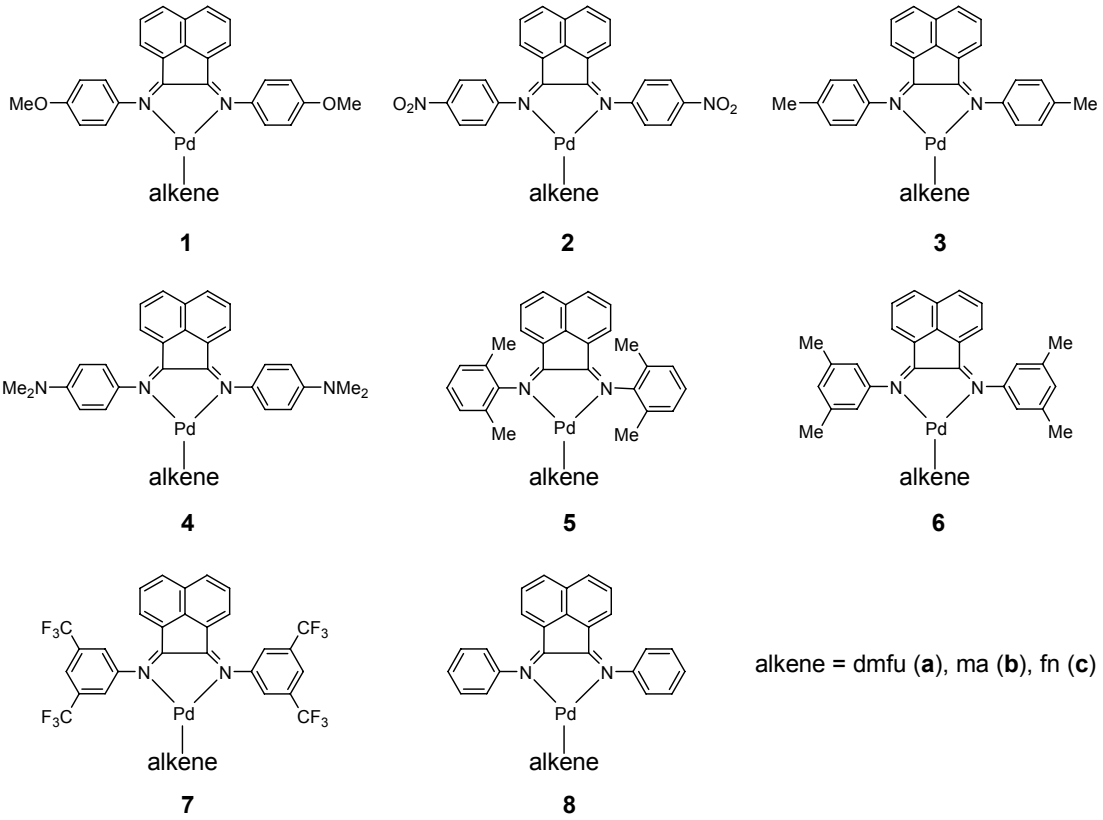
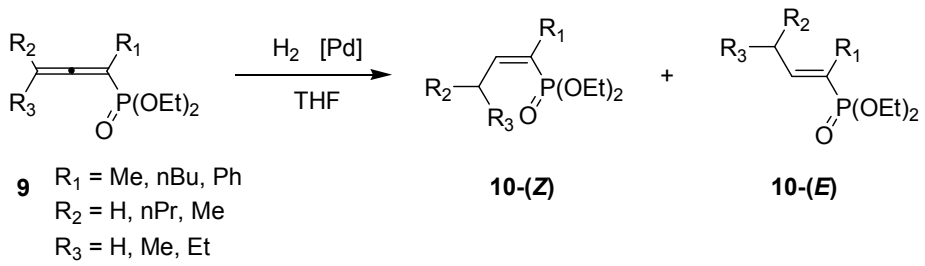


Figure 5-1. Palladium(0)-alkene complexes used in this study as hydrogenation catalysts with dimethyl fumarate (dmfu), maleic anhydride (ma) and fumaronitrile (fn) as alkene.

5.2.2 Hydrogenation of the 1,2-dienyl phosphonates (9)

The palladium(0)-alkene complexes **1a** and **3c** were applied in the hydrogenation of 1,2-dienyl phosphonates **9**. The hydrogenations were conducted at room temperature in THF with 1 mol % of catalyst under a hydrogen gas pressure of about 1 bar. Results of the hydrogenations using these catalysts have been compiled in

Table 5-1. Surprisingly the catalytic hydrogenation of these substrates gives only trisubstituted 1-alkenyl phosphonate **10** (Scheme 5-3).



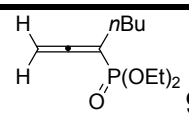
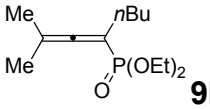
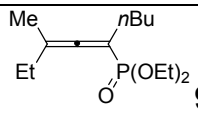
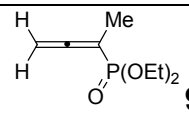
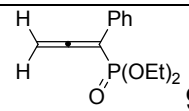
9 R_1 = Me, nBu, Ph; R_2 = H, nPr, Me; R_3 = H, Me, Et

10-(*Z*) **10-(*E*)**

Scheme 5-3. Hydrogenation of 1,2-dienyl phosphonates **9**.

So far, to the best of our knowledge, such activity, chemo-, stereo- and positional selectivity in homogeneous catalytic hydrogenation of allenes have not been described either with rhodium[6,7] or palladium[11] complexes. Hence, full positional selectivity is obtained, since the reduction proceeds *via* the unique 2,3-hydrogenation reaction. Moreover, the complete chemoselectivity is also noteworthy, since no overreduction is observed. In addition to the excellent chemo- and positional selectivities, excellent yields and stereoselectivities, up to 99% for the (*Z)*-alkene **10-(*Z*)**, are observed (entries 1 and 2, table 5-1).

Table 5-1. Hydrogenation of different 1,2-dienyl phosphonates (**9a**-**9e**) catalyzed by [Pd(Ar-bian)(η^2-alkene)].[a]

Entry	1,2-Diene	Catalyst	Conversion (%)[b]	**10-(*Z*)** (%)[c]	Yield (%)[d]
1	 **9a**	**1a**	>99	>99	94
2		**3c**	>99	>99	94
3	 **9b**	**1a**	>99	>99	95
4	 **9c**	**1a**	>99	>99	85
5	 **9d**	**1a**	>99	>99	91
6		**3c**	-	-	-
7	 **9e**	**1a**	>99	>99	95

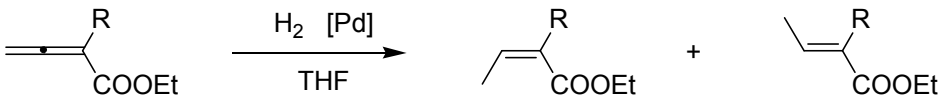
[a] Reaction conditions 0.2 mmol 1,2-diene, 3 mL THF, 1 mol % of catalyst, 1 atm H_2, 20ºC. [b] Conversion determined by ^{1}H NMR. [c] Determined by ^{1}H NMR. [d] Isolated yields.

