

Roles of Base in the Pd-Catalyzed Annulative Chlorophenylene Dimerization

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ABSTRACT

By using computation, the detailed mechanism of the Pd-catalyzed annulative chlorophenylene dimerization has been elucidated and the roles of the base have been identified. It is shown that the initial steps of this reaction are the active catalyst formation and the first C–Cl bond activation proceeds via the “base-assisted oxidative addition” mechanism. Overall, these steps of the reaction proceed via 16.2 kcal/mol free energy barrier for the C–Cl bond activation and are highly exergonic. Importantly, the base directly participates in the C–Cl bond cleavage introduces a mechanistic switch of the Pd(0)/Pd(II) oxidation and makes the reaction more exergonic. The following steps of the reaction are palladacycle and Pd-aryne formations, among which the palladacycle formation is found to be favorable: it proceeds with a moderate C–H activation barrier and is slightly exergonic. Although the Pd-aryne formation requires a slightly lower energy barrier, it is highly endergonic: therefore, the participation of the Pd-aryne complex, or its derivatives, in the Pd-catalyzed annulative chlorophenylene dimerization in the presence of Cs₂CO₃ seems to be unlikely. Again, base plays important roles in the palladacycle formation: it participates in the “bay” C–H bond activation, and facilitates the driving of the reaction forward by removing a proton to the solution via the bicarbonate-to-carbonate exchange mechanism. Addition of the second C–Cl bond to palladacycle intermediate, i.e. Pd(II)/Pd(IV) oxidation, is a rate-limiting step of the entire Pd-catalyzed annulative chlorophenylene dimerization in the presence of Cs₂CO₃: it occurs with 35.8 kcal/mol free energy barrier and is exergonic by 25.1 kcal/mol. The following polycyclic aromatic hydrocarbon (PAH) formation is a multi-step process and requires less free energy barriers. An alternative pathway, namely, cyclooctatetraene (COT) formation requires a higher energy barrier and is not feasible. This finding is consistent with experiments that show no COT

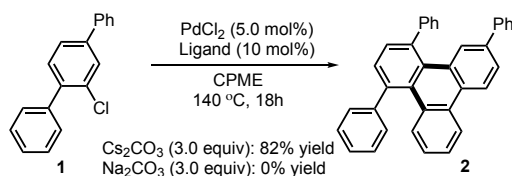
product in the utilized conditions. The calculations also indicate that the observed diminishing of the yield of the Pd-catalyzed annulative chlorophenylene dimerization reaction upon the use of Na-carbonate instead of Cs-carbonate is the result of not only poor solubility of Na-carbonate in the used experimental conditions, but also of a prohibitively large free energy barrier required for the second C–Cl activation, i.e. Pd(II)-to-Pd(IV) oxidation.

Introduction

The high π -electron density, low redox potentials, strong π - π stacking interactions, and high stability of the polycyclic aromatic hydrocarbons (PAHs) make them potentially attractive materials for use in optoelectronic, fluorescent bioimaging, pharmaceutical, and agrochemical industries.¹ Ongoing extensive research has (a) revealed that the physicochemical properties of PAHs are functions of the topology of their ring structures and degree of π -extension,¹ and (b) identified multiple synthetic strategies for the control over the preparation of PAHs or other π -extended aromatic materials. Current synthetic toolbox for this purpose includes (but is not limited to) cross-coupling, Diels-Alder, cyclodehydrogenation (such as Scholl reaction), and cyclotrimerization.² However, recent advances in transition metal catalyzed selective C–H functionalization³ have opened new horizons for effective synthesis of PAHs and related species.

A prominent example of this is the annulative π -extension (APEX) of unfunctionalized aromatics, reported by Itami and coworkers.⁴ This step- and atom-economic synthesis allows direct transformation of easily available unfunctionalized arenes to PAHs and nanographenes. Briefly, it is shown that the use of PdCl₂ as a catalyst, PⁿBu(Ad)₂ as a ligand, and Cs₂CO₃ as a base facilitates the annulative dimerization of chlorophenylenes through double C(sp²) – H bond functionalization.⁴ Fascinatingly, the change of base from Cs₂CO₃ to Na₂CO₃ decreases yield of the reaction from 82% to 0%, and the use of sterically less bulkier phosphines is shown to be less effective (see Scheme 1).

