

Review

Diarylplatinum(II) Compounds as Versatile Metallating Agents in the Synthesis of Cyclometallated Platinum Compounds with *N*-Donor Ligands

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Abstract: This review deals with the reactions of diarylplatinum(II) complexes with *N*-donor ligands to produce a variety of cycloplatinated compounds including *endo*-five-, *endo*-seven-, *endo*-six- or *exo*-five-membered platinacycles. The observed reactions result from a series of oxidative addition/reductive elimination processes taking place at platinum(II)/platinum(IV) species and involving C–X (X = H, Cl, Br) bond activation, arene elimination, and, in some cases, C_{aryl}–C_{aryl} bond formation.

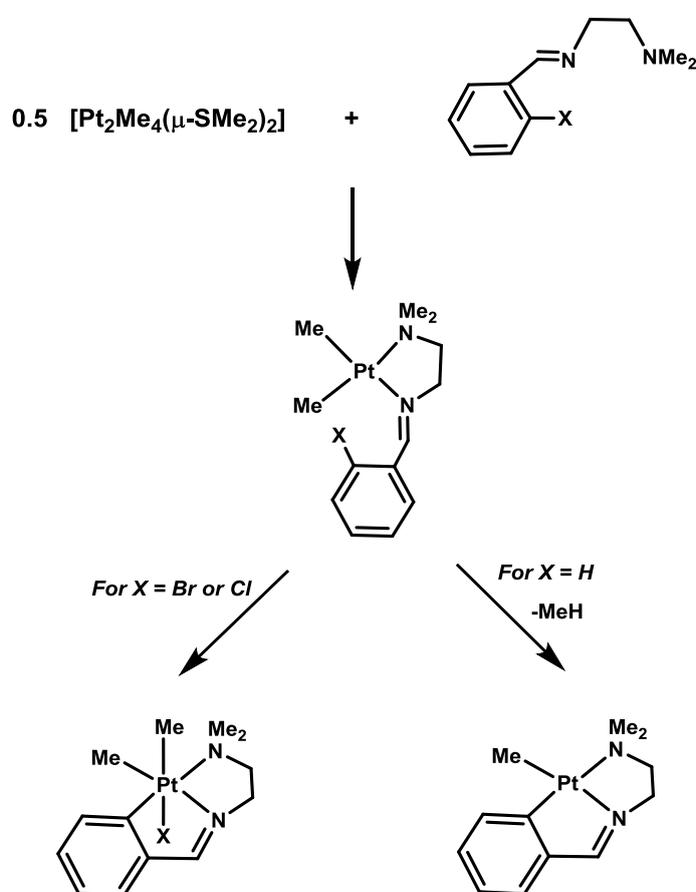
Keywords: platinum; cyclometallation; *N*-donor ligands; diarylplatinum(II) precursors; synthesis

1. Introduction

In recent years, research involving platinum complexes has focused on the study of their photophysical properties and their biological activities. Cyclometallated platinum compounds containing *N*-donor ligands have attracted a great deal of attention because of their potential interest in both areas [1–17]. For this reason, the development of new methods for the preparation of cycloplatinated compounds containing *N*-donor ligands is a pursued goal. In contrast to cyclopalladation reactions for which Pd(OAc)₂ is a very useful precursor leading to formation of a wide variety of palladacycles [18,19], an analogous “universal” starting material is unknown for cycloplatination reactions. Recent reports on cycloplatination reactions proved that *cis*-[PtCl₂(dmsO)₂] is a reasonable metallating agent leading to higher yields and cleaner reactions than the more classical

$K_2[PtCl_4]$ starting material [20–30]. In these systems, the labile sulfoxide ligands are easily replaced for nitrogen atoms, thus affording the required initial coordination of the nitrogen-donor ligand, which is followed by *ortho*-metallation. On the other hand, the lower electrophilicity of platinum(II) compared to palladium(II) facilitates oxidative addition as an alternative pathway. Thus, for electron-rich platinum precursors such as $[PtMe_2(dmsO)_2]$ [31–36] or dimer $[Pt_2Me_4(\mu-SMe_2)_2]$ [37–43], the initial coordination of the ligand is followed by a cyclometallation step which, in this case, consists on oxidative addition followed by reductive elimination of methane. As shown in Scheme 1, in addition to formation of cyclometallated platinum(II) compounds, dimethylplatinum precursors allow formation of stable cyclometallated platinum(IV) compounds arising from intramolecular activation of C–X bonds (X = Cl, Br) [41–43] of adequately designed ligands. In recent years, several diarylplatinum(II) compounds containing labile ligands such as dimethylsulfoxide or dialkylsulfide have also been tested as metallating agents for *N*-donor ligands. The obtained results indicate that they may produce a variety of cycloplatinated compounds and these processes will be reviewed in the present article.

Scheme 1. Synthesis of cyclometallated platinum(II) and platinum(IV) compounds from a dimethylplatinum(II) precursor [41].