Substitution at C-3 by methyl or ethyl groups does not affect the positional selectivity (2,3-hydrogenation) and the stereoselectivity (entries 1, 3 and 4). Meanwhile, slight modification of the substituants R_1 on the carbon 1 does not change the observed stereoselectivity (entries 1, 5 and 7) the effect of the phosphonate moieties is apparently predominant to determine the stereoselectivity.

Contrary to the hydrogenation of the *n*-butyl-substituted 1,2-dienyl phosphonate **9a** (entries 1 and 2) in which both of the catalysts (**1a** and **3c**) were highly active and selective, the results of the hydrogenations of the methyl-substituted 1,2-dienyl phosphonate **9d** (entries 5 and 6) are marked by the lack of activity of **3c**. This complete absence of reaction could be attributed to the lack of activation of the pre-catatalyst **3c**, which may result from the stronger coordination of the fumaronitrile ligand to the palladium as compared to dimethylfumarate homologue. Indeed, the strength of the alkene-palladium bonds decreases in the order: maleic anhydride > fumaronitrile > dimethylfumarate.[15]

5.2.3 Hydrogenation of the 2,3-dienoates (11 and 13)

The palladium(0)-alkene complexes **1**-**8** were applied in the hydrogenation of 2,3-dienoates **11** and **13**. The hydrogenations were conducted at room temperature in THF with 1 mol % of catalyst under a hydrogen gas pressure of about 1 bar. Results of the hydrogenations using these catalysts have been compiled in Table 5-2. The same excellent chemo- and positional selectivity as was obtained for the 1,2-dienyl phosphonates **9** is observed, since only trisubstituted 1-alkenyl esters **12** and **14** are formed (Scheme 5-4).



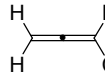
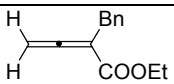
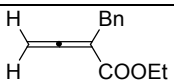
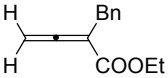
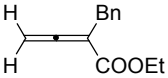
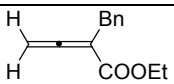
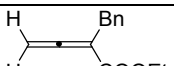
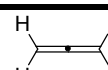
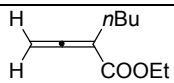
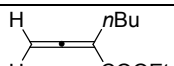
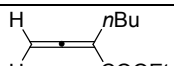
		(*Z*)	(*E*)
11	R = Bn	**12-(*Z*)**	**12-(*E*)**
13	R = *n*Bu	**14-(*Z*)**	**14-(*E*)**

Scheme 5-4. Hydrogenation of 2,3-dienoates **11** and **13**.

With this substrate, the chemo- and positional selectivity of the hydrogenation is conserved, but we observe a lack of stereoselectivity. Indeed, the *Z/E* ratio typically

varies between 80/20 and 93/7. In some cases an opposite selectivity is observed with a ratio *Z*/*E* varying between 20/80 and 40/60.

Table 5-2. Hydrogenation of Ethyl 2-benzylbuta-2,3-dienoate **11** and of Ethyl 2-*n*-butylbuta-2,3-dienoate[16] **13** catalyzed by [Pd(Ar-bian)(η^2-alkene)].[a]

Entry	2,3-Dienoate	Catalyst	Time (h)	Conversion (%)[b]	Ratio *Z*/*E* (%)[c]
1	 **11**	**1a**	5	34	**12** 93/7
			24	>99	90/10
2		**5a**	5	32	88/12
			24	>99	91/9
3		**6a**	24	>99	34/66
4		**2a**	24	>99	93/7
		2b	24	>99	83/17
5		**3a**	24	>99	91/9
		3b	24	>99	83/17
6		**4a**	24	>99	61/39
		4b	24	>99	80/20
7		**1b**	24	>99	47/53
		1c	24	>99	85/15
8	 **13**	**1a**	1.75	>99	**14** 90/10
			24	>99	80/20
9		**1b**	1.75	>99	85/15
			6	>99	77/23
10		**5a**	1	-	-
			24	>99	23/77
11		**7a**	24	>99	~20/80
		8a	24	>99	~20/80

[a] Reaction conditions 0.2 mmol 2,3-dienoate, 3 mL THF, 1 mol % of catalyst, 1 bar H_2, 20ºC. [b] Conversion determined by ^{1}H NMR. [c] Determined by ^{1}H NMR.

The complex [Pd(*p*-MeO-C_6H_4-bian)(η^2-dmfu)] (**1a**) (entries 1 and 8, Table 5-2) turned out to be one of the most selective catalyst for the hydrogenation of 2,3-dienoates **11** and **13**. Meanwhile, for the hydrogenation of ethyl 2-benzylbuta-2,3-dienoate **11** (entries 1-7, Table 5-2), the highest selectivity with full conversion was obtained with [Pd(*p*-NO_2-C_6H_4-bian)(η^2-dmfu)] (**2a**) (entry 4), Pd(*p*-Me-C_6H_4-bian)(η^2-dmfu) (**3a**) (entry 5), [Pd(*m,m'*-Me_2-C_6H_3-bian)(η^2-dmfu)] (**5a**) (entry 2) and **1a**. From these results, it seems that the electronic effect induced by the substituent on the aryl group of the ligand does not have a major effect on the stereoselectivity of the hydrogenation. However, the stereoselectivity seems higher with the [Pd(Ar-bian)(η^2-dmfu)] type catalyst (**a**) compared to the [Pd(Ar-bian)(η^2-ma)] type (**b**) (entries 4 and 5, and regarding entries 8 and 9). The hydrogenation of these two 1,2-dienoates shows a large substrate dependence concerning the activity. Employing **1a** as the catalyst, the hydrogenation of ethyl 2-*n*-butylbuta-2,3-dienoate **13** is faster than that of the benzyl analogue **11**; after 1.75 hours full conversion is obtained for **13**, whereas after 5 hours only 34% conversion of **11** (respectively entries 8 and 1, Table 5-2) had been obtained. This substrate dependence does not seem to affect the observed stereoselectivity of the semi-hydrogenation, which is approximately the same, however after 24 hours of reaction in both cases the ratio *Z*/*E* decreased significantly. This tendency is clearly confirmed by using the maleic anhydride derivative (entry 9).

5.2.4 Stereoselectivity and *Z-E* isomerization

Most of the studies refer to simple cyclic or acyclic allenes such as propadiene,[11] 1,2-cyclononadiene[6] or eventually monofunctionalized as the 1-methoxy-propa-1,2-diene.[7] The allenes that have been used in this study are slightly different to that, their functionalization with group as phosphonate, ester or sulfone[1] conjugated to the insaturation, allows delocalisation of the electron density that could be at the origin of the complete positional selectivity. Even if the positional selectivity is the same, the complex constants with palladium from ethyl 2-benzylbuta-2,3-dienoate **11** and of ethyl 2-*n*-butylbuta-2,3-dienoate **13** are different, this thermodynamic consideration should explain the substrate dependence observed.