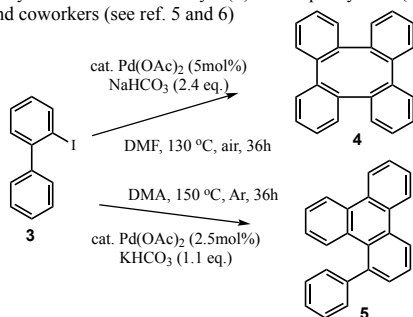
Scheme 1. The Pd-catalyzed Annulative Chlorophenylene Dimerization Reaction, Reported by Itami and Coworkers (see ref. 4).



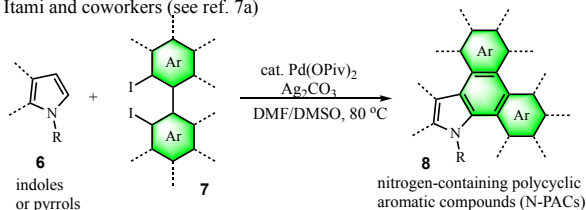
Inspiring work by Shi and coworkers has shown that the product, *i.e.* polyaromatic hydrocarbons (PAHs) *vs* arene-fused cyclooctatetraenes (COTs) formation, via the C–H bond functionalization, depends on the reaction conditions. For example, they have reported that Pd(OAc)₂ catalyzed direct arylation and cyclization of *o*-iodobiaryls forms tetraphenylenes or arene-fused cyclooctatetraenes (COTs) (Scheme 2a).⁵ In this reaction, the use of neither Cs₂CO₃ nor KHCO₃ gives higher yield than NaHCO₃, and the use of bulky phosphine ligand (Davephos) has a negative impact on the reaction yield. Intriguingly, performing the reaction under argon gas, instead of air, and switching the base from NaHCO₃ to KHCO₃ has led to formation of PAHs instead of COTs (Scheme 2a).⁶

Scheme 2. Selected Examples for the Synthesis of Polycyclic Aromatics Compounds.

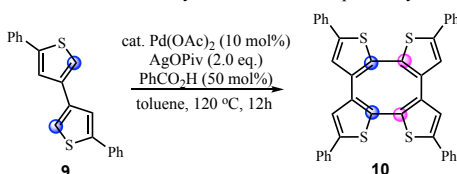
(a) Arylation and cyclization of o-iodobiaryls (**3**) to tetraphenylenes (**4**) and PAHs (**5**), reported by Shi and coworkers (see ref. 5 and 6)



(b) Palladium-catalyzed APEX reaction of indoles and pyrroles with diiodobiaryls, reported by Itami and coworkers (see ref. 7a)



(c) Synthesis of heteroarene-fused cyclooctatetraenes: reported by Miura and coworkers (see ref. 7b)

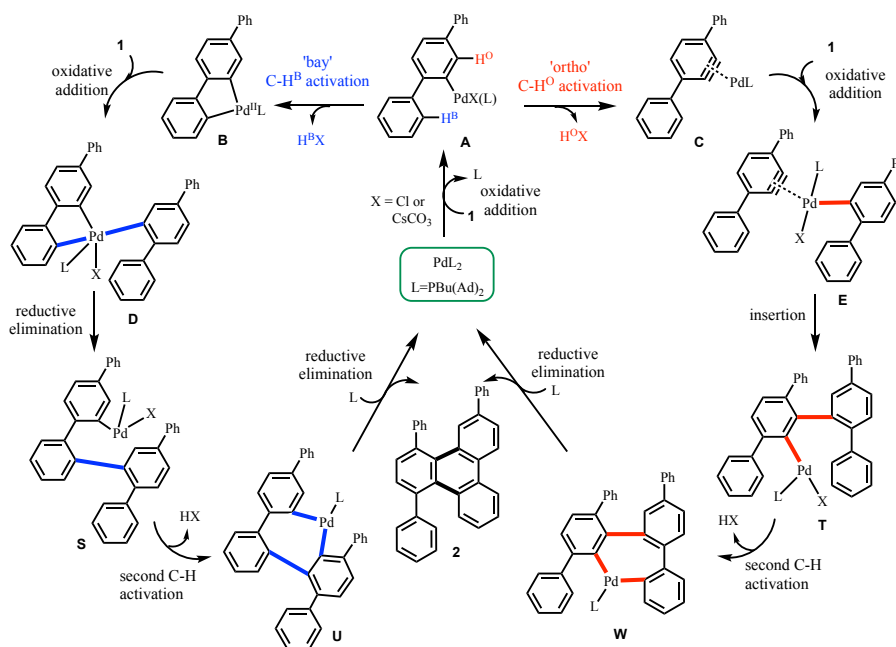


Growing number of the transition metal catalyzed synthesis of PAHs and related species via the selective C-H functionalization (as example, see Scheme 2b and 2c)⁷ make it critical to better understand the mechanism and controlling factors of the reported catalytic annulative coupling reactions. It is conceivable to expect that the understanding of details of these reactions will enable us to improve the yield and product selectivity, and will broaden the substrate scope. Previously, the Itami group have proposed a multistep mechanism for the Pd-catalyzed annulative dimerization of chlorophenylene (**1**) that includes (i) oxidative addition of the C–Cl bond to Pd(0) to form Pd-aryl intermediate **A**, (ii) the first C–H bond activation, either of ‘bay’ C–H^B or ‘ortho’ C–H^O bonds, leading to formation of the palladacycle **B** or Pd-aryne **C** intermediates, respectively, (iii) C–Cl oxidative addition of a second equivalent of substrate **1** to either palladacycle **B** or Pd-aryne **C** intermediates leading to the formation of intermediates **D** or **E**, respectively, and (iv) reductive elimination or insertion to form intermediates **S** and **T**, (v) the second C–H bond activation, and (vi) reductive elimination to form the final product **2** (see Scheme 3).⁴ However, this proposed mechanism left several key questions unanswered, including (a) What is the nature of the catalytic active species?, (b) What are the barriers, reaction energies, and the rate-limiting and selectivity-determining steps of the reaction?, (c) What are the factors controlling the stability and formation of the proposed palladacycle and aryne intermediates?, and (d) What is a true nature of the proposed intermediates. Furthermore, it is critical to elucidate roles of the base in the reaction, and understand reasons of diminishing of the yield of the reaction upon changing the base from Cs₂CO₃ to Na₂CO₃.

In order to answer these questions and improve the efficiency of the Pd-catalyzed annulative chlorophenylene dimerization, we launched a comprehensive computational and mechanistic study. Briefly, we have elucidated the mechanism of the Pd-catalyzed annulative chlorophenylene

dimerization, and shed lights on the role of the base in the reaction. We expected that the findings of these computational studies will enable the further development of the synthesis of versatile PAHs.

Scheme 3. The Proposed Mechanism for the Pd-catalyzed Annulative Chlorophenylene (**1**) Dimerization Reaction.



Computational Methods

Geometry optimizations and frequency calculations for all reported structures were performed with the Gaussian 09 suite of programs⁸ at the B3LYP-D3BJ/[6-31G(d,p) + Lanl2dz (Pd, Cs)] level of theory with the corresponding Hay-Wadt effective core potential for Pd and Cs, and Grimme's empirical dispersion-correction (D3) with Becke-Johnson (BJ) damping for B3LYP⁹ (below, called as B3LYP-D3BJ/BS1). Frequency analysis was used to characterize each minimum with zero imaginary frequency and each transition state (TS) structure with only one imaginary frequency. Intrinsic reaction coordinate (IRC) calculations were performed for all TSs to ensure their true nature. Bulk solvent effects were incorporated for all calculations using the self-consistent reaction field polarizable continuum model (IEF-PCM).¹⁰ As a solvent we chose dichloromethane (with dielectric constant of 8.93) which is a closest alternative of the cyclopentyl-methyl-ether (CPME, with dielectric constant of 4.76) used in the experiments. The calculated Gibbs free energies are corrected to the experimentally-used temperature, 413.15 K (G_{413}). In the text, the B3LYP-D3BJ/BS1 results at 413.15 K (G_{413}) will be primarily used, while the G_{298} values will be discussed where that will be appropriate and will be included in Supporting Information.

In order to validate the [B3LYP-D3BJ]/BS1 calculated results we also performed single point energy calculations (i.e. at the [B3LYP-D3BJ]/BS1 calculated geometries) for selected intermediates and transition states by utilizing an extended basis set BS2 = 6-311+G(d,p) + SDD (Pd and Cs), and Stuttgart effective core potential for Pd and Cs¹¹ (below, called as [B3LYP-D3BJ]/BS2 approach). Since both the [B3LYP-D3BJ]/BS2 and [B3LYP-D3BJ]/BS1 methods led to same conclusions, here we discuss only [B3LYP-D3BJ]/BS1 results because of their

completeness, while the data obtained for the selective structures at the [B3LYP-D3BJ]/BS2 are included in Supporting Information.

Results and Discussion

A. Catalyst generation and the first C–Cl bond addition. As it could be expected, the mixing of PdCl₂ with phosphine ligands and base leads to formation of the Pd(0)-phosphine pre-reaction complex. Previously, the role of phosphine ligands in the Pd(0)/Pd(II) oxidation by aryl halides has been extensively studied.¹² Our computational data, presented below, are consistent with findings of previous investigations and show that in the mixture of Pd[PⁿBu(Ad)₂]₂ (below, called as **PdP2**) and 2-Cl-diphenyl (**Cl-diPh** or chlorophenylene, **1a**), the C–Cl oxidative addition does not occur prior to the dissociation of one of phosphine ligands, i.e. formation of the mono-phosphine Pd-complex, **PdP**.

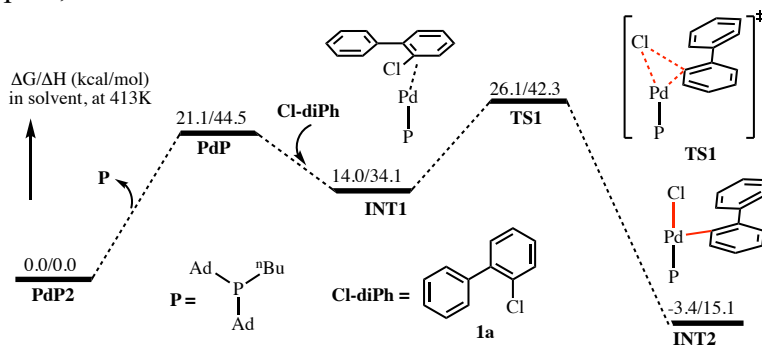


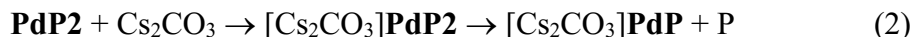
Figure 1. The calculated free energy surface of the **PdP2** + **1a** oxidative addition reaction.

As shown in Figure 1: (a) the **PdP2** → **PdP** + **P** reaction is endergonic by 21.1 kcal/mol, (b) the coordination of one equivalent of **1a** to Pd-monophosphine complex **PdP** is 7.1 kcal/mol exergonic, and (c) the C–Cl bond activation at the transition state **TS1** requires 12.1 kcal/mol free energy barrier calculated relative to the pre-reaction complex, **INT1**. The overall process



requires a total of 26.1 kcal/mol free energy and is exergonic by 3.4 kcal/mol.

However, until now, little is known about the impact of base on the Pd(0)/Pd(II) oxidation by aryl halides. Partly, because this is a very complex issue and depends both on solubility and aggregation states of the base in the course of the reaction. Here, in our computational study, we assumed that Cs-carbonate is soluble in experimental conditions, i.e. the Cs₂CO₃ molecules exist in the reaction mixture. In this case, the initial step of the above discussed C–Cl oxidative addition is found to be coordination of base to **PdP2**: the **PdP2** + Cs₂CO₃ → [Cs₂CO₃]**PdP2** reaction is calculated to be exergonic by 8.3 kcal/mol (see Figure 2a). The subsequent phosphine dissociation from the resulting [Cs₂CO₃]**PdP2** adduct is only 5.5 kcal/mol endergonic, instead of 21.1 kcal/mol for the base-free process. Thus, in the presence of Cs₂CO₃, the formation of mono-phosphine complex, i.e. reaction



is 2.8 kcal/mol exergonic. Close analysis of [Cs₂CO₃]**PdP** (below called as compound **A_Cs**) revealed the presence of two stabilizing interactions: i) an unusual Pd–Cs (which has been previously reported by Schaefer and coworkers¹³), and ii) Pd–CO₃ interactions with distances of Pd–Cs = 3.823 Å and Pd–O = 2.138 Å (see Figure 2b). Thus, the presence of Cs₂CO₃ in the reaction

mixture changes the nature of catalytic active species from **PdP** to $[\text{Cs}_2\text{CO}_3]\text{PdP}$ (i.e. **A_Cs**), and makes its formation energetically favorable.

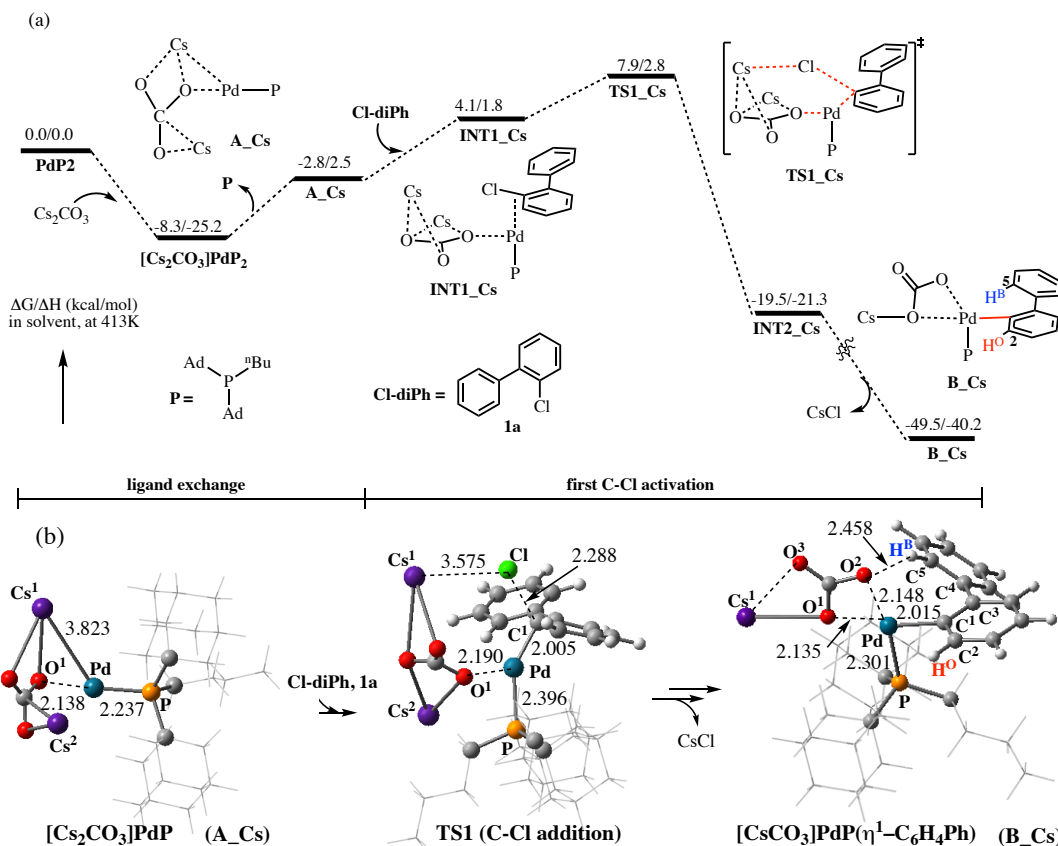
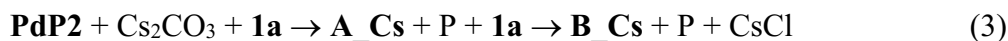


Figure 2. (a) Free energy surface for ligand exchange and first C–Cl bond addition steps; (b) Structures and important geometry parameters (distances are in Å) of the reactant $[\text{Cs}_2\text{CO}_3]\text{PdP}$, C–Cl addition transition state **TS1_Cs**, and product of the 2-electron oxidation reaction $[\text{Cs}_2\text{CO}_3]\text{PdP} + \mathbf{1a} \rightarrow [\text{CsCO}_3]\text{Pd}^{\text{II}}\text{P}(\eta^1\text{-C}_6\text{H}_4\text{Ph}) + \text{CsCl}$.

The subsequent C–Cl oxidative addition by intermediate **A_Cs** (at the transition state **TS1_Cs**, see Figure 2) occurs with a 10.7 kcal/mol free energy barrier, relative to **A_Cs** + **1a**. Intriguingly, in the presence of Cs_2CO_3 , the Pd(0) and Cs-cation act collectively to activate the C–Cl bond. