COMMUNICATION

Palladium-Mediated Intramolecular Dearomatization of Ligated Dialkylterphenyl Phosphines†

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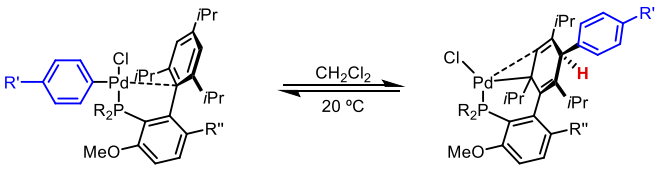
Aryl-Pd(II) chlorides stabilized by dialkylterphenyl phosphine ligands undergo a thermal isomerization process leading to the formation of allyl-Pd(II)-chloride species. The transformation involves the intramolecular functionalization of a C-H bond of the terphenyl group mediated by the Pd(II) center.

Ligand design has become instrumental for understanding chemical reactivity as well as for promoting new metal-mediated transformations.[1-2] The potential of tailor-made ligands has been nicely illustrated by palladium-catalyzed cross-coupling reactions,[3] in which both catalytic performance and applicability have been largely enhanced by judicious structural modifications of the ancillary ligands.[4-5] Currently, the stage of cross-coupling chemistry is still mostly dominated by phosphines. In recent years, efforts have been focused on the synthesis of heteroleptic phosphines[6] PR_2R', which combine two different organic substituents at the phosphorus atom.[7] The modular synthesis of heteroleptic phosphines permits to adjust their stereoelectronic properties for a particular application by varying the nature of only one of the R groups.[7a,8]

Among such designer phosphines, the large family of Buchwald's dialkylbiaryl phosphines[7b] exhibits the widest scope.[9] Besides the classical P-M coordination, the non-phosphine containing aryl ring can participate in weak M···C_{arene} interactions offering additional stabilization to unsaturated metal species.[10] However, the proximity of said arene ring to the palladium center makes it more prone toward attack by a nucleophile. Thus, palladium-mediated dearomatization of the non-phosphine containing arene in biaryl phosphine-ligated Pd(II) complexes were reported (Scheme 1).[11] Far from being a disadvantage, the *in situ* modified phosphine ligands generated an improved catalytic system for C-F bond forming reactions.[11a] Related intramolecular dearomatization of ligated phosphines induced by Ni(II) has also been reported.[12]



Scheme 1 Dearomative rearrangement of biaryldialkyl phosphines

Over the last few years, our group has been engaged in the synthesis of a family of dialkylterphenyl phosphines PR_2Ar' (Ar' = terphenyl radical). Previous to our work, only a few members of this family were known,[13] but the chemistry of this kind of ligands remained underexplored. We prepared a series of dialkylterphenyl phosphines with linear, branched and cyclic R substituents and with different substitution patterns on the terphenyl group, Ar', and analyzed their steric and electronic parameters.[14] Considering the impact of dialkylbiaryl phosphines in palladium-catalyzed cross-coupling, we have recently investigated the behavior of the analogous terphenyl phosphines in the context of palladium-catalyzed aryl amination reactions.[15] In this contribution we focus on the reactivity of Pd(II) complexes with PR_2Ar' ligands, reporting a palladium-mediated intramolecular arene C-H functionalization of the terphenyl phosphine bonded to palladium.

When evaluating the catalytic performance of Pd(II) precatalysts bearing PR_2Ar' ligands in C-N cross-coupling reactions, the best results were found with precatalysts having the bulkiest R groups (*iso*-propyl and cyclopentyl) at the P atom, i.e. $PiPr_2Ar^{Xyl2}$ (**L1**) and $P(Cyp)_2Ar^{Xyl2}$ (**L2**). In order to isolate possible intermediate species, we decided to examine in more detail the different steps involved in the mechanism proposed

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† Dedicated to Professor Robin N. Perutz on the occasion of his 70th birthday.