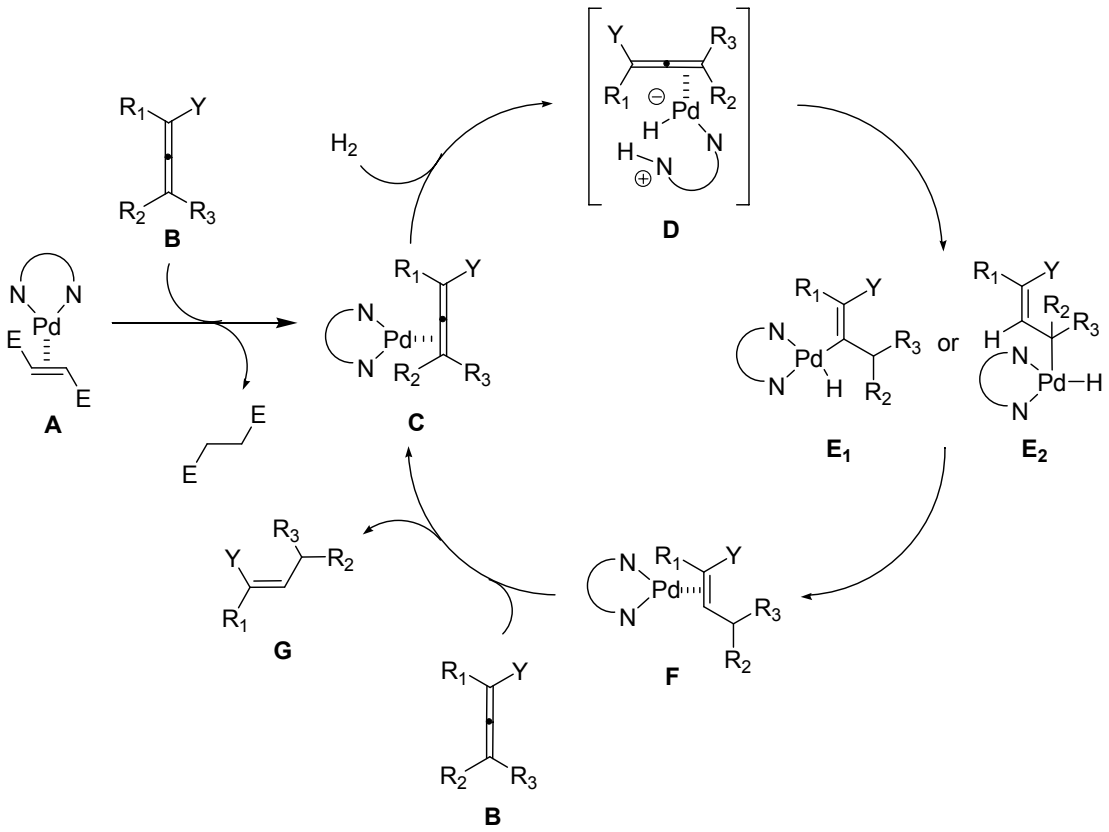
The main question was how to explain the low stereoselectivity observed in some cases? Two hypotheses were taken into consideration; (i) a real lack of stereoselectivity of our catalysts and (ii) an isomerization process occurring after the semi-hydrogenation of the allene. Regarding all the results, the steric and electronic effects induced by the catalyst are not deemed to be the origin of the, in some cases, seemingly 'reversed' stereoselectivity. More probably, *Z*-*E* isomerization has taken place after initial stereoselective hydrogenation. Indeed, the second hypothesis has been confirmed by a simple experiment: after full conversion of the allene into alkene (and the determination of the stereoselectivity by proton NMR on the crude mixture immediately after reaction), the reaction mixture (including the Pd-complex) was subsequently stirred for another period (4 hours) under nitrogen atmosphere. Monitoring of the *Z*/*E* ratio showed that it was changing in favour of the (*E*)-isomer, even in the absence of hydrogen pressure. Hence, the (*Z*)-alkene is the primary reaction product, from which the minor product (*E*)-alkene may be formed by an H_2-assisted palladium-catalyzed isomerization reaction[13b] or, as we observed, without the assistance of H_2. Hence, when we employed this and similar palladium catalysts and reaction times of 24 hours, we can assume that the observed stereoselectivity is somewhat smaller than the real stereoselectivity of the catalyst. So, the numbers in Table 5-2 for reactions proceeding during 24 h represent minimum values as far as the amount of the (*Z*)-alkene is concerned.

The 2,3-dienoates **11** and **13** seem to be more sensitive toward isomerization than the 1,2-dienyl phosphonates **9**. Isomerization occurs under mild conditions. The differences in the apparent stereoselectivity may be explained by considering two factors involved: (i) the higher thermodynamic stability of the (*E*)-alkene relative to the (*Z*)-isomer and (ii) the higher complex constant between palladium and the alkene **12** and **14** compared to the complex constant of palladium with the alkene **10**.

5.2.5 Mechanistic aspects

Since we have not studied the kinetics, nor have any experiments aimed at trapping of intermediates been performed, the mechanism of the selective hydrogenation of allenes using [Pd(Ar-bian)(η^2-alkene)] catalysts remains largely unknown. However, we suspect that the mechanism might in part be similar to the mechanism proposed for the semi-hydrogenation of alkynes using this type of

catalysts.[13] On the basis on these and previous results, a mechanism for this reaction is proposed in Scheme 5-5.



Scheme 5-5. Proposed catalytic cycle for the selective hydrogenation of allenes.

The catalytic cycle starts by the activation of the catalyst precursor **A** by hydrogenation of the coordinated alkene. Next, the more electron rich C=C bond in **B** coordinates to palladium instead of the alkene ligand to form a [Pd(Ar-bian)(η^2-allene)] complex **C**. In analogy with the mechanism for the alkyne hydrogenation,[13b] we propose heterolytic hydrogen cleavage by **C** to afford the monohydridopalladium complex **D**. This intermediate **D** may undergo highly stereoselective hydropalladation to generate the palladium hydride $\mathbf{E_1}$ or $\mathbf{E_2}$ after transfer of the N–H hydrogen atom to Pd.[17] A new [Pd(Ar-bian)(η^2-alkene)] complex **F** is produced by reductive elimination from $\mathbf{E_1}$ or $\mathbf{E_2}$. The final product **G** is obtained by dissociation of the product alkene from the intermediate **F**, at the same time regenerating the catalytically active species **C** through the coordination of the starting allene. The stereoselectivity observed supports the idea that the reaction most likely proceeds via the intermediate $\mathbf{E_1}$, in which the mutual *trans* orientation of the palladium and phosphonates or ester moieties may determine the stereoselectivity. Substitution of the generated (*Z*)-alkene

by allene (**F** → **C**) is crucial for the chemoselectivity of the reaction. This substitution process is acceptable since a complete chemoselectivity is observed during our experiments, the complex constant is probably higher in the case of the palladium η^2-allene complex than for the palladium η^2-alkene complex.

5.3 Conclusion

The use of pre-catalyst complexes, consisting of palladium(0), a rigid bidentate nitrogen ligand and an alkene, for the reaction of hydrogenation of different functionalized allenes has been explored. Hydrogenation of 1,2-dienyl phosphonates **9a-9e** has been performed successfully with high chemo-, positional and stereoselectivity leading to di- or trisubstituted (*Z*)-1-alkenyl phosphonates **10-(*Z*)**. The same full chemo- and positional selectivities were observed for the hydrogenation of the 2,3-dienoates **11** and **13**, but a lower stereoselectivity was obtained in forming the (*Z*)-1-alkenyl esters (**12-(*Z*)** and **14-(*Z*)**). The high chemoselectivity towards the alkene can be explained by the higher preference for coordination of the allene to palladium compared to the resulting alkene. Testing similar [Pd^0(Ar-bian)] catalysts revealed that the coordination strength of the alkene co-ligands has an influence on the stereoselectivity. An isomerization process of the (*Z*)-alkene to its (*E*)-isomer on palladium species resulting from catalyst decomposition is most certainly involved in this decrease of observed stereoselectivity. For all active [Pd(Ar-bian)(η^2-alkene)] catalysts, over-reduction is absent. This could be interesting for applications regarding oil purification processes or for the synthesis of trisubstituted alkenes that are otherwise difficult to obtain.

5.4 Experimental Section

5.4.1 General considerations

All reactions were carried out by using standard Schlenk techniques under an atmosphere of dry nitrogen unless otherwise specified. The solvents were dried according to standard procedures[18] and distilled before use. ^{1}H and ^{13}C NMR spectra were recorded at 298K on a Varian Mercury 300 spectrometer (300.13 and 75.48

MHz respectively). The chemical shift values are referenced to external TMS with high frequency shifts signed positive. Chemical shifts (δ) and coupling constants (J) are expressed in ppm and in Hertz (Hz) respectively and the multiplicity as s = singulet, d = doublet, dd = double doublet, t = triplet, pst = pseudo triplet, m = multiplet, br = broad; data in parenthesis are given in the following order: multiplicity, number of protons, labelling of the proton and coupling constants in Hz.
Dimethylfumarate (Merck), maleic anhydride (Acros), fumaronitrile (EGA), were used as received. $Pd(dba)_2$[19], *p*-MeO-C_6H_4-bian,[20] *p*-NO_2-C_6H_4-bian,[20] *p*-Me-C_6H_4-bian,[20] *p*-NMe_2-C_6H_4-bian,[20] *o.o'*-Me-C_6H_4-bian,[20] *m,m'*-Me-C_6H_4-bian,[20] *m,m'*-CF_3-C_6H_4-bian,[20] Ph-bian,[20] palladium(0)-alkene complexes **1-8**,[15] 1,2-dienyl-phosphonates,[21] 2,3-dienoates,[22] were prepared according to literature procedures.

5.4.2 Hydrogenation experiments

The hydrogenation reactions were performed by dissolving, in a Schlenk tube, 0.2 mmol of the relevant allene and 0.02 mmol of the appropriate palladium complex in 3 mL of dry THF, under nitrogen atmosphere. Subsequently, the Schlenk tube was connected to a gas inlet and flushed with hydrogen to set a hydrogen atmosphere (1 atm) and the solution was stirred at 20ºC for 24h. The reaction mixture was then filtered over celite and the crude mixture was analysed by ^1H NMR spectroscopy. The solvent was removed in vacuo and flash chromatography on silica gel with a mixture petroleum ether/diethyl ether (1/2) as the eluent afforded the correspondent product.

5.4.3 Acknowledgement

Many thanks to Prof. Shengming Ma and Hao Guo for the allenes and the discussions on the obtained results.

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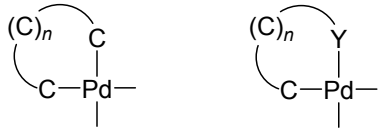
Samenvatting

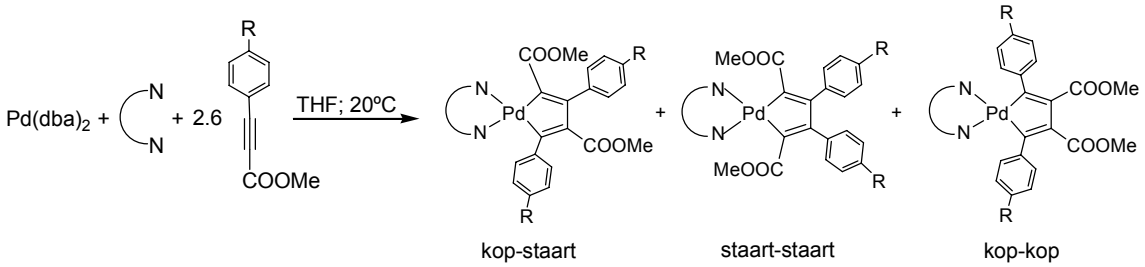
Er is, nu en in de toekomst, een toenemende behoefte aan chemische reacties die minder energie kosten en minder afvalproducten leveren dan huidige processen, maar die tegelijkertijd ook een hogere selectiviteit vertonen. Het gebruik van katalysatoren speelt een belangrijke rol in dit geheel, teneinde deze doelstellingen te halen. Chemici dragen hier een deel in bij door onderzoek te verrichten naar de synthese van nieuwe meer selectieve katalysatoren voor bestaande en nieuwe reacties. Hierdoor zal er tevens een toename optreden in de kennis en het begrip van bestaande processen. Uiteindelijk proberen we het beste compromis te vinden tussen kosten in termen van energie, financiële middelen, milieu en uitvoering.

Deze dissertatie omvat de synthese, karakterisering en in sommige gevallen de toepassing van katalyse van verscheidene cyclische palladium complexen. ***Hoofdstuk 1*** begint met een introductie van de coördinatie- en organometaalchemie, waarna dieper wordt ingegaan op de organopalladiumchemie van cyclische complexen; met name de synthese en de reactiviteit van palladacyclische en cyclogepalladeerde verbindingen (Schema 1) worden belicht, alsmede hun eventuele toepassing als katalysator.



Schema 1. Palladacyclische Pd(C^C) en cyclogepalladeerde Pd(C^Y) complexen.

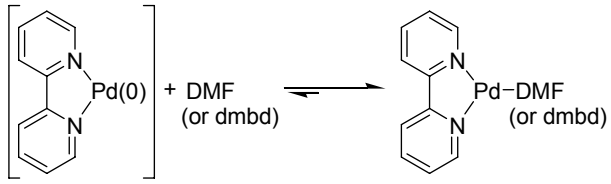
In ***Hoofdstuk 2*** wordt de vorming van palladacyclopentadienen uit asymmetrische alkynen beschreven. De complexen worden gevormd door een reactie van een asymmetrisch alkyn met $Pd(dba)_2$ en bidentaat stikstof liganden (bipy, tmeda, phen en Ar-bian) zoals aangegeven in Schema 2. Asymmetrische alkynen zoals methyl fenylpropynoaat of methyl (4-methoxyfenyl)propynoaat geven een volledig regioselectieve vorming van kop-staart gekoppelde palladacyclopentadienen, terwijl de reactie met methyl (4-nitrofenyl)propynoaat leidt tot de vorming van zowel kop-staart als staart-staart gekoppelde producten.



Schema 2. Vorming van palladacyclopentadienen uit asymmetrische alkynen.

