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Through-Space Intramolecular Palladium Rearrangement in Substituted Aryl Complexes: Theoretical Study of the Aryl to Alkylpalladium Migration Process

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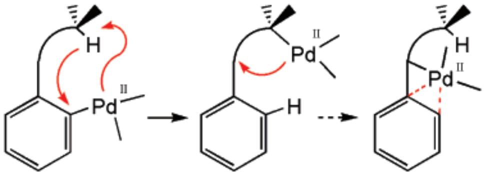

DFT/B3LYP calculations have been carried out to study intramolecular 1,*n* palladium shifts ($n = 3-5$) between sp^2 and sp^3 carbon atoms in alkylarylpalladium systems. Such shifts, which also involve a concomitant exchange with a hydrogen atom of the alkylaryl ligand, are quite often a pivotal step of several organic transformations mediated by palladium complexes. We show that the intimate mechanism for the 1,3 shift corresponds to a Pd(IV) pathway, whereas a Pd(II) pathway is favored in the case of 1,5 migrations. In the case of 1,4 migrations, both mechanisms are competitive. The Pd(IV) pathway can involve either a true Pd(IV) intermediate (oxidative addition/reductive elimination mechanism) or a Pd-(IV) transition state (oxidative hydrogen migration mechanism). The energy barrier is very high for the 1,3 palladium shift, making this process very unlikely, in contrast to the other ones which have enthalpy barriers ranging between 22.8 kcal mol^{-1} (for the 1,5 shift) and 31.9 kcal mol^{-1} (for the least favorable 1,4 shift studied here). All of these results are in line with our previous results for palladium shifts between two sp^2 carbon atoms. In addition, the sp^2 to sp^3 shifts have been found to be rather exothermic owing to the possibility for the alkylaryl ligand in the product to achieve a η^3 coordination mode. This η^3 coordination mode results either from the shift itself (1,3 case) or from a subsequent rearrangement that comprises a chain-running mechanism within the alkyl chain bound to the metal (for $n > 3$).

Introduction

Multistep organic synthetic reactions mediated or catalyzed by palladium complexes are extraordinarily numerous and diversified.[1,2] This versatile nature of palladium can be traced to the fact that palladium complexes can formally exit in three oxidation states, Pd(0), Pd(II), and Pd(IV). The reversible interconversion between these oxidation states underlies most of the mechanistic patterns that are usually put forth to account for these reactions. Yet, whereas the interconversion between the 0 and +2 oxidation states is now well established, both experimentally and theoretically, the interconversion between the +2 and +4 oxidation state is more controversial. This can be traced to the scarcity of well-characterized Pd(IV) complexes,

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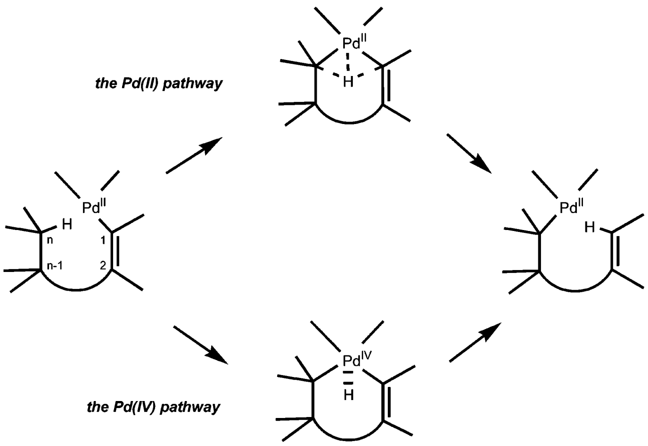
SCHEME 1. General Pathways for the Aryl-to-Alkyl Pd Shift



especially with palladium−carbon bonds.[3−8] In that context, the recent discovery of reactions that involve a step made of a through-space shift of palladium between two carbon atoms, associated to a simultaneous C−H bond activation,[9−25] is quite intriguing from the mechanistic point of view: As shown in Scheme 1 two different *intramolecular* pathways may be envisioned a priori: (i) either a two-step process that goes via a C−H oxidative addition on the palladium atom to yield a hydridopalladium (IV) intermediate which subsequently undergoes a C−H reductive elimination toward a neighboring carbon atom or (ii) a one-step process in which the oxidation state +2 of the palladium atom is retained. In this case, it could be considered either as a metathesis reaction of the C−H σ bond with the Pd−C bond or as a concomitant 1,n shift of both the hydrogen and the palladium atoms.

Such migration processes have been reported several times for 1,4 migrations, either between two sp^2[10−14,16,18,20−22,24] or between an sp^3 and an sp^2 carbon atoms.[9,15,17,19] These experimental studies have also shown the importance of this migration process from a synthetic point of view, since it allows the attachment of groups in positions that are otherwise difficult to substitute by usual chemical reactions.[25] However, they could not assess unambiguously which of the two pathways sketched in Scheme 1 is operative. We have recently addressed this issue, via DFT-B3LYP calculations, for 1,n aryl-to-aryl ($n = 3-6$)[26] and 1,5 vinyl-to-aryl[27] to palladium shifts. From these calculations, three different intimate mechanisms, rather than two, were found to be possibly at work: (i) the Pd(II) mechanism, which could be classified as a σ-bond metathesis mechanism but which was shown to correspond more to a through-space proton transfer between the two carbon atoms;[26,27] (ii) an oxidative addition/reductive elimination two-step mechanism in which a true Pd(IV) intermediate is involved; and (iii) an oxidative hydrogen migration one-step mechanism[28,29] in which the Pd(IV) species is a transition state rather than an intermediate. In the Pd(IV) transition states the imaginary frequency (which is associated to the hydrogen motion) was found to be rather low (between 150i cm^{-1} and 600i cm^{-1}), much lower than in the Pd(II) transition step (where it ranges between 1100i cm^{-1} and 1400i cm^{-1}).[26] The intimate mechanism for the 1,3 shift was shown to correspond to an oxidative hydrogen migration Pd(IV) pathway, whereas a Pd(II) pathway seemed to be favored in the case of 1,5 and 1,6 migrations. In the case of 1,4 migrations, *the Pd(II) and Pd(IV) mechanisms were found to be competitive, a key delineating factor being the geometrical constraints*. The energy barrier computed for the 1,3 palladium shift was very high, making this process very unlikely (at least in gas phase), in contrast to the other ones for which enthalpy barriers ranging between 18 and 28 kcal mol^{-1} were obtained. These results not only account for the feasibility of the 1,4 and 1,5 migrations, but they also raise the possibility of 1,6 migrations. Moreover, the fact that for the 1,4 migration the Pd(II) and Pd(IV) pathways were found to be competitive does not contradict the deuterium-labeling experiments, which have afforded some evidence for the involvement of Pd(IV) intermediates in some 1,4 vinyl-to-aryl palladium migration.[22] In their most recent paper, Larock et al. have also stressed the importance of steric hindrance as a significant factor.[24]