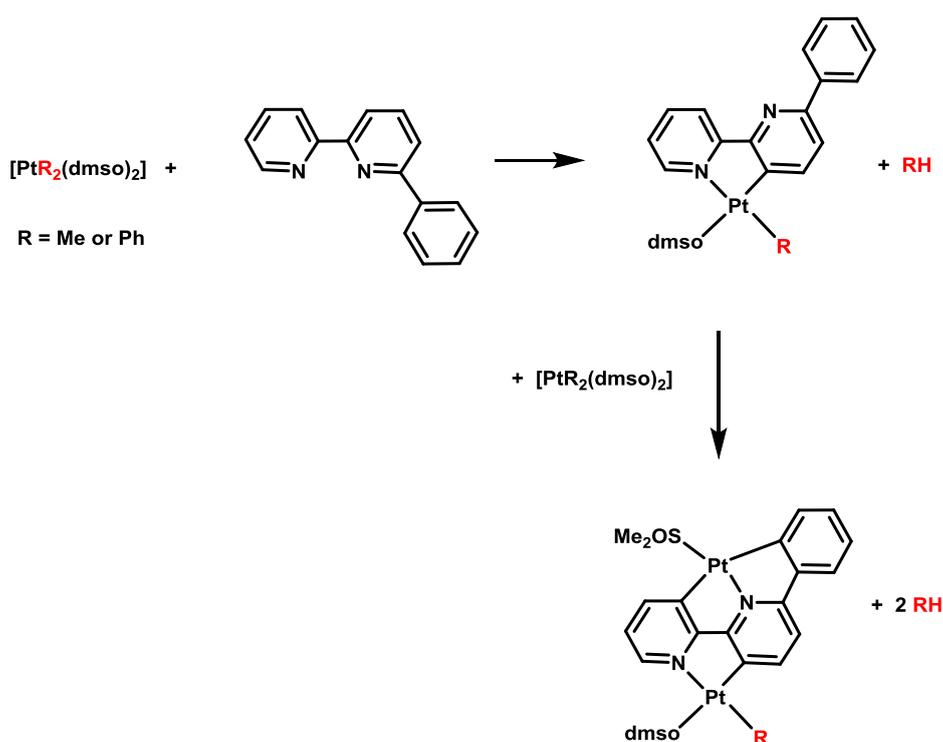


2. Activation of C–H Bonds at Diarylplatinum(II) Precursors

Diphenylplatinum(II) compounds such as $[PtPh_2(dmsO)_2]$ [31–33,44,45] or $[PtPh_2(SMe_2)_2]$ [46–49] have been often used as metallation precursors analogous to those containing dimethylplatinum(II)

moieties. In these reactions, the labile dimethylsulfoxide or dimethylsulfide ligands can be readily replaced by *N*-donor ligands, and the intramolecular C–H bond activation proceeds with elimination of benzene. Although, diphenylplatinum(II) derivatives are reported to be less prone to cyclometallation than the corresponding dimethyl derivatives, metallation of 2-phenylpyridines, benzo[*h*]quinoline or imines containing biphenyl, pyridyl or pyrimidine fragments has been achieved [44–48]. In addition, “rollover” cyclometallation of substituted bipyridines, including multiple C–H bond activation, and functionalized *N*-(2'-pyridyl)-7-azaindolyl ligands has been achieved using diarylplatinum precursors (see Scheme 2) [31–33,49,50].

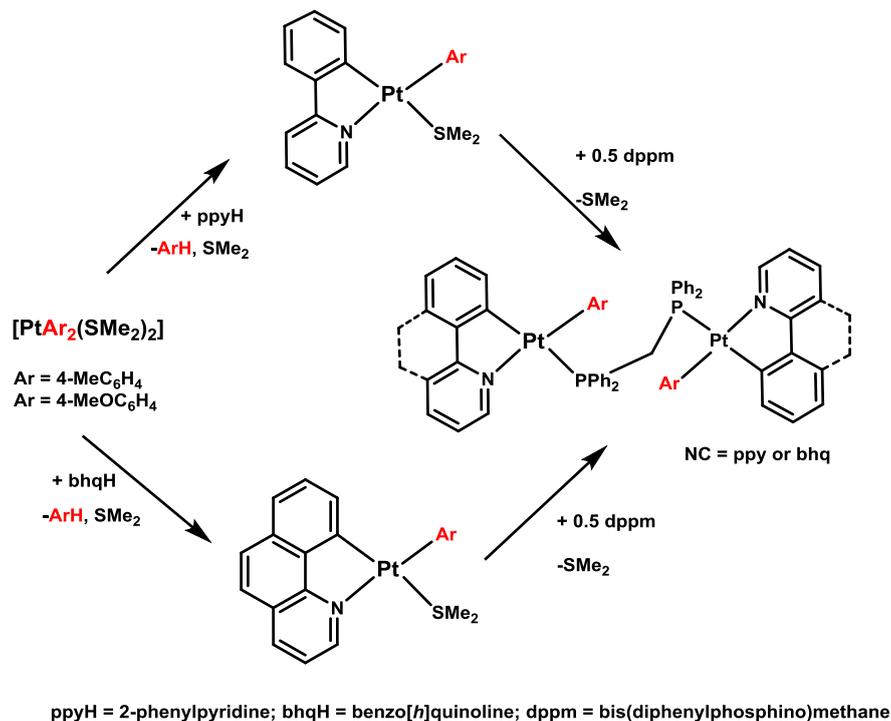
Scheme 2. Examples of “rollover” and multiple C–H bond activation of substituted bipyridines [31].