De regioselectiviteit van de oxidatieve cyclisatie van een tweede alkyn molecuul met het tussenproduct [Pd(NN)(η^2-alkyn)] geeft aan dat er een subtiel samenspel is van sterische en electronische faktoren. Gezien de soms geringe stabiliteit van het gevormde palladacyclopentadieen, wordt voorgesteld dat dit proces reversibel is. Sluitend bewijs hiervoor werd gevonden door de waargenomen stabiliteit van een mengsel van regio-isomeren en een uitwisselingsreactie gepaard gaand met het vrijkomen van het initieel gecoördineerde alkyn.

In **Hoofdstuk 3** worden experimenten besproken die als doel hebben het mechanisme van de 3-componenten synthese van diënen op te helderen. Onderzoek betreffende de kinetiek en het mechanisme van de vorming van het palladacyclopentadieen [Pd(bipy)(CCOOMe$_4$)] vanuit [Pd(bipy)(η^2-DMF)] en [Pd(bipy)(η^2-dmbd)] suggereert de vorming van een niet te detecteren, reactief tussenproduct, dat beschreven kan worden met het evenwichtsmengsel van een [Pd(bipy)(η^2-DMF)] complex en een [Pd(bipy)(η^2-alkyn)] complex (Schema 3).

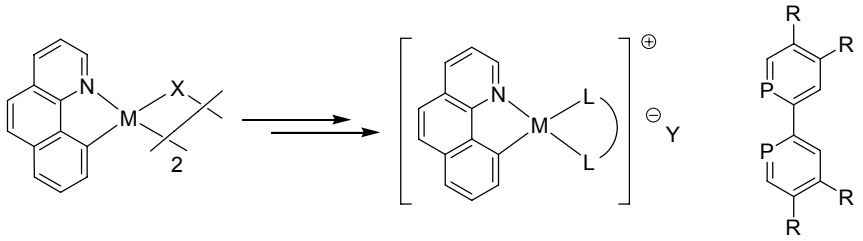


Schema 3. Ongedetecteerd reactief tussenproduct, verondersteld in het vormingsmechanisme van palladacyclopentadieen complexen.

De waargenomen lage selectiviteit in de katalytische synthese van dienen kan worden veroorzaakt door de hoge reactiviteit van dit Pd^0-waardige tussenproduct, welke kan worden gevormd door reductieve eliminatie van het dieen product.

Er wordt betoogd dat er twee parallelle katalytische cycli doorlopen kunnen worden en voorts, dat het mogelijk is de katalyse zo te sturen dat hoofdzakelijk het dieen wordt verkregen. Tenslotte wordt een plausibel mechanisme voor het katalytische 3-componenten proces voorgesteld.

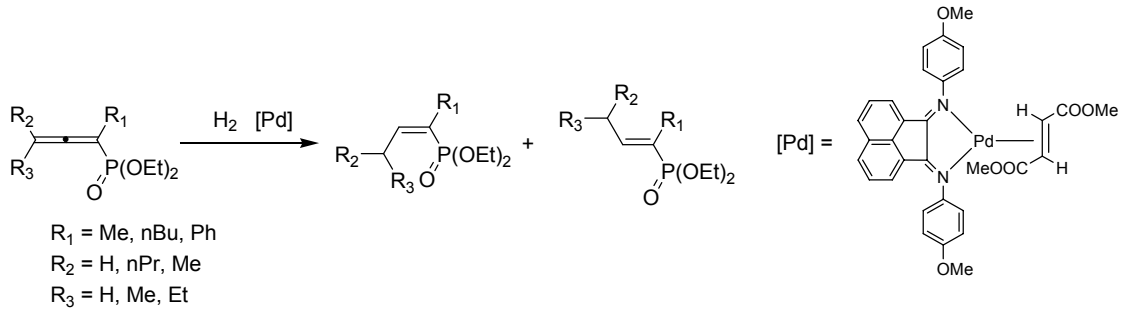
In **Hoofdstuk 4** wordt de aandacht gericht op de synthese en karakterisering van cyclometallische platina- en palladium verbindingen van het type $[M(C\text{^}N)(LL)]^+$ met als LL chelerende liganden zoals 2,2'-difosfininen en 2,2'-bipyridylen (Schema 4). Als de cyclogepalladeerde complexen worden gebruikt als katalysator in koper- en fosfine-vrije Sonogashira reacties, dan wordt er een goede stabiliteit en activiteit van deze complexen gevonden, die echter vergelijkbaar zijn met voor deze reactie al bestaande en gepubliceerde katalysatoren. Vervolgens wordt er een kort overzicht gegeven van de eigenschappen van 2,2'-di-fosfinines en wordt er een voorstel gedaan hoe deze te synthetiseren, ter introductie van het (tot dusver niet succesvolle) onderzoek van de synthese van 0-waardige cyclische palladium verbindingen met $N\text{^}C^-$ liganden (van het type $[Pd(C\text{^}N)L_n]^-$) vergelijkbaar met de actieve verbinding $[Pd(C\text{^}P)L_n]^-$. Deze $[Pd(C\text{^}P)L_n]^-$ verbinding wordt verwacht de katalytisch actieve component in de Mizoroki-Heck reactie te zijn.



Schema 4. Cyclometallisch platina- en palladiumverbindingen van het type $[M(C\text{^}N)(LL)]^+$ en 2,2'-di-fosfinine liganden.

Als laatste wordt in **hoofdstuk 5** de selectieve partiële hydrogenering van verschillende gefunctionaliseerde allenen beschreven, gekatalyseerd door 0-waardige palladium complexen met als liganden bis(arylimino)acenafteen en een alkeen. Er is aangetoond dat deze katalysatoren een excellente activiteit vertonen. Hydrogenering van 1,2-dienylfosfonaten is succesvol uitgevoerd met hoge chemo- ,

positionele- en stereoselectiviteit waarin di- of tri-gesubstitueerde (*Z*)-1-alkenyl fosfonaten worden verkregen (Schema 5).



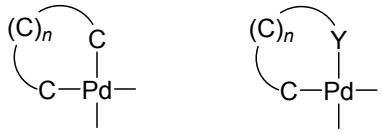
Schema 5. Hydrogenering van 1,2-dienyl fosfonaten met de [Pd(*p*-MeO-C_6H_4-bian)(η^2-dmfu)] katalysator.

Naast 1,2-dienyl fosfonaten kunnen ook 2,3-dienoaten worden gehydrogeneerd, tevens met een hoge chemo- en positionele selectiviteit, zij het wel met lagere stereoselectiviteit. Deze lagere stereoselectiviteit bij de hydrogenering van 2,3-dienoaten wordt waarschijnlijk veroorzaakt door een palladium-gekatalyseerde isomerisatie van het (*Z*)-alkeen product naar het (*E*)-alkeen. De belangrijkste eigenschap van de reactie is, dat er geen ongewenste overreductie plaats vindt indien de actieve [palladium(Ar-bian)] katalysator wordt gebruikt.

