Organometallic nucleophiles and Pd: What Makes ZnMe₂ Different? Is Au like Zn?

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ABSTRACT: The cis/trans isomerization of [PdMeAr(PR₃)₂] complexes (Ar = C₆F₅, C₆F₅Cl) can take place spontaneously (via dissociation and topomerization, studied experimentally) or catalyzed by ZnMe₂. The later mechanism, studied by DFT methods, involves methyl exchange between Pd and Zn. The study of this catalyzed isomerization shows that, in contrast with the typical acidic behavior of Zn in ZnMeCl, Zn in ZnMe₂ (or, more exactly, the ZnMe bond) behaves as a strong basic center, able to attack the relatively high in energy acceptor orbital at Pd in fairly electron rich Pd complexes such as [PdArMeCL₃] or [PdMeCl₂]. This makes the two reagents very different in Negishi couplings. The catalyzed isomerization occurs via transmetalation, thus both processes are connected. A comparison of the Pd/Zn intermediates and transition states with those found previously for Pd/Au transmetalations reveals very similar structures with intermetallic distances in the order of or noticeably shorter than the sum of the vDW radii, regardless of the nature of the metal (metalophillic Au or non metallophillic Zn). These short distances are associated to the involvement of the metals in 3c2e electron deficient bonds during R group transmetalation. In this respect there is a remarkable similarity with the structurally known behavior of main-group electron-deficient compound, which supports a unified view of the transmetalation processes.

INTRODUCTION

The Negishi reaction is a powerful process for the formation of C–C bonds.⁶,¹² Although it is the reaction of choice for couplings involving sp² carbon atoms due to the high reactivity of organozinc reagents,⁴,⁶,¹⁵ mechanistic studies on Negishi coupling have focused mainly on Ar–Ar cross-coupling,³,⁶ while studies with sp² carbon centers are comparatively scarce.⁵,⁶,⁷,⁸,¹⁰ As for other palladium catalyzed couplings of organic electrophiles (R’X) and nucleophiles (MR₃),¹⁵ the reaction pursues the selective formation of R’–R”, but homocoupling byproducts, presumably formed via undesired transmetalations, frequently contaminate the reaction. For instance, formation of the so-called reduction product ArH (Ar = 2-C₆H₅CO₂Et) in the Negishi cross-coupling reaction of ArI and ZnEt₂ has been proved very recently to arise from hydrolysis of ZnArEt₂ (formed in an undesired transmetalation) and not via β-H elimination from Pd-Et.¹⁵ In this reaction, the “reduction” product Ar-H, the cross-coupling product Ar-Et, and the two homocoupling products Et-Et and Ar-Ar are observed, confirming active participation of isomerizations and undesired transmetalations.¹³ The number and percentage of undesired products was much less when ZnEtCl was used instead of ZnEt₂. In order to understand this difference we decided to closely examine the behavior of ZnMe₂, as nucleophile towards cis-[PdArMe(PR₃)] (1) (Ar = C₆Cl₅F₂ = RF (Ia); Ar = C₆F₅ = P (1b)), a Pd center with relatively low electrophilicity. This kind of complex is the one from which Ar–Me cross-coupling should occur in a synthesis.

Scheme 1. A general Pd catalyzed cross-coupling cycle highlighting the existence of isomers and the importance of isomerization equilibria.

One specific question that we wanted to answer in this study is whether ZnMe₂ would be able to catalyze isomerization reactions of [PdR’R’L₂] complexes. Isomerizations are important and can be determinant for the outcome of the reaction. This problem has been thoroughly discussed in the context of Stille reactions,¹⁵ but is also operative for other cross-coupling processes. In the case studied here this isomerization might operate on the last intermediates in the cycle, preceding reductive elimination, as show in Scheme 1 where we highlight how two isomers, cis and trans, can be produced in the oxidative addi-
tion and also in the transmetalation steps of a cycle, but only the cis isomer can give rise to the coupling product.

The results of this investigation have revealed some interesting peculiarities of ZnMe₂ (and presumably ZnEt₂ but no other ZnR₂ with bulkier R groups) that make it very different from ZnRX (X = halide). Moreover, the transmetation intermediates or reagents found in the calculations reveal that the formation of short Pd-M bonds is a feature shared by Zn and Au nucleophiles.