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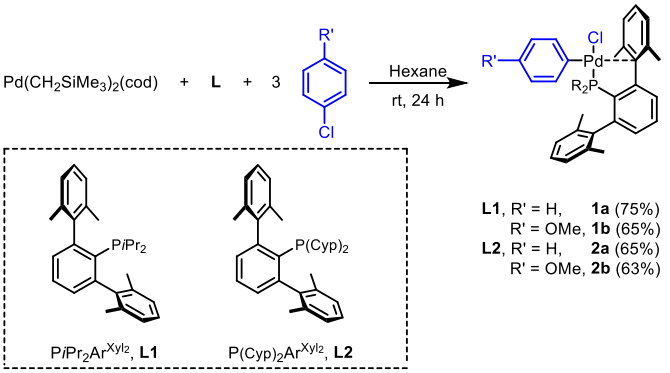
for aryl amination reactions.[16] We focused on the oxidative addition step and prepared the complexes Pd(Ar)Cl(PR_2Ar^{Xyl2}), in an independent manner,[17] by the reaction of ArCl with $Pd(CH_2SiMe_3)_2$(COD) (cod = 1,5-cyclooctadiene), a precursor for Pd(0) species, in the presence of one equivalent of the terphenyl phosphine ligand at room temperature (Scheme 2).



Scheme 2 Synthesis of Pd(Ar)Cl(PR_2Ar^{Xyl2}) complexes **1**-**2**.

Compounds **1** and **2** were isolated in good yields as air-stable brown or pale yellow solids. They were fully characterized by microanalysis and NMR spectroscopy. The room temperature $^{31}P\{^1H\}$ NMR spectra for **1** and **2** consisted of single resonances around 55 ppm for the P*i*Pr_2Ar^{Xyl2} derivatives, **1a**-**1b**, and *ca*. 46 ppm for those bearing $P(Cyp)_2Ar^{Xyl2}$, **2a**-**2b**, indicating the presence of only one isomer in solution. Their ^1H NMR spectra at 25 °C were consistent with the rotation, in a swift manner, of the phosphine ligands around the P-C_{ipso} bond at this temperature. Taking as an example complex **1b**, the four methyl substituents of the xylyl rings originated a broad singlet centered at 2.2 ppm together with unresolved resonances due to protons in the aromatic region. Upon cooling to -20 °C, the interconversion of the flanking rings was hindered, emerging two singlets at 2.28 and 2.06 ppm (6H, 6H) for the Me groups and well-defined signals for the aromatic xylyl protons (see ESI, Fig. S1).

To unambiguously establish the molecular structures of **1** and **2,** X-ray diffraction studies were carried out with complex **2b**. As illustrated in Fig. 1, the Pd^{II} center lies in a distorted square-planar environment (τ_4 value of 0.18)[18] formed by the chloride ion, the aryl group and the phosphorous atom, the fourth coordination site being occupied by the *ipso*-carbon atom of the closer xylyl ring of the terphenyl moiety. The groups with the stronger *trans* influence, the phosphine and the aryl ring, are in a mutually *cis* disposition. The Pd···C_{ipso} bond length of 2.426(2) Å fits within the range 2.22-2.45 Å found for the η^1-coordinate arene to a d^8-ML_3 fragment,[19] and is comparable with those reported for analogous biaryl phosphines derivatives.[17] The C_{ipso}-Pd-Ar and P-Pd-Cl angles are deviated about 18 and 8 °, respectively, from linearity, the size of these deviations being similar to that already described.[11b]

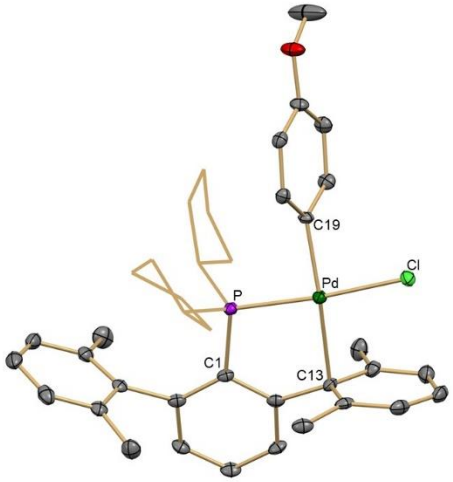
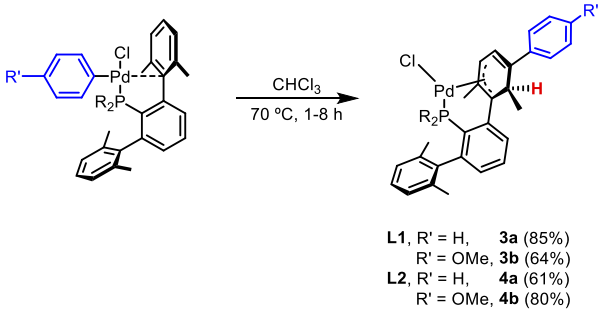


Fig. 1 Molecular structure of **2b**. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are shown at 50% probability. Selected bond lengths [Å] and angles [°]: Pd-P 2.2575 (7), Pd-Cl 2.3518(7), Pd-C13 2.426(2), Pd-C19 2.002(2); Cl-Pd-C19 84.57(8), P-Pd-C13 83.50(7), P-Pd-Cl 172.02(2), C13-Pd-C19 162.01(9).