Summary

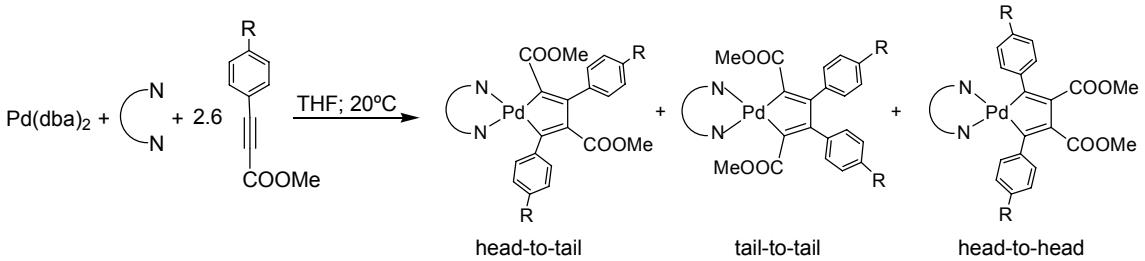
The quest for performing chemical reactions with less energy, less waste but at the same time with higher selectivities, is keeping a drive on the preoccupations of society. Catalysis plays an important role in this respect. Chemists can contribute to this quest by looking for new, more selective catalysts and viable 'atom-economic' reactions. That means an increase of the knowledge and understanding of existing (and enabling discovery of new) processes, in order to reach the best compromise between energy consumption, cost, environment and performance.

This thesis deals with the synthesis, characterization and in some cases the application in catalysis of various cyclic complexes of palladium. ***Chapter 1*** starts with an introduction concerning the coordination and organometallic chemistry. Next, the field of organopalladium chemistry involving cyclic complexes is discussed in more details. The synthesis, the reactivity and in some cases the application as catalyst of palladacyclic and cyclopalladated compounds (Scheme 1), are presented.



Scheme 1. Palladacyclic Pd(C^C) and cyclopalladated Pd(C^Y) complexes.

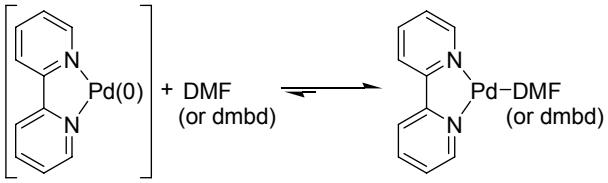
In ***Chapter 2***, the formation of palladacyclopentadiene from dissymmetric alkynes is described. The complexes were generated by reacting an (unsymmetric) alkyne with $Pd(dba)_2$ and these bidentate nitrogen ligands (bipy, tmeda, phen and Ar-bian) in the ratio indicated in Scheme 2.



Scheme 2. Synthesis of palladacyclopentadiene from dissymmetric alkynes.

Dissymmetric alkynes such as methyl phenylpropynoate or methyl (4-methoxyphenyl)propynoate give completely regioselectively rise to the formation of 'head-to-tail' coupled palladacyclopentadiene products only. Whereas, the reaction with methyl (4-nitrophenyl)propynoate leads to the formation of 'head-to-tail' coupled products as well as 'tail-to-tail' coupled products. The regioselectivity of the oxidative cyclization of a second molecule of alkyne with the [Pd(NN)(η^2-alkyne)] intermediate formed reveals the involvement of a subtle interplay between steric and electronic factors. In view of the sometimes limited stability of this palladacyclopentadiene, it is suggested that its formation is reversible. Conclusive evidence was obtained from the observed stability of a mixture of regioisomers and of an exchange reaction together with the release of the initial coordinated alkyne.

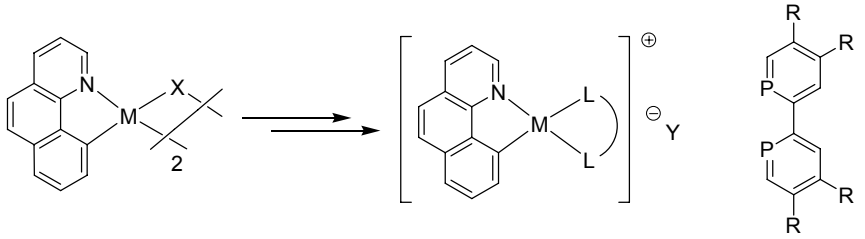
[Pallada-2,3,4,5-tetrakis(carbomethoxy)-2,4-cyclopentadiene(Ar-bian)] complexes are known catalysts for the conversion of dimethyl-2-butynedioate organic halide and tetramethyl tin to conjugated (*Z*,*Z*)-dienes. ***Chapter 3*** concerns experiments aimed at elucidating the general mechanism of this three-components synthesis of dienes. The kinetic and mechanistic investigation of the formation of the palladacyclopentadiene [Pd(bipy)(CCOOMe)$_4$] from [Pd(bipy)(η^2-DMF)] and [Pd(bipy)(η^2-dmbd)] suggests the formation of an undetected reactive intermediate, which could be described as an equilibrium mixture of [Pd(bipy)(DMF)] and [Pd(bipy)(alkyne)] species (Scheme 3).



Scheme 3. Undetected reactive intermediate hypothesized in the mechanism of formation of palladacyclopentadiene complexes.

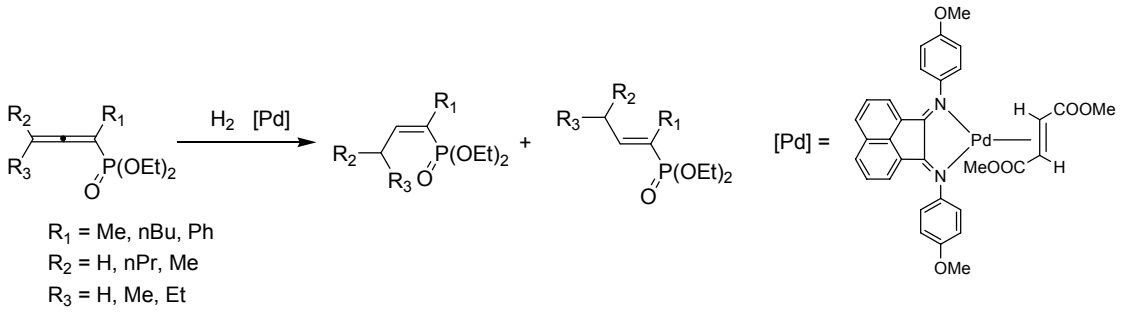
The low selectivity observed in the catalytic synthesis of diene is suggested to be due to the high reactivity of this zerovalent intermediate, which arises from the reductive elimination of the diene product. It is demonstrated that two concomitant catalytic cycles occur and that it is possible to direct the catalysis to predominantly obtain the diene. These results have led to the proposal of a viable general mechanism for the catalytic three-components process.

Chapter 4 focuses on the synthesis and characterization of cyclometallic platinum and palladium compounds of the type $[M(C^{\wedge}N)(LL)]^{+}$ with chelating ligands LL such as diphosphine or bipyridine (Scheme 4). The use of the cyclopalladated complexes as catalyst in copper- and phosphine-free Sonogashira reaction shows that the catalyst stability and activity obtained with these ligands are relatively good, but are rather similar compared to reported catalysts. A brief presentation of the properties of 2,2'-biphosphinines and their synthesis is proposed in order to introduce our (hitherto unsuccessful) investigation concerning the synthesis of zerovalent palladacycles with $N^{\wedge}C^{-}$ ligands of the type $[Pd(C^{\wedge}N)L_n)]^{-}$ that are similar to active species $[Pd(C^{\wedge}P)L_n)]^{-}$, suggested to be the catalytically active species in Mizoroki-Heck reaction.