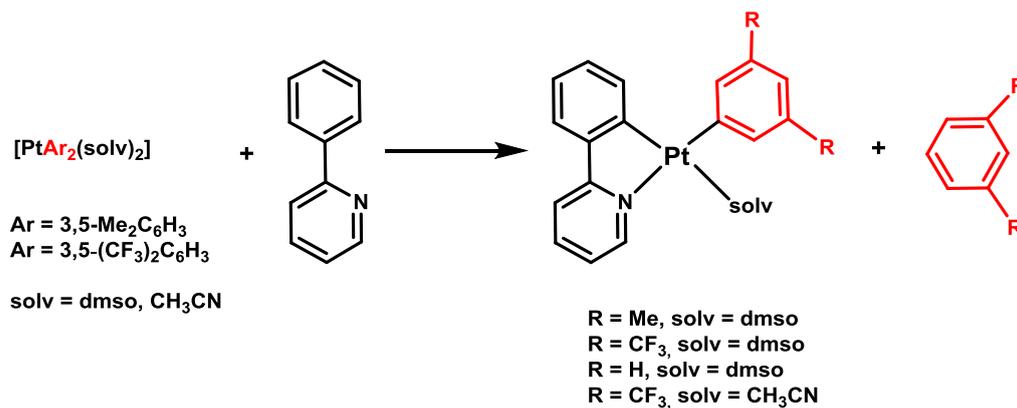
Other diarylplatinum(II) compounds such as $[PtAr_2(SMe_2)_2]$ ($Ar = 4-MeC_6H_4$; $4-MeOC_6H_4$) have been shown to be efficient metallation agents in front of 2-phenylpyridine or benzo[*h*]quinoline ligands, and the assembly of the resulting cyclometallated organoplatinum complexes through bridging diphosphine ligands has been reported (see Scheme 3) [51,52].

In these systems, the cyclometallation process involves oxidative addition of the C–H bond to the platinum(II) center to produce a platinum(IV) hydride complex, and subsequent reductive elimination of arene. Complexes having more electron-donating substituents at the aryl group undergo faster cyclometallation, however, as shown in Scheme 4, compounds $[Pt(Ar)(PhPy)(dmsO)]$ containing a cyclometallated phenylpyridine could be obtained from compounds $[PtAr_2(dmsO)]$ even when the aryl groups contain electronwithdrawing substituents such as $Ar = 3,5-(CF_3)_2C_6H_3$ [45].

Scheme 3. Synthesis and assembly of cyclometallated platinum compounds containing aryl ligands [51,52].



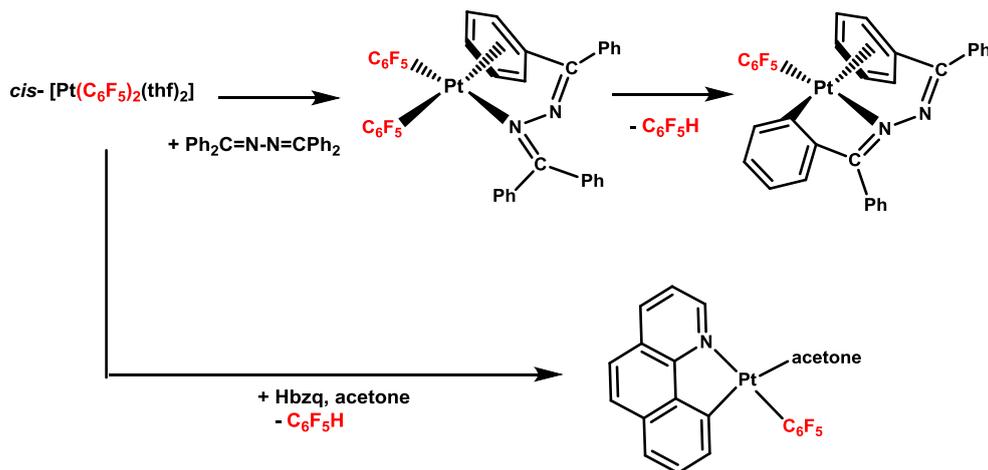
Scheme 4. Further examples of cyclometallation at diarylplatinum(II) compounds [45].



Moreover, the perfluorinated compound *cis*-[Pt(C₆F₅)₂(thf)₂] (thf = tetrahydrofuran) has also been used as a metallation precursor in the reactions with *N*-donor ligands leading to cyclometallated platinum compounds containing a tridentate [C,N,(η²-phenyl)] [53] or a bidentate [C,N] [54] ligand as shown in Scheme 5.

Evidence from the fact that *cis* configuration of the platinum precursor is not required comes from the fact that double cyclometallation of 3,6-bis(2-thienyl)-1,2,4,5-tetrazine has been achieved from the precursor *trans*-[Pt(2,4,6-Me₃C₆H₂)₂(dmsO)₂] in a reaction leading to a dinuclear platinum(II) compound [55].

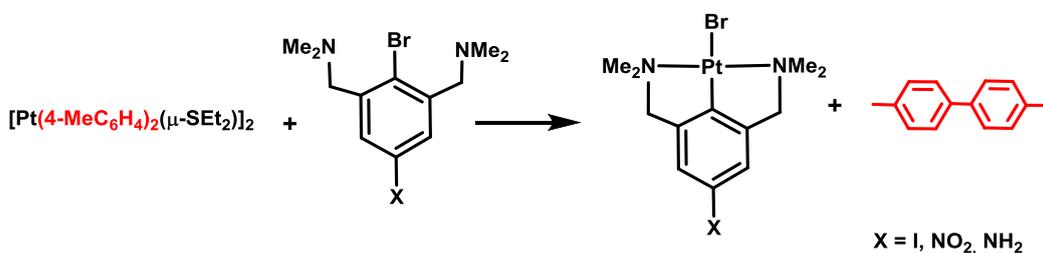
Scheme 5. Reactivity of compound $cis\text{-}[\text{Pt}(\text{C}_6\text{F}_5)_2(\text{thf})_2]$ (thf = tetrahydrofurane) with *N*-donor ligands [53,54].



3. Activation of C–X Bonds (X = Br, Cl or H) at Diarylplatinum(II) Precursors: Seven- versus Five-Membered Platinacycles

As shown in Scheme 6, the reactions involving intramolecular C–Br bond activation and subsequent reductive elimination of 4,4'-bitolyl have been reported as a convenient method for the synthesis of pincer- $[N,C,N]$ cyclometallated platinum(II) compounds when $[\text{Pt}(4\text{-MeC}_6\text{H}_4)_2(\mu\text{-SEt}_2)]_2$ was used as platinum precursor [56–59].

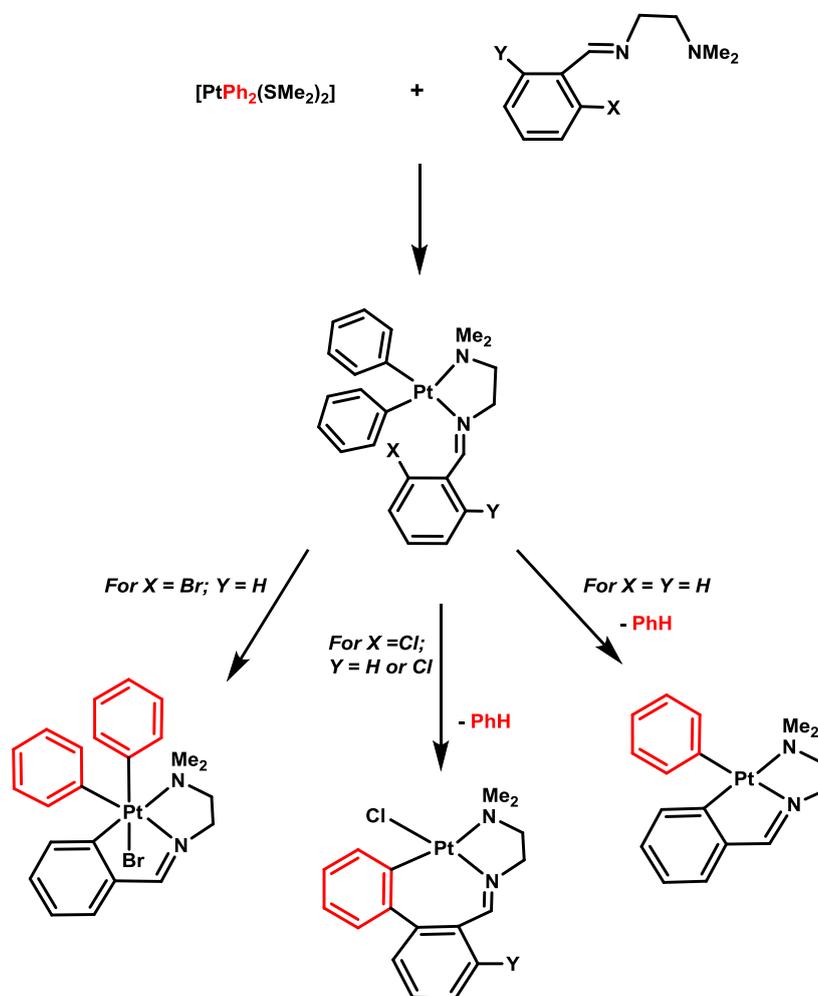
Scheme 6. Synthesis of $[N,C,N]$ cyclometallated compounds via C–Br bond activation followed by reductive elimination [56].



The reactions of potentially tridentate $[C,N,N']$ ligands $\text{RCH}=\text{NCH}_2\text{CH}_2\text{NMe}_2$ ($\text{R} = \text{C}_6\text{H}_5$, 2- BrC_6H_4 , 2,6- $\text{Cl}_2\text{C}_6\text{H}_3$ and 2- ClC_6H_4) with $[\text{PtPh}_2(\text{SMe}_2)_2]$ have been studied [60] in order to compare the results with those obtained when $[\text{Pt}_2\text{Me}_4(\mu\text{-SMe}_2)_2]$ was used as precursor. These reactions gave, in addition to cyclometallated platinum(II) and platinum(IV) compounds analogous to those described for the dimethylplatinum precursor, a new type of platinum(II) compound with a seven-membered metallacycle when $\text{X} = \text{Cl}$ (Scheme 7). In agreement with previous results for the chemistry of dimethylplatinum analogues [41–43], a concerted mechanism is suggested for intramolecular C–X bond activation [61]; for $\text{X} = \text{Br}$ a platinum(IV) compound is obtained at room temperature, while for $\text{X} = \text{H}$ a platinum(II) compound is formed along with reductive elimination of benzene after refluxing in toluene the corresponding coordination compounds. Unexpectedly, under the conditions required for

intramolecular activation of the C–Cl bond, a seven-membered metallacycle including a biaryl linkage is formed.

Scheme 7. Synthesis of cyclometallated platinum(II) and platinum(IV) compounds from a diphenylplatinum(II) precursor [60].

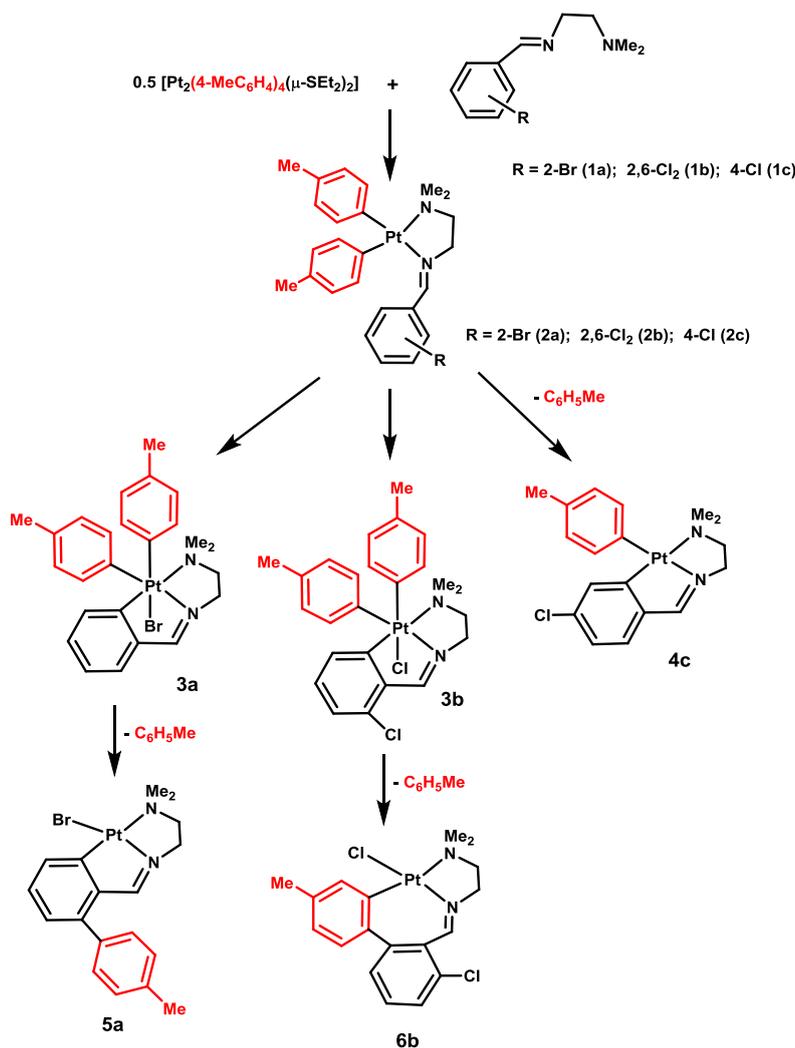


It is interesting to point out that despite the involvement of triarylplatinum(IV) species in these processes and the known susceptibility of such compounds to undergo reductive elimination of two aryl ligands to release a free biaryl [56], no evidence of such reductive elimination of biphenyl was observed.

In order to gain insight into the different processes that might take place when diarylplatinum compounds are used as metallating substrates, the study of the reactions of *cis*- $[\text{Pt}(4\text{-MeC}_6\text{H}_4)_2(\mu\text{-SEt}_2)]_2$ with imines of general formula $\text{RCH}=\text{NCH}_2\text{CH}_2\text{NMe}_2$ in which the aryl group R may contain either Br, Cl, H or F in the *ortho* positions was undertaken [62]. Dinuclear compound *cis*- $[\text{Pt}(4\text{-MeC}_6\text{H}_4)_2(\mu\text{-SEt}_2)]_2$, previously used as metallating agent as stated above, was selected for this study since the presence of an electron-donor methyl substituent in the aryl ring could facilitate the activation of the *ortho* C–X bonds. In addition, the position of the methyl substituent in the final products is relevant in order to confirm the mechanism of the process. As shown in Scheme 8, the reactions proceed as expected, yielding as final products a cyclometallated platinum(IV) compound **3a** (for X = Br), a cyclometallated platinum(II) compound **4c** (for X = H) and a seven-membered

platinum(II) compound **6b** for X = Cl. In the latter case, it was possible to detect a platinum(IV) compound (**3b**) as a precursor of the seven membered platinacycle. In addition, the presence of the methyl substituent, initially *para* to platinum, in a *meta* position in compound **6b** suggests that the C_{aryl}–C_{aryl} bond is formed in a reductive elimination reaction from the platinum(IV) compound. A subsequent cyclometallation process takes place through C_{aryl}–H bond activation at the biaryl fragment and elimination of one molecule of toluene.

Scheme 8. Synthesis of cyclometallated platinum(II) and platinum(IV) compounds from *cis*-[Pt(4-MeC₆H₄)₂(μ-SEt₂)₂] [62,63].

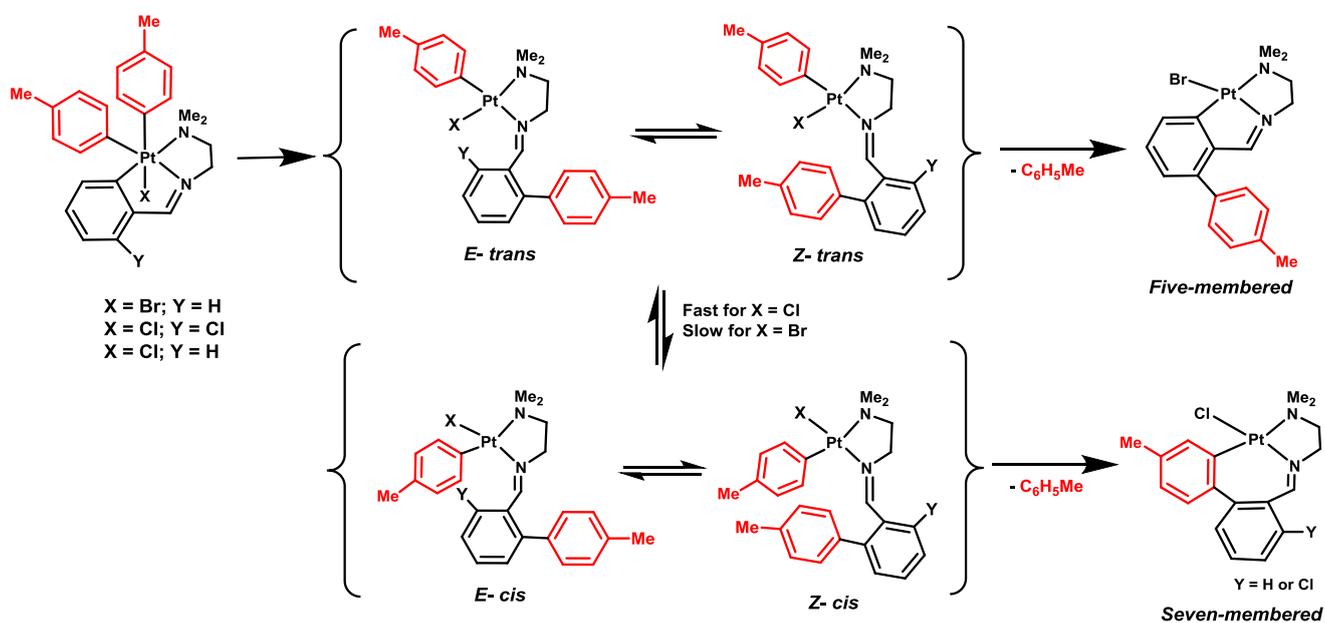


An initial attempt to produce a seven-membered platinacycle from the more inert bromide platinum(IV) compound [PtBr(4-MeC₆H₄)₂(C₆H₄CH=NCH₂CH₂NMe₂)] was carried out in refluxing toluene and led to a complex mixture of compounds in which the major component was surprisingly a five-membered platinacycle with an “*exo* C_{aryl}–C_{aryl}” bond (**5a**). To analyze the factors governing the selective formation of either five or seven-membered platinacycles from the corresponding cyclometallated platinum(IV) compounds, a kinetic-mechanistic study of these processes was carried out [63]. Based on these studies, the mechanism depicted in Scheme 9 is proposed. In all cases, a common reductive elimination reaction occurs to form a non-cyclometallated intermediate containing a

dangling biaryl moiety, which leads to the selective formation of five or seven-membered platinacycles through a *trans* (X, NMe₂)-*cis* (X, NMe₂) isomers equilibrium. The *trans* form leads exclusively to the five-membered compound, as observed for X = Br. A fast *trans* to *cis* isomerization process takes place for X = Cl, and in the obtained *cis* isomer the steric hindrance forces a *Z* conformation of the imine, for which only formation of the seven-membered platinacycle is plausible. Along this work, using the reaction conditions extracted from the kinetic studies, both *E-cis* and *E-trans* intermediates could be detected and crystallographically characterized.

The reactions of diarylplatinum(II) substrates have been also tested with imine ligands containing a single nitrogen atom. Initial work was based on the reaction of [PtPh₂(SMe₂)₂] with imine 2-BrC₆H₄CH=NCH₂C₆H₅ [64,65] and further work was carried out using *cis*-[Pt(4-MeC₆H₄)₂(μ-SiEt₂)₂] and imines 2-BrC₆H₄CH=NCH₂(4-ClC₆H₄) and 2,6-Cl₂C₆H₃CH=NCH₂(4-ClC₆H₄) [62]. In these reactions, both intramolecular activation of C–Br or C–Cl bonds lead eventually to formation of seven-membered platinacycles.

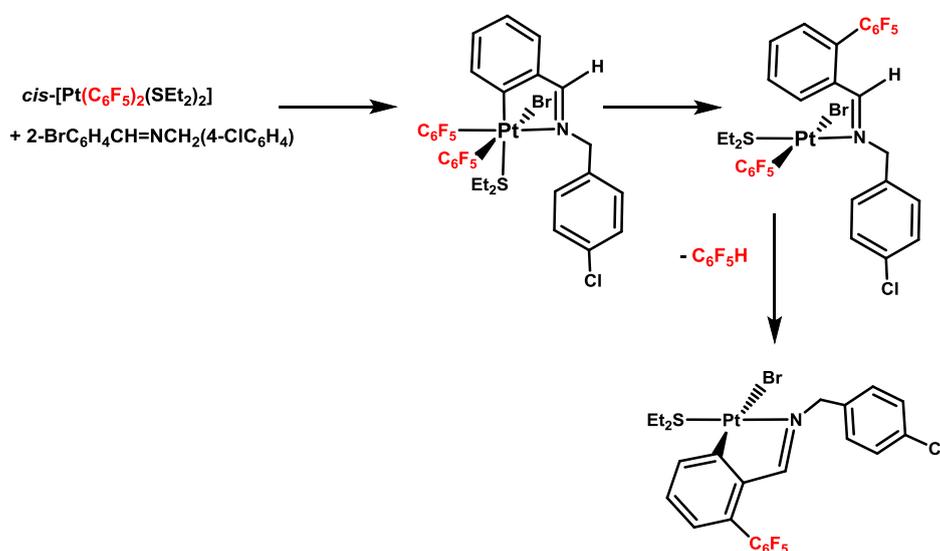
Scheme 9. Proposed mechanism for the formation of five and seven-membered platinacycles [63].



Although for these reactions the corresponding non-cyclometallated intermediates containing a dangling biaryl moiety were not detected, an analogous mechanism to that proposed for ligands containing two nitrogen donor atoms should operate. Accordingly, the cyclometallated platinum(IV) compound initially formed undergoes a process involving reductive elimination to form a biaryl that remains coordinated through the nitrogen atom to platinum(II), and this step is followed by C_{aryl}–H bond activation and reductive elimination of arene (benzene or toluene) to yield a seven-membered platinum(II) metallacycle. Taking into account the results described above for ligands containing two nitrogen atoms, isomerization to the adequate isomer should be more facile for ligands containing one single nitrogen, thus allowing formation of seven-membered platinacycles even for the less prone bromo derivatives.

On the other hand, although intramolecular C–F bond activation has been achieved upon reaction of $[\text{Pt}_2\text{Me}_4(\mu\text{-SMe}_2)_2]$ with ligand $\text{C}_6\text{F}_5\text{CH}=\text{NCH}_2\text{CH}_2\text{NMe}_2$ [41–43] such process has not been observed for precursors $\text{cis-}[\text{PtPh}_2(\text{SMe}_2)_2]$ or $\text{cis-}[\text{Pt}(4\text{-MeC}_6\text{H}_4)_2(\mu\text{-SEt}_2)]_2$. This result can be related with the strength of the C–F bond and the lower reactivity of the later substrates toward intramolecular activation of σ bonds. In order to achieve $\text{C}_{\text{aryl}}\text{-C}_{\text{aryl}}$ coupling leading to a fluorinated biphenyl moiety, a new preparative strategy based on the reaction of $\text{cis-}[\text{Pt}(\text{C}_6\text{F}_5)_2(\text{SEt}_2)_2]$ with imine $2\text{-BrC}_6\text{H}_4\text{CH}=\text{NCH}_2(4\text{-ClC}_6\text{H}_4)$ was tested. In this process, a five-membered metallacycle, in which the formed $\text{C}_{\text{aryl}}\text{-C}_{\text{aryl}}$ is not included, was obtained. In this case, formation of a seven-membered platinacycle, which requires C–F bond activation, is not favored and indeed is not observed. The kinetic-mechanistic studies carried out for this system [66] indicate initial formation of platinum(IV) compound arising from the activation of the C–Br bond of the imine. This process is followed by a $\text{C}_{\text{aryl}}\text{-C}_{\text{aryl}}$ reductive elimination and a final $\text{C}_{\text{aryl}}\text{-H}$ bond activation leading to a five-membered cyclometallated platinum(II) compound with elimination of pentafluorobenzene as shown in Scheme 10. In this case, ^{19}F NMR monitoring of the process allows the detection of all proposed intermediates.

Scheme 10. An example of $\text{C}_{\text{aryl}}\text{-C}_{\text{aryl}}$ reductive coupling leading to a fluorinated biphenyl moiety [66].

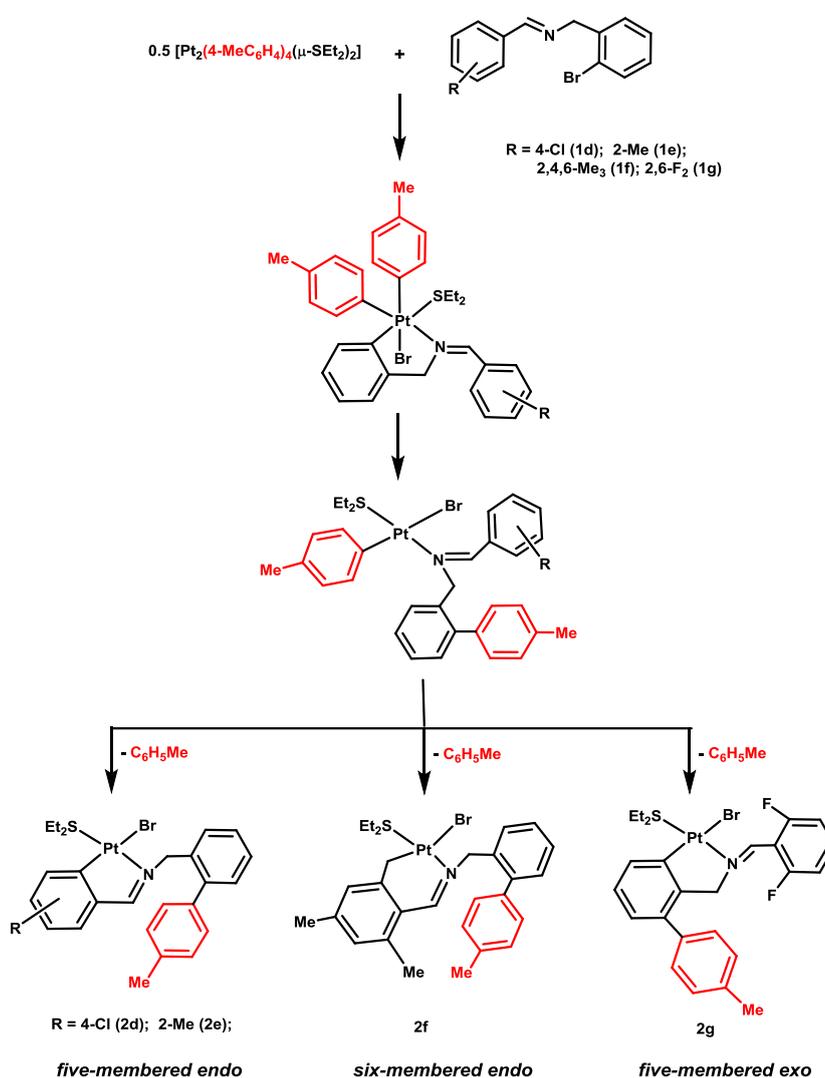


4. Six- versus Five-Membered and *endo*- versus *exo*-Platinacycles

In all cases reported above, the $\text{C}_{\text{aryl}}\text{-C}_{\text{aryl}}$ coupling processes leading to either seven- or five-membered platinacycles involve formation of stable *endo*-metallacycles. In order to analyze whether formation of a biaryl linkage is also possible for *N*-benzylidenebenzylamines for which formation of less stable *exo*-metallacycles is preferred, the reactions of $\text{cis-}[\text{Pt}(4\text{-MeC}_6\text{H}_4)_2(\mu\text{-SEt}_2)]_2$ with imines containing a C–Br bond at an *ortho* position of the more flexible benzyl ring have been studied and are summarized in Scheme 11 [67,68]. According to the obtained results, these reactions proceed through activation of the C–Br bond to produce a platinum(IV) compound with a five-membered *exo*-metallacycle, followed by $\text{C}_{\text{aryl}}\text{-C}_{\text{aryl}}$ bond formation between the benzyl group of the imine ligand and one of the *para*-tolyl ligands leading to a biaryl linkage. The subsequent $\text{C}_{\text{aryl}}\text{-H}$ bond activation does not necessarily take place at the biaryl system; instead, a $\text{C}_{\text{aryl}}\text{-H}$ bond of the benzylidene group is

activated to produce a five-membered *endo*-metallacycle with elimination of a toluene molecule (ligands **1d** and **1e**). For ligand **1f**, the mesityl group was chosen in order to block the *ortho* positions of the benzylidene group and drive the reaction towards the benzyl group of the ligand. Instead, an aliphatic C–H bond of the mesityl group is activated to produce a six-membered *endo*-metallacycle. This result, analogous to those reported for cyclopalladation reactions [69,70] can be related to the higher stability of the *endo versus exo*-metallacycles (the so-called *endo effect*), which allows to overcome the low tendency to form six-membered rings and to activate a sp^3 C–H bond [18]. For imine $2,6-F_2C_6H_3CH=NCH_2(2-BrC_6H_4)$, the fluoro substituents block cyclometallation at the benzylidene ring, and drive the reaction towards formation of a five-membered *exo*-metallacycle (**2g**). As a whole, the obtained results indicate that intramolecular C–X bond activation at the saturated arm of *N*-benzylidene-benzylamines may promote formation of a biaryl linkage between one of the tolyl ligands and the benzyl group of the imine ligand. However, the biaryl linkage is not necessarily involved in the subsequent metallation process which leads to either *endo*-five, *endo*-six or *exo*-five-membered platinacycles as shown in Scheme 11.

Scheme 11. Synthesis of cyclometallated platinum(II) compounds from *N*-benzylidenebenzylamines and $cis-[Pt_2(4-MeC_6H_4)_2(\mu-SEt_2)]_2$ [67,68].



Finally, it is interesting to point out that analogous processes from cyclometallated platinum(IV) complexes obtained from dimethylplatinum(II) precursors such as $[\text{PtMe}_2\text{X}\{\text{C}_6\text{H}_4\text{CH}=\text{NCH}_2\text{R}'\}\text{L}]$ ($\text{X} = \text{Cl}, \text{Br}$; $\text{R}' = \text{aryl}$; $\text{L} = \text{SMe}_2, \text{PPh}_3$) have been recently reported [71,72]. In this case, $\text{C}_{\text{sp}^2}\text{--}\text{C}_{\text{sp}^3}$ reductive elimination involving the metallated ring and one methyl ligand takes place and is followed by formation of five or six-membered platinacycles.

5. Conclusions

As a whole, several diarylplatinum(II) compounds displaying monomeric or dimeric structures in which the square-planar coordination of the platinum is completed with labile ligands such as dimethylsulfoxide or dialkylsulfides have been shown to be useful in the synthesis of several classes of platinacycles containing *N*-donor ligands. The observed reactions result from a series of oxidative addition/reductive elimination processes involving platinum(II)/platinum(IV) species. The initial coordination of the ligand takes place easily by substitution of the labile ligands and/or cleavage of the dinuclear structure and is followed by intramolecular C–X ($\text{X} = \text{Br}, \text{Cl}, \text{H}$) bond activation leading to cyclometallated platinum(IV) compounds. When C–H bond activation is involved, straightforward reductive elimination of a molecule of arene leads to formation of a cyclometallated platinum(II) compound. However, cyclometallated platinum(IV) compounds are formed for $\text{X} = \text{Br}$ or Cl and subsequent reductive elimination from these species leads to $\text{C}_{\text{aryl}}\text{--}\text{C}_{\text{aryl}}$ bond formation. When the formed biaryl moiety remains coordinated to the platinum through one or two nitrogen atoms, as for ligands $\text{RCH}=\text{NCH}_2\text{R}'$ or $\text{RCH}=\text{NCH}_2\text{CH}_2\text{NMe}_2$, a further step involving C–H bond activation at either the formed biaryl fragment, or at other available aromatic or aliphatic positions produces a cyclometallated platinum(II) compound with reductive elimination of one molecule of arene. In this process, in addition to the more prevalent *endo*-five-membered platinacycles, other metallacycles such as *endo*-seven, *endo*-six or *exo*-five-membered can be obtained. In summary, a careful choice of the aryl groups in both the platinum precursor and the employed ligands allows the synthesis of a great variety of cycloplatinated compounds.

Acknowledgments

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Conflicts of Interest

The authors declare no conflict of interest.

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