RESULTS

Non-catalyzed isomerization of trans- and cis-[PdArMe(PPh₃)₂] (Ar = C₆F₅, C₆Cl₃F₃). The isomeric complexes cis-[PdArMe(PPh₃)₂] (1) (Ar = Rf- C₆Cl₃F₃ (1a); Ar = C₆F₅ (1b)) and trans-[PdArMe(PPh₃)₂] (2) (Ar = C₆Cl₃F₃ = Rf (2a); Ar = Pf = C₆F₅ (2b)) can be isolated and are sufficiently slow towards coupling to allow for monitoring of the exchange processes they undergo (Figure 1). A

Starting with the cis isomer (1a), the spectrum shows that formation of the coupling product Rf-Me is slower than isomerization, but fast enough to have to consider it in the kinetic equations of isomerization. The kinetic fitting details are given as supplementary information (SI). The two complexes isomerize in THF solution at room temperature to an equilibrium with Kₑq = 1.9 (Scheme 2). This value corresponds to an energy difference of about 0.38 kcal/mol in favor of the more stable trans isomer. The observed rate constant of this equilibration, kₑq, has an inverse linear dependence on the concentration of added phosphine in the medium, indicating a two-step dissociative process, shown highlighted in blue in Scheme 2, which is similar to that previously proposed for diaryl-palladium complexes.

A rate value ΔG°top = 27.7 kcal/mol was found for the spontaneous isomerization, corresponding to the topomerization step in a three-coordinated intermediate. The behavior of 1b is similar and the experimental data are almost identical (see SI).

Scheme 2. Isomerization equilibrium (black) and mechanism (blue) of cis-[PdArMe(PPh₃)₂] (1) to trans-[PdArMe(PPh₃)₂] (2) isomerization.

ZnMe₂ catalyzed isomerization of trans- and cis-[PdArMe(PPh₃)₂]. The catalyzed isomerization reaction ZnMe₂ + 1 = ZnMe₂ + 2 cannot be experimentally measured separately from the competing non-catalyzed one because, as discussed below, ZnMe₂ is a strong methylating reagent and its role as catalyst (in which it is not consumed) will be competing with its activity as reagent (in which it is consumed producing changes in concentration). This problem prevents to establish the reaction conditions required for experimental kinetic studies. Thus, data for the ZnMe₂ catalyzed isomerization pathway had to be obtained by DFT methods (wB97XD-PCM-THF/SDD-6-31G*/B3LYP/SDD-6-31G*), which afforded the interesting profile shown in Figure 2 for Ar = C₆F₅.

Figure 1. ¹⁹F NMR spectrum (at 470.48 MHz, in THF, 25 °C; ref. CFCl₃) of coupling vs. isomerization competence of cis-[PdRMe(PPh₃)₂] (1a).

Figure 2. DFT profile of the ZnMe₂ catalyzed 1b/2b isomerization. Gibbs energies are shown in kcal/mol (L = PMe₃, black lines; PPh₃, blue lines). NOTE: The experimental value of the equilibrium fixes the energy of 2b in THF solution in -0.4, relative to zero for 1b.

An examination of the profile shows that, in the catalyzed pathway, isomerization and transmetalation are directly connected (see below), as the ZnMe₂ catalyzed isomerization of [PdArMe(PPh₃)₂] occurs via Me/Me transmetalation. Thus this computational study of isomerization provides as well details...
on the main features of a transmetalation in a system lacking typical bridging groups such as halides. The highest catalyzed isomerization barrier corresponds to the transmetalation on the cis complex (1b) and is in the order of energy (26.3 kcal/mol; note that calculations for these systems have easily 1-3 kcal/mol errors) of the experimental value for the non-catalyzed isomerization (27.7 kcal/mol), but still clearly higher than for transmetalations involving halides.\textsuperscript{9,10} It is interesting to keep in mind that the ZnMe\textsubscript{2} catalyzed isomerization will follow a law rate\textsubscript{cat} = k\textsubscript{cat}[ZnMe\textsubscript{2}][Pd], while the uncatalyzed isomerization will follow the law rate\textsubscript{uncat} = k\textsubscript{uncat}[Pd]. The total rate will be rate\textsubscript{total} = (k\textsubscript{cat} + k\textsubscript{uncat}[ZnMe\textsubscript{2}])[Pd]. For not very different isomerization barriers (k\textsubscript{cat} and k\textsubscript{uncat}, of similar magnitude, as it is the case) the contribution of the two pathways will dramatically change depending of Pd concentration and obviously the contribution of the catalytic pathway will increase in conditions of high ZnMe\textsubscript{2} concentration ([ZnMe\textsubscript{2}]>>[Pd]). This is the case of synthetic Pd catalyzed processes, where ZnMe\textsubscript{2} is used as reagent and the initial ZnMe\textsubscript{2}/Pd ratio can be easily 10\textsuperscript{-1}. On the contrary, for small concentrations of ZnMe\textsubscript{2} ([ZnMe\textsubscript{2}]<<[Pd]), the catalyzed isomerization pathway can be slower than the uncatalyzed one.

The catalyzed isomerization process in Figure 2, from cis (1b) to trans (2b), is beautifully illustrated by sequence of structures shown in Figure 3.\textsuperscript{19} Since the two profiles are almost symmetrical around the central intermediates I\textsubscript{1}, except for the change of isomer, we comment these details only for the left half of the profile.