Scheme 4. Cyclometallic platinum and palladium compounds of the type $[M(C^{\wedge}N)(LL)]^{+}$ and 2,2'-biphosphinine ligand.

Finally, in ***Chapter 5***, the partial hydrogenation of various functionalized allenes catalyzed by zerovalent palladium catalysts bearing bis(arylimino)acenaphtene and alkene ligands is reported. It is shown that these catalysts provide excellent activities as well as chemo- and positional selectivities. Hydrogenation of 1,2-dienyl phosphonates has been performed successfully with high chemo-, positional and stereoselectivity leading to di- or trisubstituted (*Z*)-1-alkenyl phosphonates (Scheme 5).



R_1 = Me, nBu, Ph
R_2 = H, nPr, Me
R_3 = H, Me, Et

Scheme 5. Hydrogenation of the 1,2-dienyl phosphonates derivatives with the [Pd(*p*-MeO-C_6H_4-bian)(η^2-dmfu)] catalyst.

Furthermore, 2,3-dienoates can also be hydrogenated with high chemo- and positional selectivities, but with a lower stereoselectivity. This lower stereoselectivity is probably due to palladium-catalyzed isomerization of the (*Z*)-alkene product to its (*E*)-isomer. Importantly, undesired over-reduction is absent in all cases when employing the active [Pd^0(Ar-bian)(η^2-alkene)] catalysts.

Résumé

La réalisation de réactions à moindre coût énergétique, produisant moins de déchets mais devant offrir de meilleures sélectivités, est un défi permanent de la société actuelle. Les chimistes contribuent à cette quête en recherchant de nouveaux catalyseurs plus sélectifs et offrant de meilleurs rendements. Une partie de cette recherche consiste en l'augmentation des connaissances et en une meilleure compréhension des réactions décrites, de manière à atteindre le meilleur compromis entre le coût, le rendement et l'aspect environnemental.

Cette thèse présente la synthèse, la caractérisation et dans certains cas l'application en catalyse, de différents composés cycliques du palladium. Le ***Chapitre 1*** débute par une présentation de la chimie de coordination et de la chimie organométallique. La chimie organométallique des composés cycliques du palladium est ensuite traitée plus en détails. La synthèse, la réactivité et, pour certains, l'application en catalyse des palladacycles et des composés cyclopalladés (Schéma 1) sont notamment présentées.

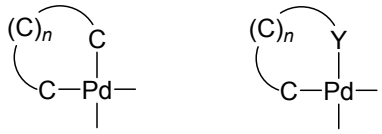


Schéma 1. Palladacycles Pd(C^C) et composés cyclopalladés Pd(C^Y).

Dans le ***Chapitre 2***, la formation de palladacyclopentadiène à partir d'alcynes dissymétriques est décrite. Ces complexes sont générés en faisant réagir un alcyne dissymétrique avec le $Pd(dba)_2$ et un ligand bidentate azoté (bipy, tmeda, phen et Ar-bian) en respectant la stœchiométrie indiquée dans le Schéma 2.

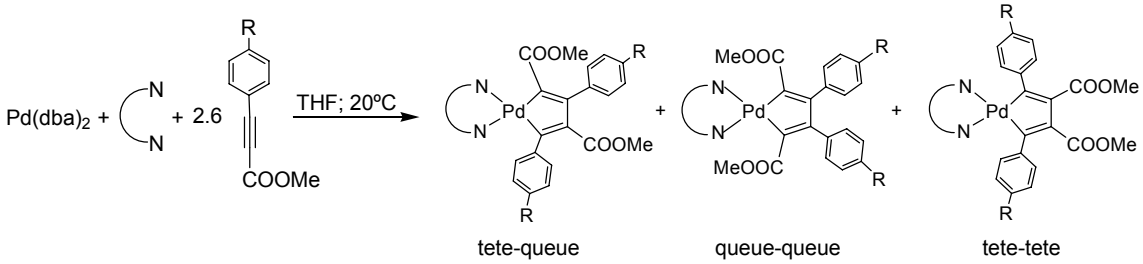


Schéma 2. Synthèse de palladacyclopentadiène à partir d'alcynes dissymétriques.

Les alcynes dissymétriques tels que le phénylpropynoate de méthyle ou le (4-méthoxyphényl)propynoate de méthyle permettent de former un unique régioisomère, le palladacyclopentadiène issu du couplage tête-queue. Le (4-nitrophényl)propynoate de méthyle conduit, quant à lui, à la formation d'un mélange de deux régioisomères issus des couplages tête-queue et queue-queue. La régiosélectivité de ce couplage entre 2 alcynes *via* l'intermédiaire [Pd(NN)(η^2-alcyne)] est la résultante d'un subtil mélange de critères stérique et électronique. La réversibilité de la formation de ces palladacyclopentadiènes a été suggérée et une réaction d'échange d'alcyne, avec libération de l'alcyne initialement présent dans le palladacyclopentadiène, tend à confirmer cette hypothèse.

Les complexes de type [Pallada-2,3,4,5-tetrakis(carbomethoxy)-2,4-cyclopentadiene(Ar-bian)] sont connus pour être catalytiquement actifs dans la synthèse de diènes conjugués (*Z*,*Z*) à partir de diméthyl-2-butynedioate, d'halogénure organique et de tétraméthyles d'étain. Le ***Chapitre 3*** relate les travaux effectués afin d'élucider le mécanisme général de cette synthèse à trois composés. L'étude cinétique et mécanistique de la formation de [Pd(bipy)$(CCOOMe)_4$], à partir des précurseurs [Pd(bipy)(η^2-DMF)] et [Pd(bipy)(η^2-dmbd)], a révélé la probable existence d'un intermédiaire hautement réactif. Cet intermédiaire pourrait être décrit comme un mélange de [Pd(bipy)(DMF/alkyne)] en équilibre dynamique (Schéma 3).

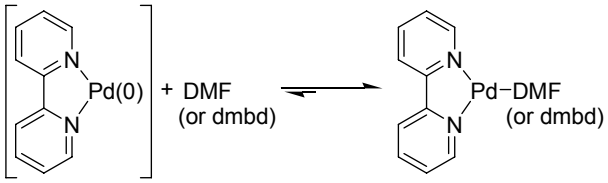


Schéma 3. L'intermédiaire hautement réactif proposé dans le mécanisme de formation des palladacyclopentadiènes.

La faible sélectivité observée dans la synthèse des diènes est probablement due au caractère hautement réactif du complexe à 14 électrons du palladium issu de l'élimination réductrice conduisant au diène. Il est démontré qu'au moins deux cycles catalytiques sont en concurrences et qu'il est possible d'orienter la réaction afin d'obtenir majoritairement le diène. L'ensemble des résultats a permis l'élaboration d'un mécanisme général de cette réaction à trois composants.

Le ***Chapitre 4*** concerne la synthèse et la caractérisation de complexes cyclométallés du platine et du palladium du type $[M(C^{\wedge}N)(LL)]^{+}$ avec des ligands chélatants tels que les biphosphines ou les bipyridines (Schéma 4). Certains de ces complexes cyclopalladés ont été utilisés comme catalyseurs dans la réaction de Sonogashira (sans cuivre et sans phosphine). Les résultats expriment la grande activité ainsi que la stabilité de ces complexes, mais restent comparables à ceux de la littérature. Une rapide présentation des propriétés des 2,2'-biphosphinines est faite de manière à introduire nos travaux concernant la synthèse d'un composé cyclopalladé mono anionique zérovalent du type $[Pd(C^{\wedge}N)L_n)]^{-}$. Ce complexe aurait une structure comparable à l'espèce $[Pd(C^{\wedge}P)L_n)]^{-}$ qui est suggérée comme étant l'entité catalytiquement active dans la réaction de Mizoroki-Heck.

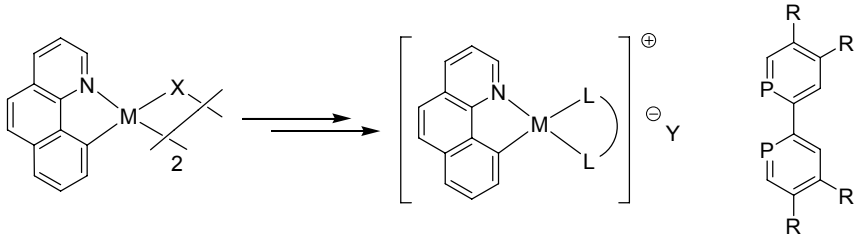


Schéma 4. Complexes cyclométallés du platine et du palladium du type $[M(C^{\wedge}N)(LL)]^{+}$ et le ligand 2,2'-biphosphinine.

Finalement, dans le ***Chapitre 5***, l'hydrogénation catalytique de différents allènes fonctionnalisés est présentée. Le catalyseur utilisé est un complexe zérovalent du palladium qui a pour ligand un bis(arylimino)acénaphtène et un alcène. Il s'avère que ces complexes sont très actifs et qu'ils offrent des chimio- et régiosélectivité importantes. L'hydrogénation des dérivés du phosphonate de 1,2-diényle a été réalisée avec succès. La chimio- et la régiosélectivité ainsi que la stéréosélectivité sont excellentes, ce qui conduit à la formation de dérivés di- ou tri substitués du phosphonate de (*Z*)-1-alcényle (Schéma 5).

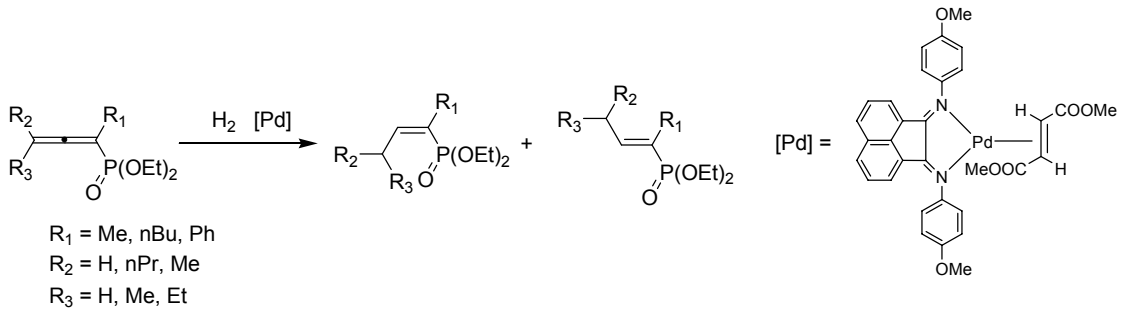


Schéma 5. Hydrogénation des dérivés du phosphonate de 1,2-diényle catalysée par le complexe [Pd(*p*-MeO-C_6H_4-bian)(η^2-dmfu)].

Les dérivés du 2,3-diènoate ont également été hydrogénés avec de bonnes chimio- et régiosélectivité mais avec une stéréosélectivité inférieure. Cette faible stéréosélectivité pourrait résulter de l'isomérisation catalytique sur palladium du produit formé. Il est important de noter l'absence d'hydrogénation totale du substrat, et ce quel que soit le substrat étudié.

List of Abbreviations

Ar-bian	bis(arylimino)acenaphtene
bipy	2,2'-bipyridine
bipy*	4,4'-bis(tertiobutyl)-2,2'-bipyridine
bp	2,2'-biphosphinine
bzq	benzo[*h*]quinoline
dba	dibenzylideneacetone
DMAC	*N*,*N*-dimethylacetamide
DMF	*N*,*N*-dimethylformamide
dmba	*N,N*-dimethylbenzylamine
dmbd	dimethyl-2-butynedioate
dmfu	dimethylfumarate
dppe	bis(diphenylphosphino)ethane
dppp	bis(diphenylphosphino)propane
FAB	fast atom bombardment
fn	fumaronitrile
GC	gas chromatography
ma	maleic anhydride
MS	mass spectrometry
NMR	nuclear magnetic resonance
phen	1,10-phenanthroline
TBAA	tetra-*n*-butylammonium acetate
THF	tetrahydrofuran
tmbp	4,4'-5,5'-tetramethyl-2,2'-biphosphinine
tmeda	*N*,*N*-tetramethylethylenediamine

List of Publications

A. Holuigue, G. Lutteke, C.J. Elsevier, L. Canovese, F. Visentin, *to be submitted*.
Mechanistic and Kinetic Investigation of the Conversion of Dimethyl-2-butynedioate to Conjugated (*Z*,*Z*)-Dienes Catalyzed by [Pd(4-CH_3-C_6H_4-bian)$(CCOOMe)_4$]

A. Holuigue, L. Canovese, F. Visentin, K. Goubitz, J. Fraanje, C. Sirlin, M. Pfeffer, C.J. Elsevier, *to be sumitted*.
Synthesis and Characterization of Palladacyclopentadienes Obtained from Dissymmetric Alkynes.

A.V. Gaikwad, A. Holuigue, M.B. Thathagar, J.E. ten Elshof, G. Rothenberg, Chemistry a European Journal (2007), 13(24), 6908-6913.
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J.-B. Sortais, N. Pannetier, A. Holuigue, L. Barloy, C. Sirlin, M. Pfeffer, N. Kyritsakas, Organometallics (2007), 26(8), 1856-1857.
Cyclometalation of Primary Benzyl Amines by Ru(II), Rh(III) and Ir(III) Complexes.

H. Guo, Z. Zheng, F. Yu, S. Ma, A. Holuigue, D. Tromp, C.J. Elsevier, Y. Yu, Angewandte Chemie International Edition (2006), (45), 4997-5000.
[Pd(Ar-BIAN)(alkene)]-Catalyzed Highly Chemo-, Regio-, and Stereoselective Semihydrogenation of 1,2-Allenyl Phosphonates and Related Compounds.

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Cycloruthenated Primary and Secondary Amines as Efficient Catalyst Precursors for Asymmetric Transfer Hydrogenation.

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