When CD_2Cl_2 samples of **1b** and **2b** were left in solution, at room temperature, for several days new species were generated with well differentiated ^{31}P NMR signals at 79.9 and 64.9 ppm, respectively, regarding the parent compounds. Since the rate of appearance of such species at room temperature was very slow, complexes **1b** and **2b** were heated in chloroform at 70 °C. Conversion of **1b** into the new complex **3b** was accomplished in only one hour, whereas **2b** required two hours to form **4b** (Scheme 2). Complexes **1a** and **2a** bearing the parent phenyl ring also achieved the said transformations but in longer reaction times (5h and 8h, respectively). In all cases, the reaction is accompanied by a change in the color of solutions from light brown to bright yellow.



Scheme 3 Thermal rearrangements of complexes **1**-**2**.

New complexes **3** and **4** were obtained as yellow crystalline materials by slow diffusion crystallization techniques. They were very stable to air, even in solution. As noted above, their $^{31}P\{^1H\}$ NMR spectra were characterized by the presence of a unique resonance shifted between 20-25 ppm to higher frequency relative to the parent compounds. ^1H and $^{13}C\{^1H\}$ NMR spectra of these derivatives attested for the lack of symmetry exhibited by these molecules. Differentiated pattern of resonances were observed for each of the substituents on

the terphenyl fragment and at phosphorous. Most significant, however, is the presence of certain characteristic resonances common to all these compounds. Thus, for example, one of the methyl substituent on the xylyl rings gives rise to a doublet around 1 ppm with a coupling constant of *ca*. 7 Hz. This methyl group is coupled with a C-H proton that originates a broad doublet of quartets at *ca*. 2.5 ppm also due to the coupling with the P atom (J_{HP} = 25 Hz). The ^{13}C signal of said methine group is observed at *ca*. 44 ppm (J_{CP} = 4 Hz). Finally, two aromatic CH protons of the terphenyl ring resonate at lower frequency (between 5.5-6-0 ppm) than expected. Elemental analyses confirmed that complexes **3** and **4** were isomers of the parent complexes **1** and **2**, respectively.

The molecular structures of **3** and **4** were elucidated by X-ray diffraction studies undertaken with complexes **3a** and **4b** (Fig. 2). In both species the metal center is ligated by the P and Cl atoms and displays short contacts (mean value ca. 2.084-2.275 Å) with three carbons of the nearest flanking ring of the terphenyl fragment, consistent with η^3-allyl bonding.[11a,20] The σ-aryl group is now located at the 3-position of the xylyl ring bonded to palladium. The formation of this new C-C bond produces dearomatization of the said ring, as reflected by the elongation of C17-C18 (mean value ca. 1.515 Å) and C13-C18 (mean value ca. 1.540) bond distances and the shortening of C16-C17 bond length (mean value 1.348 Å). Interestingly, in the dearomatized ring the hydrogen atom formerly bonded to carbon at the 3-position (C17 in Fig. 2) is now attached to the 2-position (C18 in Fig. 2), which accounts for the splitting of resonance due to the CH_3 group located at the same carbon atom in ^1H NMR spectra of these species. Both, the hydrogen atom and the Pd center are in anti face.

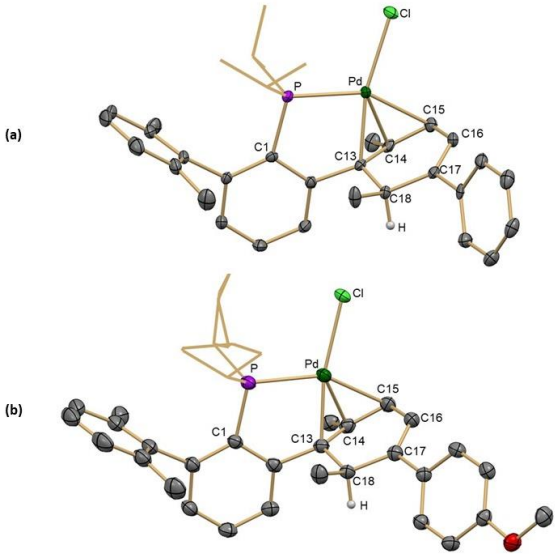


Fig. 2 Molecular structure of complexes **3a** (a) and **4b** (b). Hydrogen atoms are omitted for clarity. Thermal ellipsoids are shown at 50% probability. Selected bond lengths [Å] and angles [°] of **3a**: Pd-P 2.2673(6), Pd-Cl 2.3915(7), Pd-C13 2.084(2), Pd-C14 2.154(2), Pd-C15 2.270(2); P-Pd-C13 84.99(6), P-Pd-Cl 107.76(2), Cl-Pd-C13 166.75(6). Selected bond lengths [Å] and angles [°] of **4b**: Pd-P 2.2688(7), Pd-Cl 2.4121(6), Pd-C13 2.085(2), Pd-C14 2.156(2), Pd-C15 2.279(3); P-Pd-C13 84.84(7), P-Pd-Cl 105.95(2), Cl-Pd-C13 168.84(7).

The thermal rearrangement leading to complexes **3** and **4** involves the intramolecular functionalization of an aromatic C-H bond, which is converted into a C-C bond in the final products. This transformation is probably facilitated by the palladium-arene interaction that exists in precursors **1** and **2**, which activates the nearest flanking ring of the terphenyl phosphine towards the nucleophilic attack of the σ-aryl ligand.[12b] Buchwald and co-workers have examined in detail the mechanism of the reversible dearomative rearrangement found for biaryl phosphines-Pd(II) complexes.[11b] The observed 1,4-addition of Pd-aryl bond components to the coordinated lower ring of the biaryl moiety is proposed to occur through a concerted 1,2-insertion[21] followed by a 1,3-allylic shift.

Presumably, the dearomative rearrangement of terphenyl phosphines in complexes **3** and **4** could also proceed via the insertion of the metal olefin moiety into the Pd-aryl bond. But, there are some important differences that deserve to be commented. The most striking feature concerns with the stereochemistry of the rearranged products **3** and **4** with respect to the biaryl analogues (Fig.3). Although in both systems the σ-aryl group is added to the carbon at the 3-position of the closer arene ring to the Pd center, in the case of therphenyl phosphines complexes the sp^3-hybridized carbon atom is not located at this particular position, but rather at the 2-position of the ring due to concomitant migration of the hydrogen atom from C-3 to C-2. No such a hydrogen shift has been reported for the biaryl phophines analogues.[22] It should also be noted that while dearomatization with the Pd(II)-coordinated biaryl phosphines appears to be a reversible process at room temperature, the transformations involving the terphenyl phosphine complexes are irreversible. Experimental and computational studies aiming at elucidating the mechanism of this isomerization process is currently underway in our laboratory.

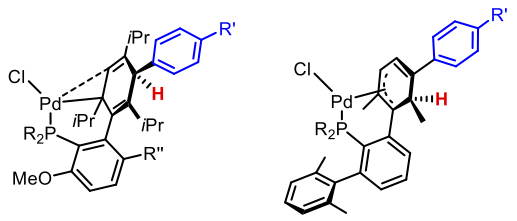


Fig. 3 Stereochemistry of products resulting from intramolecular dearomatization of biaryl phosphines (left) and terphenyl phosphines (right).

Conclusions

We have demonstrated the ability of dialkylterphenyl phosphine ligands in complexes of the type Pd(Ar)Cl(L) (L = P*i*Pr$_2$Ar^{Xyl2} and P(Cyp)$_2$Ar^{Xyl2}) to coordinate in a bidentate fashion, involving the P atom and one of the ipso carbon atoms of a flanking xylyl ring of the terphenyl group. Such a weak interaction activates the arene ring towards nucleophilic attack.

Thus, upon heating, the σ-aryl-Pd(II) complexes undergo irreversible intramolecular rearrangements to Pd(II)-allyl species, resulting from the formal insertion of a double bond of the closer xylyl into the Pd-aryl bond with concomitant dearomatization of said ring. Although this transformation shares similarities with that reported for biaryl phosphines ligands, the observed stereochemistry of the rearranged products makes the difference. Complexes **3** and **4** constitute rare examples of products of the migratory insertion of an arene into a Pd-aryl bond.[11b] Compounds of this type have been invoked as possible intermediates in Pd(II)-catalyzed C-H arylation reactions.[23]

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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The process has not been observed for dicyclohexyl based phosphines such as BrettPhos (see ref. 11b).

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