Figure 3. Snapshots of the computed ZnMe\textsubscript{2} catalyzed isomerization reaction. The structures are represented in capped stick mode using the Mercury software.\textsuperscript{20} Color code: reddish Pd, light blue Zn, yellow-orange P, deep blue F, grey C and white H.

At the beginning of this pathway, an almost barrierless intermediate structure is observed (cis\textsubscript{1}) suggesting some kind of attractive interaction in the order of 3.7 kcal/mol between the two reacting molecules.\textsuperscript{21} Particularly interesting, the transition state TS\textsubscript{1}, through which a phosphine substitution by one entering Me–Zn bond is taking place, shows a bipyramidal trigonal coordination for Pd, with the two apical sites occupied by one Me and one PMe\textsubscript{2} ligand; two of the three sites of the equatorial plane are occupied by the C\textsubscript{F\textsubscript{3}} group and the Zn atom of ZnMe\textsubscript{2}; finally, the third position is in dispute between the leaving PMe\textsubscript{2} already at a long Pd–P distance, and one Pd–Me bond that, by this time, is already oriented towards that position (this ligand substitution is indicated by two pink dashed lines connecting the exchanging ligands to the Pd center). Increasing involvement of the Me group on Pd and eventual PMe\textsubscript{2} dissociation affords intermediate I\textsubscript{2} where the two metals are connected by two Me bridges and a Pd–Zn bond. From that point, recoordination of the phosphine in the appropriate coordination position produces the trans isomer found in the calculations, cis\textsubscript{1}–PMe\textsubscript{2}. The Pd–Zn distance in cis\textsubscript{1} is almost identical (2.93 Å, Table 1) to the sum of the van der Waals radii (3.02 Å), which indicates a very minor interaction, perhaps still highly electrostatic in nature and associated to polarization of the electronic clouds of the metals and their ligands. This seems to be supported by the fact that this interaction does not stand changes in Pd coordination: the putative cis\textsubscript{1}–PPh\textsubscript{3} and trans\textsubscript{1}–PPh\textsubscript{3}, bearing a more voluminous phosphine ligand, could not be computationally characterized.

Table 1. Selected geometrical parameters of the computed structures reflecting the changes in bond distances and angles along the isomerization via transmetalation. Molecule labels are as in Figure 2. Me\textsuperscript{0} is the Me group initially on Pd. Me\textsuperscript{1} and Me\textsuperscript{2} are the two Me groups originally on Zn. Me–Pd and Me–Zn stand for the corresponding Csp\textsuperscript{3}–Pd or Csp\textsuperscript{3}–Zn distances.

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<th>Molecule–L</th>
<th>Distance (Å)\textsuperscript{*}</th>
<th>Distance (Å)\textsuperscript{*}</th>
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<td>[3.08/1.96]</td>
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\textsuperscript{*}For comparison Sr\textsubscript{vdW}(Pd+Zn) = 2.62 Å; Sr\textsubscript{vdW}(Pd+Zn) = 3.02 Å; Sr\textsubscript{vdW}(Pd+Csp\textsubscript{3}) = 2.08 Å; Sr\textsubscript{vdW}(Pd+Csp\textsubscript{3}) = 3.33 Å; Sr\textsubscript{vdW}(Zn+Csp\textsubscript{3}) = 2.08 Å; Sr\textsubscript{vdW}(Zn+Csp\textsubscript{3}) = 3.09 Å.

A clear bonding interaction between the two metal fragments is found in the transition state TS\textsubscript{1}, where the Pd–Zn bond distances (2.56 Å for PMe\textsubscript{2} and 2.79 Å for PPh\textsubscript{3}) are close to or shorter than the sum of covalent radii (2.62 Å).\textsuperscript{22} Furthermore, one of the Pd–Me distances to the Me groups on Zn is much shorter (2.68 Å for PMe\textsubscript{1} and 3.08 Å for PPh\textsubscript{1}) than the other (4.14 Å for PMe\textsubscript{1} and 4.21 Å for PPh\textsubscript{1}), supporting engagement
in coordination to Pd of one Zn–C bond, rather than involvement of the Zn atom alone. The other Zn–Me bond of ZnMe₂ is an almost inactive spectator, as supported by the variation of the Zn–Me distances along the way to I₄, one of them (Zn–Me¹ in Table 1) remains essentially unchanged along the process (1.94–1.96 Å), while the other (Zn–Me² in Table 1) elongates along the process of formation of the Me-bridging system (1.96–2.54 Å). In other words, what we are seeing in TS₁ is the formation of a bridging Me group involved in a 3-center 2-electron (3c2e) bonding system, at the expense of a Zn–Me bond.

In the next step of the evolution shown in Figure 3, intermediates I₃ show the shortest Pd–Zn bonds of each series (2.40Å for PMe₂ and 2.42 Å for PPh₃), supported by two bridging Me groups. It can also be noted that the Pd–Me distances are shorter (2.16 and 2.21 Å for PMe₂, 2.12 and 2.28 Å for PPh₃) and the Zn–Me distances are longer (2.17 and 2.54 Å for PMe₂; 2.14 and 2.52 Å for PPh₃) than before or after this point in the profile;²¹ furthermore, the longer Pd–Me distances are associated to the shorter Zn–Me distances in the same bridge. The largest Pd–Me distance is observed trans to the PPh₃ group in I₂(PPh₃), but trans to the PMe₂ ligand in I₃(PMé₃), suggesting a sequence of trans influence PMe₂ > PF > PPh₃.

A final noticeable structural change is found in the Me–Zn–Me angle, closing progressively from the initial linearity in free ZnMe₂, as this fragment progresses towards formation of intermediate I₄. This reflects, in simple terms, the increasing involvement in bonding of a second p orbital of Zn (from sp towards sp² hybridization) as the Zn atom gets involved in more bonds. Yet, the Zn–Me distance for the terminal Me group, not involved in bridges, remains unaltered from its value in free ZnMe₂.

**DISCUSSION**

**What is special in ZnMe₂ (or ZnEt₂) compared to other Zn organometallics?** ZnMe₂ is a perfectly symmetric linear molecule (sp hybridization for Zn) in the solid state (d₁₋₂₉ = 1.927(6) Å) and in the gas phase.²² It is reluctant to coordinate OEt₂ or THF in solution, which suggests that the two strongly electron donating Me groups make, altogether, a Zn center unusually electron rich; the other potentially acceptor p orbitals of Zn, well shielded by this electron density, are high in energy and not very prone to participate in bonding, keeping the compound strictly linear coordinated except in the presence of really strong ligands.²⁵ For this reason the Zn center in ZnMe₂ does not show the acidic character found for other Zn compounds (ZnCl₂, ZnMeCl). Rather on the contrary, Zn in ZnMe₂ seems to act as a Lewis base towards the square-planar Pd acidic center. This electronic richness of the Zn center is not in contradiction with the fact that quantum mechanical calculations in the literature still support polarization of the two identical Zn–Me bonds towards their carbon ends, which develop a considerable negative atomic charge (-1.33).²⁶

The Kohn-Sham orbitals shown in Figures 4 and 5 nicely support these views,²⁷ but also lead us to get a more accurate understanding of the initial structural considerations based only on bond distances. The HOMO1 and HOMO2 orbitals (A) host the four bonding electrons of ZnMe₂ (Figure 4) and altogether produce a high electron density in the vicinity of the Zn center. Alternatively, the equivalent orbital combinations B (HOMO1+HOMO 2, and HOMO2–HOMO1) allow for an easier identification of the electron density associated to the Zn–Me bond concept, and offer a more visual starting point to understand the orbital and electron density rearrangement during the evolution from cisI₁ to PdMe₃ ligand displacement by a Zn–M bond as entering ligand.

**Figure 4.** Selected Kohn-Sham orbitals: A: Molecular orbitals HOMO1 and HOMO2 for ZnMe₂. B: Alternative (HOMO2 + HOMO1) and (HOMO2 – HOMO1) combinations for ZnMe₂.

This evolution occurs via side-on coordination of one of the two Zn–Me bonds,²⁸ which eventually gets polarized towards a 3c-2e Zn- Me-Pd bond, while the other electron pair evolves to be the σ(Zn–Me) bond not involved in interaction with Pd. At the early stages of this interaction (cisI₁) the Pd–Zn distance is still a non-bonding distance (2.95 Å, almost identical to the sum of vdW radii (3.05 Å)) but the polarization of the electron clouds of the Pd and Zn orbitals giving rise to HOMO2/Pd (Figure 5) already show that the initial contact between ZnMe₂ and the Pd center is beginning to create a 3c2e Pd/Zn/Me interaction. In other words, the ligand substitution induced by ZnMe₂ occurs by nucleophilic attack of one of the two σ(Zn–Me) bonding electron pairs, fairly high in energy relative to the Pd acceptor orbital, which behaves as entering ligand towards an acceptor MO of the Pd complex. This empty Pd orbital is the same that receives the entering ligand in typical associative ligand substitution reactions on Pd. Meanwhile the HOMO1/Pd combination should begin to polarize slightly towards a Pd–Me¹ bonding orbital, although at this stage this can hardly be appreciated in Figure 5.²⁹

**Figure 5.** Selected Kohn-Sham orbitals: Incipient interactions in cisI₁, where the molecular orbitals of the Pd/Zn adduct still let to recognize those of their ZnMe₂ and Pd parents.
Whereas in the conventional structural representation of Figure 3 it seems that it is the Zn center that coordinates to the Pd center, this is a naif and misleading image as it is not the carbon or the Zn centers which are acting as the entering nucleophile, but the electron density of the bond. Figure 5 shows clearly that, from the very beginning, the interaction is defining involvement of one bond versus the other. In fact, the Pd–Me\(^2\) is shorter than Pd–Me\(^1\) in cisL\(_1\), and Me\(^1\) is already closer to the PR\(_1\) ligand that will be eventually displaced via the pentacoordinated TS\(_1\). From that point, the implication of the two electrons of the \(\sigma\)(Zn–Me) bond, now fully depending on two metal centers, Zn and Pd, produces a decrease of the electron density on Zn. This stabilizes and makes more acidic the empty p orbitals on Zn, which become acceptor of electron density from the terminal Pd–Me bond, producing the second Me bridge. With these synergistic interactions, the bimetallic Pd(µ-Me)\(_2\)Zn molecular structure is formed.

The electron density is, as discussed, the true responsible for bond formation. This multcenter interaction is difficult to depict but, assuming the typical pictorial representation of molecular structures (based in drawing bonds as bars connecting atomic centers that share bonding electron density), we could say that the Pd coordination in I\(_1\) remains essentially square planar, with the two Me groups in the coordination plane and very small deviations from an ideal square plane (all angles are 90±5º), in spite of the additional Pd–Zn bond that protrudes below that plane (Figure 3). In this view the isomerization process is pivoting around the Pd–Zn bond: when the reentering PR\(_1\), splits the Pd–Me bond trans to Rf, the cis isomer 1b will be generated; if it splits the Pd–Me bond trans to the coordinated phosphine, the trans isomer 2b will be formed.

For similar circumstances of other factors,\(^{11}\) nucleophilic attacks occur more easily for nucleophiles with high energy HOMOs and for electrophiles with low energy LUMOs.\(^{20}\) The formation of intermediate I\(_2\) by the mechanism discussed above is remarkable in that it occurs by nucleophilic attack to a LUMO in Pd that is not very low in energy, particularly in cases where the existence of two carbon ligands (Me and CF\(_3\) in this case) makes the Pd center fairly electron rich and rises the energy of its LUMO and other orbitals. It is only the high basicity of the Zn–Me bonds in ZnMe\(_2\) that makes this reaction feasible,\(^{21}\) a behavior that should be less likely with ZnMeCl.

In our recent study of the Negishi cross-coupling reaction of RfI and ZnEt\(_2\) to give Rf–Et,\(^{12}\) already commented in the introduction, we observed that important amounts of undesired Et–Et,\(^{12}\) already commented in the introduction, we observed that important amounts of undesired Et–Et and Rf–Et were formed at early stages of the reaction. This problem was much less visible when the reaction was carried out with ZnEtCl, and also diminished at later stages of the reaction with ZnEt\(_2\) when much of the initial ZnEt\(_2\) had been consumed or transformed in ZnEtCl, drastically diminishing the concentration of ZnMe\(_2\) in solution. The undesired formation of Et–Et and ZnRfEt can be understood from the undesired transmetalation in equation 1, forming [PdEt\(_2\)L\(_2\)].\(^{12}\) The stronger nucleophile ZnEt\(_2\) should be much more effective for this attack to Pd than ZnEtCl, and the more electron-rich [PdEt\(_2\)L\(_2\)] should be the least prone to undergo any electrophilic attack by, for instance, the byproduct ZnRfEt. Consequently, significant contribution of the exchange mechanism calculated and discussed here is expected to contribute very significantly to the undesired conversion of [PdRfEtL\(_2\)] to [PdEt\(_2\)L\(_2\)], producing undesired Et–Et homocoupling instead of Rf–Et cross-coupling.

\[
PdRfEtL\(_2\) + ZnEt\(_2\) \longrightarrow PdEt\(_2\)L\(_2\) + ZnRfEt
\]

For comparison we can consider transmetalations involving Pd complexes and ZnCl\(_2\) or ZnRCl and see how they behave different from those with ZnMe\(_2\) (Figure 6).\(^{30}\) The electrophilicity of the LUMO of the relatively electron rich Pd center in [PdMe\(_2\)L\(_2\)] is relatively poor (two Me groups make the Pd center electron rich, as discussed before for ZnMe\(_2\)). On the other hand, the presence of electronenagative Cl substituents that withdraw electron density from Zn stabilizes the p orbitals of Zn (as shown by the fact that complexes with THF ligands are formed). Thus the game changes: upon easy equilibrium dissociation of THF, the Zn center becomes the Lewis acid that one usually expects and, at the right of Figure 6, it is the Pd–Me bond in trans-[PdMe\(_2\)L\(_2\)] that attacks the electron poor Zn center in ZnCl\(_2\). In other words, the Pd complex is now the nucleophile (through its Pd–Me bonds) and the Zn center is the electrophile. At the left of Figure 6, the reaction courses via THF displacement by a Cl ligand to make initially a Pd–Cl–Zn bridge. This makes sense because in trans-[PdMeClL\(_2\)] the electronegative Cl substituent has reduced the electron density on Pd, and the lone pairs in Cl are more nucleophilic than the Pd–Me bond with reduced nucleophilicity. In addition, a more stable non-deficient single bridged intermediate is formed.

**Figure 6.** Transmetalation sequence calculated for the interconversion of trans-[PdMeClL\(_2\)] + ZnMeCl in trans-[PdMe\(_2\)L\(_2\)] + ZnCl\(_2\). Gibbs energies in kcal/mol. See reference 10.

**Is intermediate I\(_2\) very unusual?** It is only recently, on occasion of DFT mechanistic studies on transmetalations, that the surprising participation of transition-to-main group metal-metal interactions in these exchanges is being discovered. At first glance it is somewhat confusing how one should analyze the metal-metal interaction, as we are trained to consider metals as acidic centers, hence electrophilic centers. This study helps to better understand the bimetallic systems formed in transmetalations. In fact, the Me bridging interaction observed here is not as unusual as one might think at first glance: it is closely similar to the much more familiar chemical systems so often formed in the organometallic compounds of the main group metals, for instance in [AlMe\(_4\)], where the two 3c2e
electron deficient bridges produce Me–Al and Al–Al bonding. The R exchanges operating in the typical and classic Schlenk-type equilibria for main-group elements and the transmetalations operating on transition metals have much in common. Figure 7 highlights this similarity.

Figure 7. A comparison of the Me-bridged 3c2e bonds in Pd/ZnMe₂ transmetalation species and in Al₂Me₆.

Very interestingly, the isomerization mechanism observed in this paper shows also much similarity with the RF transmetalation from cis-[PdRF₆(AsPh₃)] to [AuCl(AsPh₃)], where the Au–Cl bond displaces a ligand from Pd and the intermediates and transition states show a strong Pd–Au bond interaction (Figure 8, from right to left).

Figure 8. Calculated transmetalation sequence interconverting the systems trans-[PdPhClL₂] + AuPhL and cis-[PdPh₂L₂] + AuClL (Gibbs energies in kcal/mol). For details see ref. 34.

Finally, in contrast with the similar stepwise pathways for the isomerization and exchange reactions of [PdR₂L₃] with ZnR₂ or with AuRL (Figure 2 and Scheme 3, respectively), it is worth highlighting the differences when halides are involved, as in Figure 6 vs. Figure 8. Thus, at the left side of Figure 8, a moderately nucleophilic Au–Ph bond (compared to Zn–Me) is able to attack the LUMO of Pd, but in this case the Pd center bears an electronegative Cl ligand that pulls out electron density from Pd, lowers the energy of the acceptor MO, and makes Pd a stronger electrophilic center. At the right side of the transmetalation process, an Au–Cl bond leading initially to formation of a single non deficient center, at clear variance with the related reaction in Figure 6, where the nucleophile is the Pd–Me bond and the electrophile is the acidic (Cl substituted) Zn center.

Figure 9 compares the high similarity of the structure calculated here for intermediate ß₁ (with Zn) and that found for the case of Au. In both structures the Pd coordination is basically square planar and in both cases there is a Pd–M (M = Zn, Au) covalent bond. Some differences (angle distortion and longer Pd–M distance relative to the sum of vdW radii found in the gold system) are expected from the fact that the Au–Cl and Zn–CH₃ moieties differ in that Cl is larger than C and also, since Cl has electron lone pairs, the Pd–Cl–Au bridge is not electron deficient. Although ZnR₂ and AuRL compounds are isoelectronic, the extraordinary similarity observed is remarkable. For the gold system we first suggested the probable participation of metallophilic interactions. This kind of interaction cannot be expected for light elements not submitted to relativistic effects, such as Zn and yet we find in this work that the interaction Pd–Zn is very strong. Hence our initial suggestion on the importance of metallophilic interactions in the Au/Pd system should perhaps be taken with caution, although metallophilic interactions can still be important in facilitating the initial approximation of the two metal centers. But the strong Pd–M interactions is definitely associated to the formation of 3c₂e bonds.

Figure 9. Structural similarity of ([Me₃P]Pd[μ-Me]₂ZnMe₂) and ([Me₃As]Pd[μ-P]([μ-Cl]Au(AsMe₃)) of Scheme 3, and it was proposed on the basis of kinetic data only. In view of the DFT data discussed above it is clear that C and D were correct but complex D, originally proposed as transition state, should be better considered as an intermediate totally similar to ß₁, and the two Au–Rf bonds (in pink), not depicted in the original proposal, must be added.

It is pertinent to recall here that sixteen years ago we reported an early gold catalyzed bimetallic process, the cis isomerization of [PdRF₆(tht)] (tht = tetrahydrothiophene), which takes minutes instead of hours when catalyzed by AuRF(tht). The mechanism proposed at that time was the same depicted in Scheme 3, and it was proposed on the basis of kinetic data only. In view of the DFT data discussed above it is clear that C and D were correct but complex D, originally proposed as transition state, should be better considered as an intermediate totally similar to ß₁, and the two Au–Rf bonds (in pink), not depicted in the original proposal, must be added.
All these examples illustrate the complex interplay of electronic effects in metal compounds, which are particularly intricate for transition metal complexes, and the subtle variations of the role of a metal center as a function of its substituents. Letting aside the steric effects that strongly correct the nucleophilicity and electrophilicity values in comparison to the acidity values, Zn changes from acidic center in ZnCl₂ to basic in ZnMe₂, and the acidity of square-planar Pd complexes associated to their acceptor molecular orbitals varies importantly with the nature of the ligands.

CONCLUSIONS

ZnMe₂ and ZnMeCl are very different nucleophiles for the transmetalation of Me groups to Pd, and presumably to other transition metals. In the former, the metal center behaves as a basic, highly nucleophilic center and the Me–Zn bond is able to react, even with fairly electron rich Pd complexes such as [PdR₂L₂], to produce L substitution and form [LRPd(μ-Me)(μ-R)ZnMe] intermediates from which transmetalation or isomerization can follow. In contrast, the metal center at ZnMeCl is acidic and has the tendency to react, in isomerization and transmetalation reactions, via intermediates or transition states using non deficient Pd(μ-Cl)Zn bridges.

The bridged structures with at least one electron deficient component (Me, Et bridges) formed in the Pd/Au and Pd/Zn transmetalation reactions show covalent intermetallic distances noticeably shorter than the sum of the vdW radii, regardless of the possible metallophilic nature of the metal (Au) or not (Zn), because its origin is the 3c2e nature of the deficient bond. In this respect there is remarkable similarity with the behavior of main-group electron-deficient compounds.

EXPERIMENTAL SECTION

General Methods. All reactions were carried out under N₂ or Ar in THF dried using a Solvent Purification System (SPS). NMR spectra were recorded onBruker Advance 400, Varian AV 400 or Varian AV 500 instruments equipped with variable-temperature probes. Chemical shifts are reported in ppm from tetramethylsilane (δH) and CCl₄ (δF), with positive shifts downfield, at ambient probe temperature unless otherwise stated. The temperature for the NMR probe was calibrated with an ethylene glycol standard. In the ¹³C and ¹⁹F NMR spectra registered in non-deuterated solvents, a coaxial tube containing acetone-d₆ was used to maintain the lock ²H signal, and the chemical shifts are reported from the CCl₄F signal in deuterated acetone. The compounds cis-[PdRfMe(PPh₃)₂] (1a) and trans-[PdRfMe(PPh₃)₂] (2a) were prepared as reported in the literature. The previously unreported 1b and 2b were prepared similarly but using C₆F₅Li.

Kinetic experiments. In a standard experiment a NMR tube cooled to -10 °C was charged with cis-[PdRfMe(PPh₃)₂] (1a) (10 mg, 1.13x10⁻² mmol), PPh₃ (0 to 6 mg; 0 to 2.3x10⁻² mmol), and THF (0.60 ml). When the mixture got dissolved a coaxial capillary containing acetone-d₆ was added and the sample was placed into the NMR probe thermostatted at 25 °C. The evolution was monitored by ³¹P NMR or by ¹⁹F NMR spectroscopy. Concentration-time data were acquired by integration of the ¹⁹F NMR signals. In order to consider the reaction as irreversible and to avoid the decomposition of the starting complex to palladium (0), only data points of the first 12% of the reaction were used.

Computational methods. PMe₂ and PPh₃ were used as ligands for the DFT computational study (level of theory wB97XD-PCM-THF/SDD-6-31G//B3LYP/SDD-6-31G*). ⁴²

ASSOCIATED CONTENT

Electronic Supplementary Information (ESI) Available: Text, figures, tables, containing experimental and kinetic details and computational information (17 pages).

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The authors declare no competing financial interests.

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(13) Secondary transmetalations are also found in cross coupling reactions with other nucleophiles (e.g. AuMe₃ as nucleophile). See for instance: Carrasco, D.; Pérez-Temprano, M. H.; Casares, J. A.; Espinet, P. Organometallics, 2014, 33, 3540-3545.


(15) The complete study of the Negishi reaction with ZnMe₂, including all the steps and other experimental investigations is in progress.

(16) In experimental mechanistic studies comparatively inert models offer the possibility to work on catalytic processes that are too fast for conventional reagents. In this respect fluorinated aryls such as C₆F₅Cl (Rf) or C₆F₅ (Pt) are excellent models of conventional aryls.


(18) Since the experimental studies show that Rf and Pt behave almost identical (see ESI), the group containing less electrons, Pf, was used in the DFT studies, but the results can also be applied to Rf, so Rf and Pf will be used indistinctly in the discussions, or referred to generally as Ar. On the other hand, we have carried out the calculations for PPh₃, and PMe₃ and the profile of the reaction includes both ligands as valuable information on how well PMe₃ performs as a model for PPh₃. These calculations also inform on the preliminary molecular interactions in cis₁, and trans₁, two states that are observed for PMe₃, but cannot be found for the corresponding more crowded PPh₃ complexes, probably because increased steric hindrance is enough to preclude their formation as intermediates. Finally, the calculated structures with PMe₃ allow for an easier observation of structural details in some figures used in this article.

(19) Represented for PMe₃ complexes for better visibility. (20) http://www.ccdc.cam.ac.uk/Solutions/FreeSoftware/Pages/FreeMercury.aspx

(21) Taking an approximate value of 8 kcal/mol for the unfavorable entropy contribution on going from 2 molecules getting bonded to give 1 molecule, the calculated estimation of about 3.7 kcal/mol suggests an extremely weak association, whatever its nature.

(22) Note that all these bonds are somewhat longer in the more crowded TS₁(PPh₃) transition state as compared to TS₂(PMe₃).

(23) The covalent radii of Pd and Zn are identical (1.31Å).


(25) Thus, anionic nucleophiles (e.g. RO−, Me−, etc.) will usually attack ZnMe₂, as in the formation of zincates. For neutral ligands, however, only few well defined complexes, always N-donor chelating or macrocyclic, are known: (a) O’Brien, P.; Hursthouse, M. B.; Motevalli, M.; Walsh, J. R.; Jones, A. C. J. Organomet. Chem. 1993, 449, 1–8. (b) Coward, K.M.; Jones, A. C.; Steiner, A.; Bickley, J. F.; Smith, L. M.; Pemble, M. E. Dalton Trans. 2000, 3480–3482.


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(28) For an early proposal of side-on coordination of C–M (M = Hg) bond as the initial step of transmetallation from a metal nucleophile, and for early studies by Ingold, Reutov, and others see references in: Reutov, O. A. Rus. Chem. Rev. 1967, 36, 163–174.

(29) Since in a [PdL2]2+ complex with perfect D4h symmetry the LUMO (\(\alpha_{6s}^2\)) produces zero overlap with \(\alpha\)-ligands approaching in the \(z\) direction, the acceptor orbital is an \(\alpha_{9s}\) orbital with contributions of the 4s, 4p, and \(d_z^2\) Pt atomic orbitals: Inorganic Chemistry, Purcell, K. F. and Kotz, J. C. W. B. Saunders Co., Philadelphia, (1977) p. 176. In this case, with much lower symmetry (C\(_4\), for the cis complex, C\(_2\) for the trans), the orbital contribution of Pt to HOMO2/Pd in cisI, contains important contributions of 4s, 3d\(_y^2\) and p orbitals with \(z\) component, and points toward the \(z\) direction. At variance with this, HOMO1/Pd contains 3d\(_x^2\), contribution instead of 3d\(_{xy}\), which makes it fairly inefficient towards Pd/Zn/Me bonding.

(30) We are using LUMO for short, but we mean the lowest empty MO that has an appropriate symmetry to rise to bond formation with the attacking full orbital of the nucleophile, which is not necessarily the LUMO if its symmetry does not provide positive overlapping.

(31) The high basicity refers to high energy of the orbitals hosting the electron density of the Zn–Me bond electron pair. The Zn–Me bond electron pair for ZnMeCl\(_2\) should be much lower in energy (less basic). Similar energetic considerations and behavior, including close relationship between basicity and nucleophile should be expected for ZnEt\(_2\), but probably not for bulkier dialkyls where high basicity might not be similarly reflected in high nucleophilicity because of steric hindrance.

(32) In that case L\(_z\) was a chelating phosphine–electron withdrawing olefin ligand.

(33) The latest structural values, determined by powder neutron diffraction at 4.5 K, show an Al–Al distance of 2.700(10) Å (Al metallic radius is 1.25 Å). The bridging CD\(_4\) groups adopt a staggered conformation with respect to each other in a molecule with C\(_3v\) symmetry, and there is no evidence in the structure for the involvement of the C–D bonds in the Al–CD\(_4\)–Al bridging bonding. See: McGrady, G. S.; Turner, J. F. C.; Iberson, R. M.; Prager, M. Organometallics 2000, 19, 4398-4401.


(37) Metallophilic interactions are usually in the order of energy of weak H-bonds.