These two theoretical investigations were restricted to the consideration of sp^2 to sp^2 palladium migrations. One also needs to analyze palladium migrations between an sp^2 carbon atom and an sp^3 carbon atom, for which there has been some experimental evidence,[9,15,17,19] in order to check whether our

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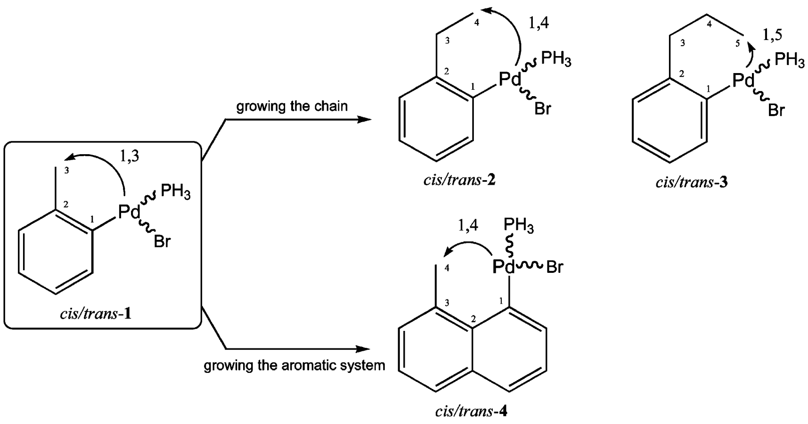
SCHEME 2. Systems Studied for the *Aryl to Alkyl* 1,*n* Pd Migration



previous mechanistic conclusions are still valid or not. We shall report herein our results for the 1,3 to 1,5 aryl-to-alkyl palladium migration.

Computational Details

The calculations were carried out at the DFT-B3LYP level[30−32] with the Gaussian 03 program.[33] The triphenylphosphine ligand PPh_3 was modeled by PH_3. The geometries were fully optimized by the gradient technique with the following basis: For Pd the LANL2DZ basis set is modified following the prescription of Couty and Hall.[34] In this modified basis, the innermost core electrons (up to 3d) are described by the relativistic orbital-adjusted effective core potential of Hay and Wadt[35] and the remaining outer core and valence electrons by a [341/541/31] basis set where the two outermost 5p functions of the standard LANL2DZ basis set have been replaced by a [41] split of the 5p function optimized by Couty and Hall.[34] For the Br atom, the quasi relativistic energy-adjusted spin-averaged effective core potential was taken from the work of the Stuttgart group, together with their [31/31] basis set,[36] to which s and p diffuse functions (with exponents of 0.0493 and 0.0363, respectively), and a d polarization function (of exponent 0.381) were added, following Radom et al.[37] The carbon, hydrogen, and phosphorus atoms were described by the standard polarized 6-31G* basis set.[38] The nature of the optimized structures, either transition states or intermediates, was assessed through a frequency calculation. Since we are dealing here with intramolecular processes, we will concentrate on enthalpy values which were obtained by taking into account zero-point energies and the thermal motion at standard conditions (temperature of 298.15 K, pressure of 1 atm). We checked in our first study[27] that the geometrical parameters obtained with this basis set are in agreement with related experimental structures of bromopalladium complexes and that the thermodynamic values obtained with this basis set were quite comparable to those obtained with larger basis sets.[39−41]

Results

We will primarily focus on the 1,3 to 1,5 palladium transfers depicted in the Scheme 2 for the monopalladated alkyl arene complexes **1**−**4**. They differ by changing either the length of the alkyl chain or the size of the aromatic system. As will be shown in the following sections, these transfers turned out to be in most cases energetically favorable along the direction shown by the arrow in the Scheme 2, viz. the aryl-to-alkyl direction. Note also that the cis/trans label here refers to the relative position of the bromine and the carbon atom covalently bound to palladium and that the transfer will connect a cis structure to a trans structure and vice versa. Both cis → trans and trans → cis transfers have been analyzed. The main conclusions turned out to be rather similar for both types of transfer. Thus, we shall report in the following our results for the trans isomer only, owing to the fact that this isomer was found to be more stable than the cis one. The reader interested in more subtle details will find the results obtained for the cis isomer in the Supporting Information. In the case of system **2**, we have also considered another intramolecular process that may be competitive with the 1,4 process, namely a 1,3 Pd migration process. The same applies for structure **3**, for which transfers other than the 1,5 transfer could occur.

The monophosphine Pd(II) bromo complexes of the Scheme 2 (**1**−**4**) may result from a previous oxidative addition reaction of the carbon−bromine bond to palladium in the corresponding monobromated precursors. Such monophosphine species appear from our previous studies to be energetically favorable.[27] In particular, we have shown that the transition states calculated for the vinyl-to-aryl Pd shift are higher in energy in the biphosphine complexes compared to the monophosphine complexes.[27] Note that these monophosphine complexes, although being formally three-coordinated, will in most cases fill the fourth valence of palladium through an agostic interaction, either with a C−H bond of the neighboring alkyl chain (except in the methyl case, vide infra) or with the C−H or the C═C bonds of one of the aromatic rings. The involvement of three-coordinated

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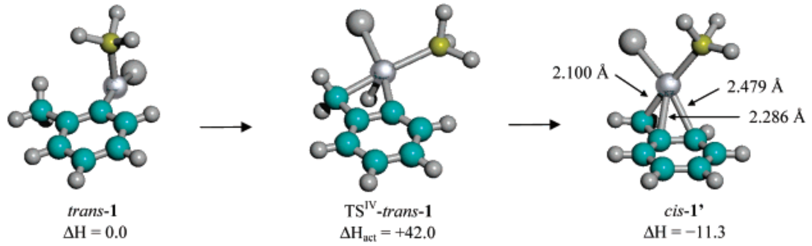

FIGURE 1. Optimized structures of the *trans*-**1** → *cis*-**1′** 1,3 Pd migration process. The prime label refers to complexes having the Pd atom bound the alkyl chain. The enthalpy values are in kcal mol^{-1}.

TABLE 1. Calculated Energies (Δ*E*) and Enthalpies (Δ*H*) for the Species Involved in the *Trans* → *Cis′* and *Trans* → *Trans′* Transformations in Structures 1 and Bz-1[a,b]

system	Δ*E*	Δ*H*	imaginary frequency[c]
1: 1,3 Pd^{IV} oxidative hydrogen migration pathway			
trans-**1**	0.0	0.0	
TS^{IV}-*trans*-**1**	+46.0	+42.0	557*i*
cis−**1′**	−10.9	−11.3	
bz-**1**: 1,3 Pd^{IV} oxidative hydrogen migration pathway			
trans-bz-**1**	0.0	0.0	
η^1-*cis*-bz-**1′**	+2.5	+2.4	
1: 1,3 Pd^{IV} oxidative addition/reductive elimination multistep pathway			
trans-**1**	0.0	0.0	
TS1^{IV}-*trans*-**1**	+47.4	+43.5	129*i*
inter1-*trans*-**1**	+46.2	+43.1	
TS^{IV}-inter-*trans*-**1**	+46.6	+42.8	17*i*
inter2-*trans*-**1**	+46.4	+43.2	
TS2^{IV}-*trans*-**1**[d]	*d*	*d*	*d*
trans−**1′**	−12.2	−12.4	

[a] The values are in kcal mol^{-1}; the zero of energy for the Pd migration in **1** and bz-**1** refers to *trans*-**1** and *trans*-bz-**1**, respectively. [b] The B3LYP total energies (in au) are for *trans*-**1**: $E = -754.276875$, $H = -754.116129$; and for *trans*-bz-**1**: $E = -986.535886$, $H = -986.266946$. [c] In cm^{-1}; refers to the unique imaginary frequency of the calculated transition state. [d] Not found.

monophosphine complexes as intermediates is also well documented experimentally.[17,39−48]

(A) 1,3 Pd Migration: Toluene System (1). As for the 1,3 aryl-to-aryl palladium shift in polycyclic aromatic hydrocarbons (PAHs),[26] the 1,3 phenyl-to-methyl shift in the Pd-tolyl complex goes preferentially through the oxidative hydrogen migration mechanism that involves a single Pd(IV) transition state; see Figure 1. The computed enthalpy barrier, which amounts to 42.0 kcal mol^{-1}, is somewhat lower than for the 1,3 aryl-to-aryl shift that we analyzed previously.[26] The transition state is again characterized by a short Pd−H bond (1.545 Å) and a low imaginary frequency (557*i* cm^{-1}). These two features are typical of a Pd(IV) complex. Thus, the transfer is best referred to as an oxidative hydrogen migration (OHM), according to the denomination coined by Oxgaard et al.[28,29] We have previously underlined that Pd(IV) transition state and intermediates are favored by a planar arrangement of the two organic moieties involved in the transfer, whereas the Pd(II) transition state is helped by a clamping arrangement of these two organic moieties.[26] The geometric constraints of **1** do not allow this clamping arrangement, hence the preference for a Pd(IV) transition state.

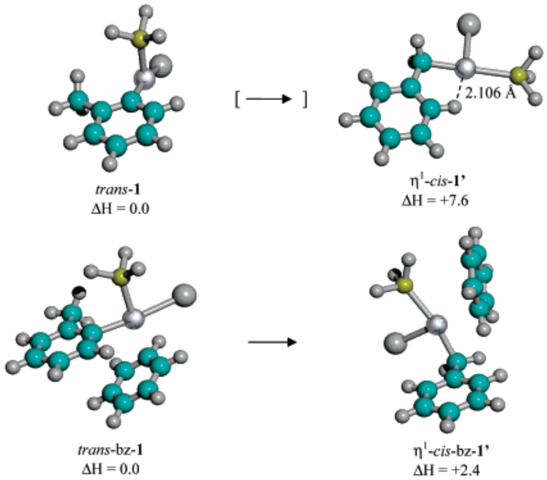

FIGURE 2. Optimized structures for the *trans*-**1** → η^1-*cis*-**1′** and *trans*-bz-**1** → η^1-*cis*-bz-**1′** 1,3 Pd migration process. The enthalpy values are in kcal mol^{-1}.

It should be noted that for the aryl-to-alkyl Pd shift analyzed here, the transferred hydrogen atom is always closer to the methyl group (the $C_{methyl}-H_{transferred}$ distance amounts to ~2.0 Å against the $C_{aromatic}-H_{transferred}$ distance which is ~2.5 Å). This was not the case when the transfer took place between two sp^2 carbons.[26] That the transition state is more reactant-like is in line with the larger exothermicity found for this transfer. This relatively high exothermicity is most likely due to (i) the destabilization of the *trans*-**1** reactant, which lacks any agostic interaction between the organic moiety and the Pd atom (such an agostic interaction would fill the fourth coordinating valence), and to (ii) the stabilization of the *cis*-**1′** product, which is in fact an η^3-benzyl Pd complex (and not the expected η^1 one), the three Pd−C(benzyl) bond distances (see Figure 1) being quite comparable to known η^3-benzyl Pd bond lengths.[49−51] The activation barrier is nevertheless quite high, see Table 1, as a consequence of the ring tension that the cyclometalated moiety experiences in the transition state (the C_1-Pd-C_3 angle and the C_1-C_3 distance in TS^{IV}-*trans*-**1** amount to 66.7° and 2.302 Å, respectively, the 1 and 3 subscripts making reference

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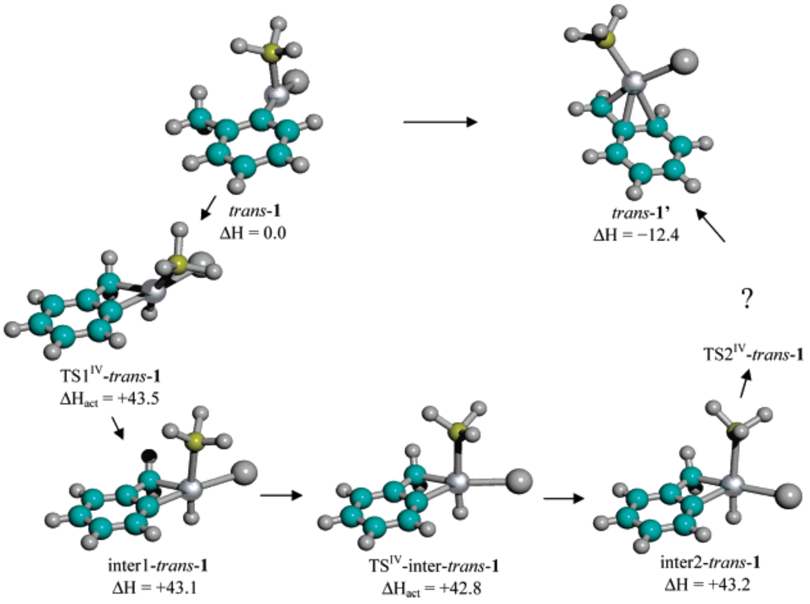

FIGURE 3. Possible oxidative addition/reductive elimination Pd^{IV} route connecting trans isomers of **1**. The enthalpy values are in kcal mol^{-1}.

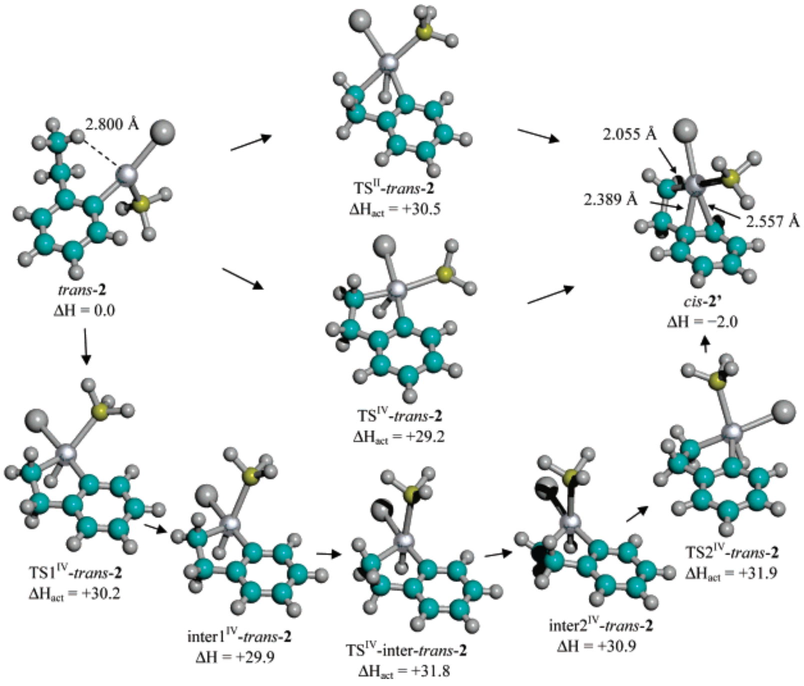

FIGURE 4. Optimized structures of the Pd(II) and Pd(IV) pathways for the *trans*-**2** → *cis*-**2′** 1,4 Pd migration process. The enthalpy values are in kcal mol^{-1}.

to the carbons involved in the 1,3 Pd shift). This high barrier makes the 1,3 migration process rather unlikely, at least in the gas phase.

Attempts to obtain the expected η^1-benzyl Pd structure systematically led to the η^3 species. In fact, the η^1 structure could be obtained only as a transition state for the torsion about the $C_{aromatic}-C_{methyl}$ bond, well above the η^3 structure (by 18.9 kcal mol^{-1}). As a result, the reaction enthalpies for a 1,3 Pd migration that would stop at the η^1 structure is +7.6 kcal mol^{-1} (see Figure 2 and Table 1). In order to get another estimate of the enthalpies for such reactions, we considered systems with an extra benzene molecule which blocks the fourth coordination site; see the *trans*-bz-**1** structures of Figure 2 (benzene was chosen because it could be also considered as participating as a solvent molecule for the reaction). This led as expected to a significant decrease of the reaction enthalpy which amounts to +2.4 kcal mol^{-1}, instead of −11.3 kcal mol^{-1}, see Table 1. From these results, the enthalpy gain in forming the η^3-benzyl complex may be estimated to be about 14 kcal mol^{-1}, a value in agreement with values that have been previously found either experimentally[52] or computationally for various Pd−benzyl complexes.[53]

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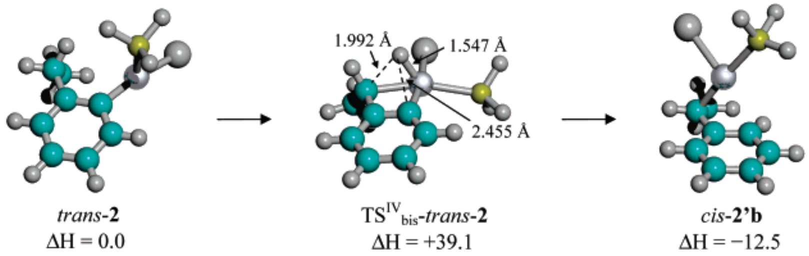


FIGURE 5. Optimized structures of the Pd(IV) pathway for the *trans*-**2** → *cis*-**2′b** 1,3 Pd migration process. The enthalpy values are in kcal mol^{-1}.

TABLE 2. Calculated Energies (Δ*E*) and Enthalpies (Δ*H*) for the Species Involved in the *Trans* → *Cis′* Transformation in Structure 2[a,b]

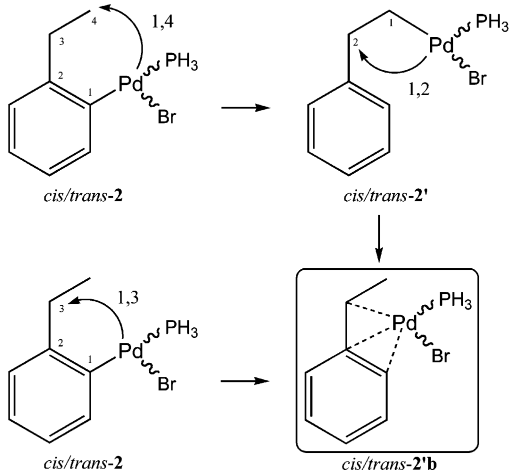
system	Δ*E*	Δ*H*	imaginary frequency[c]
2: 1,4 Pd^{II} proton-transfer pathway			
trans-**2**	0.0	0.0	
TS^{II}-*trans*-**2**	+34.3	+30.5	1393*i*
cis-**2′**	−1.5	−2.0	
2: 1,4 Pd^{IV} oxidative hydrogen migration pathway			
trans-**2**	0.0	0.0	
TS^{IV}-*trans*-**2**	+32.9	+29.2	533*i*
cis-**2′**	−1.5	−2.0	
2: 1,4 Pd^{IV} three-step oxidative addition/reductive elimination pathway			
trans-**2**	0.0	0.0	
TS1^{IV}-*trans*-**2**	+33.9	+30.2	166*i*
inter1^{IV}-*trans*-**2**	+32.7	+29.9	
TS^{IV}-inter-*trans*-**2**	+35.2	+31.8	112*i*
inter2^{IV}-*trans*-**2**	+33.7	+30.9	
TS2^{IV}-*trans*-**2**	+35.7	+31.9	198*i*
cis−**2′**	−1.5	−2.0	
2: 1,3 Pd^{IV} direct oxidative hydrogen migration pathway			
trans-**2**	0.0	0.0	
TS$^{IV}_{bis}$-*trans*-**2**	+43.3	+39.1	490*i*
cis-**2′b**	−12.0	−12.5	

[a] The values are in kcal mol^{-1}; the zero of energy for the Pd migration in **2** refers to *trans*-**2**. [b] The B3LYP total energy (in au) is for *trans*-**2**: $E = -793.589894$, $H = -793.399079$. [c] In cm^{-1}, refers to the unique imaginary frequency of the calculated transition state.

At this stage, one should mention that the results for the cis isomer do parallel the ones for the trans isomer; see the Supporting Information. A point of interest is that, although this *cis*-**1** isomer lies +5.5 kcal mol^{-1} (enthalpy value) above the *trans*-**1** isomer, the activation barrier is much lower for the *cis*-**1** → *trans*-**1′** conversion (+34.8 kcal mol^{-1}) than for the *trans*-**1** → *cis*-**1′** conversion (+42.0 kcal mol^{-1}). The *cis*-**1** → *trans*-**1′** transition state (TS^{IV}-*cis*-**1**) remains therefore below the *trans*-**1** → *cis*-**1′** transition state; see Scheme S1 and Table S1 of the Supporting Information. Thus, should there be a feasible mechanism that would first convert *trans*-**1** into *cis*-**1**, then one would have a pathway to go from *trans*-**1** to *trans*-**1′**.

It is also worth mentioning that the TS^{IV}-*trans*-**1** transition state lies close in energy to, but below, intermediates and transition states of an oxidative addition/reductive elimination multistep Pd(IV) pathway; see Figure 3 and Table 1. In this pathway, the arrangement of the ligands around the palladium atom in the intermediates is still square pyramidal, but with a negatively charged carbon atom in the apical position, namely the one originating from the methyl group (Figure 3). We could not, however, and despite repeated efforts, find a transition state for the last step of this pathway. Should it nevertheless exist, then one would have a mechanism to connect two trans isomers, hence corresponding to a *trans* → *trans′ transformation*.

SCHEME 3. Various Routes To Obtain *cis*- and *trans*-2′b from Different Starting Points



Pathways involving Pd(IV) intermediates have also been found in our previous studies, but for the 1,5 and 1,6 shifts only.[26,27] For the 1,3 and 1,4 shifts, the Pd(IV) pathways were oxidative hydrogen migration one-step pathways with a Pd(IV) transition state, and we traced the preference for the one-step Pd(IV) pathway over the multistep Pd(IV) pathway to structural requirements.[26] That the 1,3 shift analyzed here may involve a square pyramidal intermediate is therefore most likely due to the possibility of the system **1** to distort in order to achieve such a geometry. Note finally that the angular displacement of the Br atom that leads from inter1-*trans*-**1** to inter2-*trans*-**1** via TS^{IV}-inter-*trans*-**1** (which has a distorted TBP structure), see Figure 3, is a well-known feature of halogeno d^6-pentacoordinated transition-metal complexes.[54−58] All of the above findings illustrate once again the versatility of palladium to accommodate the +IV oxidation state in various geometries.

(B) 1,4 Pd Migration: Ethylbenzene System (2). The *trans*-ethylbenzene Pd complex displays several stable structures, which differ by the type of the agostic interaction that is present between palladium and the ethyl substituent. The most stable one, labeled as *trans*-**2**, is shown in Figure 4. It is characterized by a weak ϵ agostic interaction between the Pd atom and the terminal C−H bond of the ethyl chain (the Pd−H distance is 2.799 Å). As shown in Figure 4, three different pathways, viz. one Pd(II) single step, one Pd(IV) oxidative hydrogen migration, and an oxidative addition/reductive elimination three-step

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(54) Lichtenberger, D. L.; Brown, T. L. *J. Am. Chem. Soc.* **1978**, *100*, 366.

(55) Davy, R. D.; Hall, M. B. *Inorg. Chem.* **1989**, *28*, 3524.

(56) Riehl, J. F.; Jean, Y.; Eisenstein, O.; Pelissier, M. *Organometallics* **1992**, *11*, 729.

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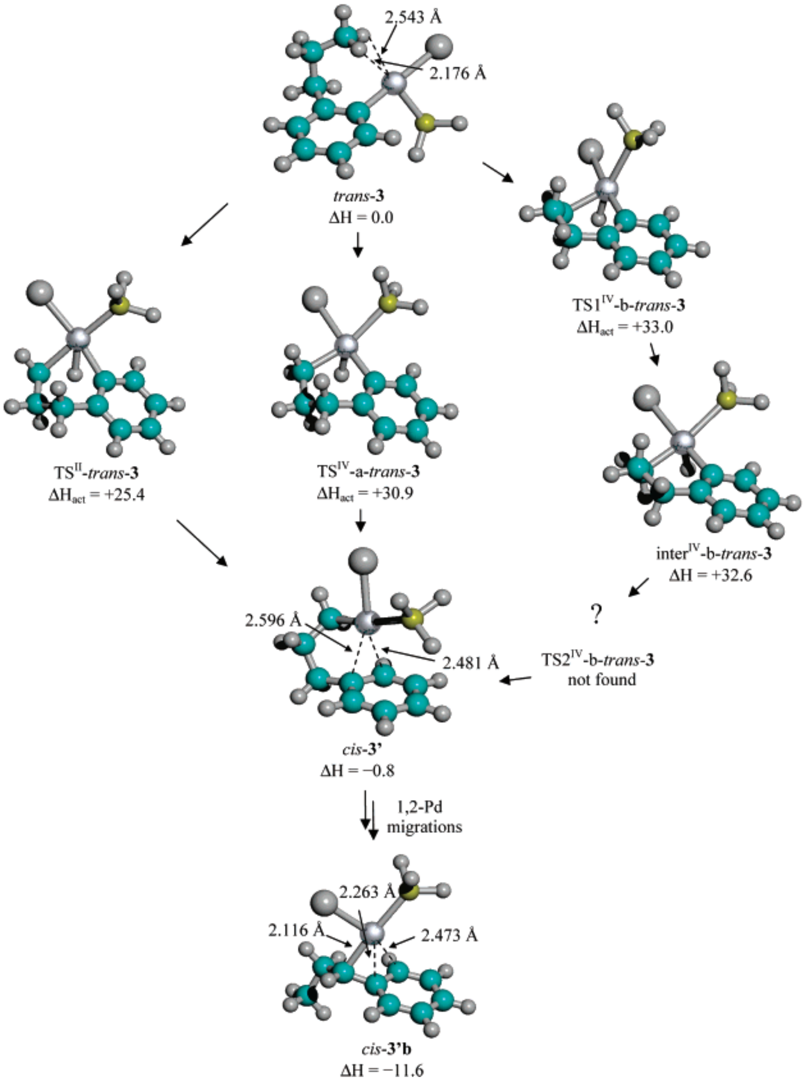

FIGURE 6. Optimized structures of the Pd(II) and Pd(IV) pathways for the *trans*-**3** → *cis*-**3′b** [1,5 + 1,2] tandem Pd migration process. The enthalpy values are in kcal mol^{-1}

pathway involving two Pd(IV) intermediates, have been obtained. As for the aryl to aryl 1,4 Pd migration,[26] we expected that these mechanisms would be competitive, with comparable energy barriers. This is indeed the case; see Table 2 and Figure 4. The Pd(IV) oxidative hydrogen migration mechanism, which is the most favorable one ($\Delta H_{\mathrm{act}} = +29.2$ kcal mol^{-1}), was ascertained by an IRC calculation. It showed that TS^{IV}-*trans*-**2** does indeed connect *trans*-**2** to *cis*-**2′**, even if the transferred hydrogen atom is far away (2.435 Å) from the C_{arom} position (compare this value to the value of 1.914 Å for the $H-C_{\mathrm{ethyl}}$ distance). Note also that the oxidative addition/reductive elimination three-step pathway involves a conformational change of the ethyl group through the $C_{\mathrm{arom}}-C_{\mathrm{ethyl}}$ bond axis (compare inter1^{IV}-*trans*-**2** and inter2^{IV}-*trans*-**2** in Figure 4) that is needed to get geometries appropriate for the transfer.

At this stage, one should stress that the resulting *cis*-**2′** structures is not the most stable one on the whole potential surface: it can rearrange via a five-step rearrangement that results in a palladium displacement from a terminal position to an inner position to yield *cis*-**2′**b; see Scheme 3 and Figure S4 of the Supporting Information (the same is true for *trans*-**2′** which results from *cis*-**2**; see Figure S5 in the Supporting Information). This rearrangement, which has been previously referred to (in metal alkyl complexes) as a “chain running”[52,59−61] leads once again to a quite stable η^3-benzyl Pd complex. The overall reaction is therefore a [1,4 + 1,2] tandem Pd migration.

Although being conceptually very simple, the 1,2 Pd/H interchange is mechanistically rather complex. It comprises several rotation, β-elimination and insertion steps—all them characterized by low enthalpy barriers (of the order of 12 kcal mol^{-1} or less)[62] —which are described in detail in the Supporting Information section (see Figures S4 and S5 and Scheme S4). It should therefore take place quite easily.

Quite interesting too is the fact that the final product **2′b** obtained from **2′** through this [1,4 + 1,2] tandem Pd migration process can be also obtained from **2** via a direct 1,3 Pd migration

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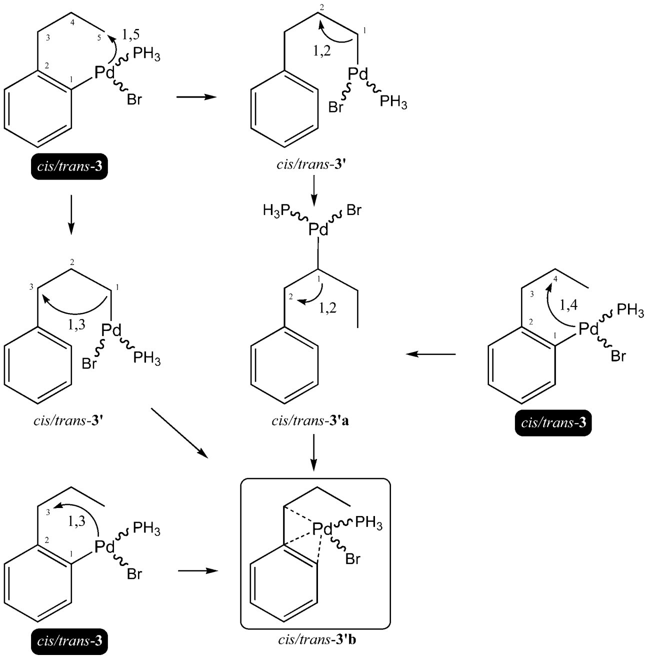
[59] Schmidt, G. F.; Brookhart, M. *J. Am. Chem. Soc.* **1985**, *107*, 1443.

[60] Brookhart, M.; Volpe, A. F.; Lincoln, D. M.; Hovarth, I. T.; Millar, J. M. *J. Am. Chem. Soc.* **1990**, *112*, 5634.

[61] See also (a) Larock, R. C.; Lu, Y.; Bain, A. C.; Russell, C. E. *J. Org. Chem.* **1991**, *56*, 4589. (b) Albéniz, A. C.; Espinet, P.; Lin, Y.-S. *Organometallics*, **1997**, *16*, 4138.

[62] A somewhat similar situation has been analyzed recently in alkenyl palladium complexes, see: (a) Hansen, A. L.; Ebran, J.-P.; Ahlquist, M.; Norrby, P.-O.; Skrydstrup, T. *Angew. Chem., Int. Engl.* **2006**, *45*, 3349. (b) Ebran, J. P.; Hansen, A. L.; Gogsig, T. M.; Skrydstrup, T. *J. Am. Chem. Soc.* **2007**, *129*, 6931.

SCHEME 4. Various Routes To Obtain *cis*-3′ and *trans*-3′b from 3 via Initial 1,5, 1,4, and 1,3 Pd Migrations



(Scheme 3 and Figure 5): as for the 1,3 migration in **1**, the barrier for this 1,3 migration is high, much higher than the barrier associated with the tandem 1,4 + 1,2 Pd migration; see Table 2. Thus, any *apparent* 1,3 Pd shift in ethylbenzene derivatives might be in fact the result of such a 1,4 + 1,2 tandem reaction. More generally, one may also anticipate that a 1,*n* Pd migration in alkylbenzene derivatives could be followed by a series of 1,2 shifts, provided that such shifts would be allowed by either the geometrical constraints of the system or the nature of the alkyl moiety. For instance, in the tandem C−H functionalization/Suzuki−Miyaura coupling reaction of 2,4,6-tri-*tert*-butylbromobenzene with phenylboronic acid investigated by Buchwald et al.[17] and which involves a 1,4 aryl- to alkylpalladium migration, a subsequent 1,2 shift *cannot* occur due to the lack of β-hydrogens. The same is true for the products of the 1,4 alkyl to aryl shifts observed by Larock et al.[15] in fused polycycles. Note that in this case the shift is from the alkyl to the aryl. In our model system **2**, the shift is energetically favorable in the opposite direction, i.e., from the aryl to the alkyl, but the energy difference is small, 2 kcal mol^{-1} only. Thus, the direction of the 1,4 shift should depend to a large extent upon the complexity of the system. In fact, in the consecutive vinylic to aryl to allylic palladium migration reported recently by the same group,[19] the second transfer is from the sp^2 to the sp^3 carbon atom, most likely driven by the isomerization of the allyl ligand from the η^1 to the η^3 coordination mode. Note also that in the intermediate undergoing the sp^2 to sp^3 1,4 shift, the expected coplanarity of the two organic moieties that are involved in the transfer should favor one of the Pd(IV) routes, either the oxidative hydrogen migration pathway or—as put forth by the experimentalists[19]—the oxidative addition/reductive elimination pathway.

(C) 1,5 Pd Migration: Propylbenzene system (3). As for the ethylphenyl complex **2**, the most stable structure obtained after the 1,5 migration in **3** has an η^3 coordination mode, see **3′b** in Figure 6. This structure is most easily accessible through a 1,5 Pd(II) migration coupled to a chain running mechanism that would involve two 1,2 Pd migrations along the alkyl chain.

TABLE 3. Calculated Energies (Δ*E*) and Enthalpies (Δ*H*) for the Species Involved in the *Trans* → *Cis*′ Transformation in Structure 3[a,b]

system	Δ*E*	Δ*H*	imaginary frequency[c]
3: 1,5 Pd^{II} migration pathway			
trans-**3**	0.0	0.0	
TS^{II}-*trans*-**3**	+28.8	+25.4	1292*i*
cis-**3′**	−0.6	−0.8	
cis-**3′b**	−11.5	−11.6	
3: 1,5 Pd^{IV} oxidative hydrogen migration pathway “a”			
trans-**3**	0.0	0.0	
TS^{IV}-a-*trans*-**3**	+34.4	+30.9	283*i*
cis-**3′**	−0.6	−0.8	
cis-**3′b**	−11.5	−11.6	
3: 1,5 Pd^{IV} oxidative addition/reductive elimination multistep pathway “b”			
trans-**3**	0.0	0.0	
TS1^{IV}-b-*trans*-**3**	+36.4	+33.0	455*i*
inter^{IV}-b-*trans*-**3**	+35.4	+32.6	
TS2^{IV}-b-*trans*-**3**	*d*	*d*	*d*
cis−**3′**	−0.6	−0.8	−
cis−**3′b**	−11.5	−11.6	−

[a] The values are in kcal mol^{-1}, the zero of energy for the Pd migration in **3** refers to *trans*-**3**. [b] The B3LYP total energy (in au) is for *trans*-**3**: $E = -832.903966$, $H = -832.683592$. [c] In cm^{-1}; refers to the unique negative frequency of the calculated transition state. [d] Not found.

We can anticipate that the geometries and the activation energies associated to this 1,2 Pd migration sequence should be very similar to those obtained for the system **2**.

As shown from Figure 6, the Pd(II) pathway for the 1,5 Pd migration is favored over both the oxidative hydrogen migration and the oxidative addition/reductive elimination Pd(IV) pathways. This is in line with our previous conclusions on sp^2 to sp^2 1,*n* Pd migrations, which were found to be in the Pd(II) domain when $n > 4$.[26] Interestingly the most stable conformation of the propyl group in *trans*-**3** leads quite naturally to *cis*-**3′** via the oxidative hydrogen migration pathway “a” shown in Figure 6. This route is preferred over the oxidative addition/reductive elimination pathway “b” which involves a conformational change of the propyl group and is characterized by higher energy intermediates and transition states. Moreover, the search for TS^{IV}-b-*trans*-**3** structure proved unsuccessful. Thus, the pathway “b” may not be operative for the trans isomer, perhaps because of an inappropriate conformation of the propyl group. These results illustrate the critical role that the conformational behavior of the alkyl chain might play in the assessment of the intimate mechanism of these Pd migrations.[26]

We have already mentioned that the palladium bound to the terminal carbon of the alkyl chain in **3′** can undergo a 1,2 Pd migration sequence that will stop at the corresponding **3′b** species. In fact, one should be aware that there is, a priori, a whole variety of Pd migrations from the aryl group to the propyl chain, ranging from a 1,5 to a 1,3 type, and that each of these can be followed by one or more Pd migrations within the propyl: thus, as shown schematically in Scheme 4, **3′b** could be obtained from **3** either via a 1,5 migration coupled to a single 1,3 Pd migration, or via a 1,4 Pd migration to the outermost methylene group in the propyl chain followed by a single 1,2 Pd displacement, or finally via an 1,3 direct Pd migration by transferring the hydrogen atom to the innermost methylene group (Figures S9−S11 in the Supporting Information). We have also determined the intermediates and transition states of the 1,3 and 1,4 Pd migration pathways for both the *cis*-**3** and *trans*-**3**

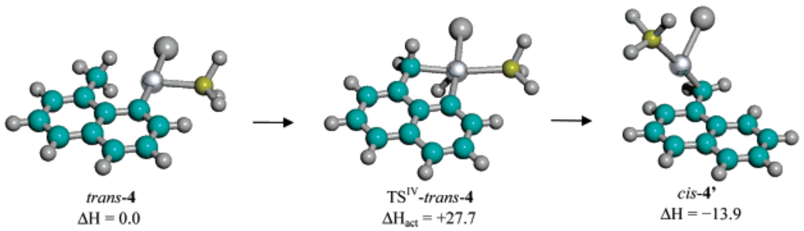


FIGURE 7. Optimized structures of the oxidative hydrogen migration Pd(IV) pathway for the *trans*-**4** → *cis*-**4′** 1,4 Pd migration process. The enthalpy values are in kcal mol^{-1}.

TABLE 4. Calculated Energies (Δ*E*) and Enthalpies (Δ*H*) for the Species Involved in the *Trans* → *Cis*′ Transformation in Structure 4[a,b]

system	Δ*E*	Δ*H*	imaginary frequency[c]
4: 1,4 Pd^{IV} oxidative hydrogen migration pathway			
trans-**4**	0.0	0.0	
TS^{IV}-*trans*-**4**	+31.2	+27.7	480*i*
cis−**4′**	−13.9	−13.9	

[a] The values are in kcal mol^{-1}; the zero of energy for the Pd migration in **4** refers to *trans*-**4**. [b] The B3LYP total energy (in au) is for *trans*-**4**: $E = -907.916498$, $H = -907.706659$. [c] In cm^{-1}; refers to the unique imaginary frequency of the calculated transition state.

isomers, see Table S5 in the Supporting Information. For the trans isomer, the 1,5 Pd(II) migration turns out to be the most favorable initiation process. Since further 1,2 Pd displacements are expected to be rather facile (vide supra), one may conclude that the easiest route to *cis*-**3′b** from *trans*-**3** should involve a [1,5 + 1,2 + 1,2] cascade reaction. Surprisingly, as shown in the Supporting Information (see Figure S8 and Table S5) for the cis isomer the 1,5 Pd(II) pathway has a comparable activation energy to that of the 1,4 Pd(IV) route (Table 3). In this case the tandem [1,4 + 1,2] process is therefore a likely alternative.

(D) 1,4 Pd Migration: Methylnaphthalene System (4). As for the 1,3 migration in the tolyl complex **1**, no Pd(II) transition state could be obtained. This is again due to the geometric constraints that prevent the two organic moieties involved in the transfer, viz. the methyl and the naphthyl groups, from adopting a clamping rearrangement around palladium. One finds instead a Pd(IV) transition state that is characteristic of an oxidative hydrogen migration mechanism; see Figure 7. Quite noteworthy are the relatively low activation energy and high exothermicity computed for this 1,4 migration process in **4** (Table 4), when compared to the 1,3 or 1,4 migration processes in **1**−**3**. This is most likely due to the combined effects of the formation of the quite stable η^3 product (as in **1**) and of the relief of steric hindrance between the methyl group and the $PdBr(PH_3)$ moiety in the reactant.

Interestingly Wang et al.[9] have observed for the Heck reaction of α-chloromethynaphtalene with various olefins, the formation, in the case of *N*-vinyl olefins, of an unexpected coupling product in which the olefin group is attached to the *peri* position of the naphtalene ring. They proposed that this could be accounted for by a 1,4 rearrangement between a naphthylmethyl and a methylnaphthyl Pd intermediate; see Scheme 5. They also suggested that these nitrogen containing olefins might be involved in the stabilization of the intermediates as coordinating ligands. Their result would imply that the methylnaphthyl intermediate is more stable (or at least close in energy to) than the naphthylmethyl intermediate, a conclusion that seems at odds with our present finding. We have also carried out calculations on the chloro Pd systems **5** and found again that, as in the bromo system **4**, the palladium is preferably bound to the methyl group (rather than to the phenyl); see Figure 8. Yet, on the basis of our results for the toluene derivative **1** (vide supra), one may expect that the presence of a coordinating system in the coordination sphere would first lead to a η^1 coordination mode and thus lead to reactants and products of similar energy.

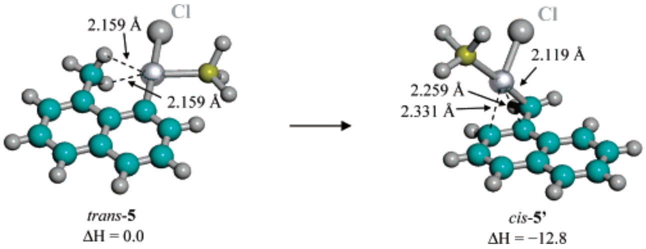
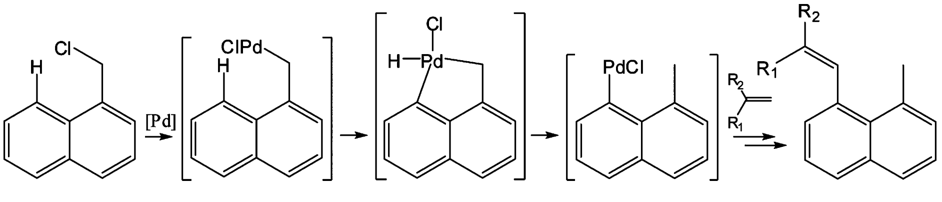


FIGURE 8. Optimized structures for the *trans*-**5** → *cis*-**5′** 1,4 Pd migration processes. The enthalpy values are in kcal mol^{-1}.

Conclusion

We have extended in this study our investigation of the 1,*n* carbon to carbon palladium shifts (which are simultaneously accompanied by a hydrogen migration) from the shift between two sp^2 carbon atoms to the shift between an sp^2 and an sp^3 carbon atom. The results show that our previous conclusions remain valid, whatever the type of carbon atom is involved. In particular, the preference for the Pd(II) route over the routes that involve either a Pd(IV) transition state (the oxidative hydrogen migration route) or a Pd(IV) intermediate (the oxidative addition/reductive elimination route) is highly dependent on the geometry of the system, namely its ability to undergo a distortion that will allow a clamping arrangement

SCHEME 5. Mechanism with the 1,4 Pd Shift Proposed by Wang et al.



with respect to the transferred hydrogen in the Pd(II) transition state. As for the 1,3 aryl-to-aryl Pd shift, the 1,3 phenyl to methyl shift is characterized by a high barrier, thus making the process unlikely despite a favorable exothermicity. This relatively large exothermicity is the result of an additional stabilization provided by the η^3 coordination mode of the benzyl ligand obtained. On the other hand, for the 1,n phenyl to alkyl shift ($n > 3$) the energy barrier is much more accessible, especially in the case of the propylphenyl system ($n = 5$). For $n = 4$, the Pd(II) and Pd(IV) routes are competitive, whereas for $n = 5$, the Pd(II) mechanism becomes more favorable. Quite interestingly, too, for $n > 3$ the stabilization by the η^3 coordination mode mentioned above appears to be a triggering factor for the occurrence of successive 1,2 shifts that may ultimately lead to a product that seems to arise from an apparent 1,3 shift in the alkylphenyl starting complex.

Supporting Information Available: Text, Figures, Schemes and Tables giving details for the various *cis* → *trans* processes and for other possible intramolecular rearrangement processes. Cartesian coordinates, absolute energies and enthalpies of the calculated structures reported in the text. This material is available free of charge via the Internet at http://pubs.acs.org. Cartesian coordinates of calculated structures reported in the Supporting Information Section are available, on request, from the corresponding author.

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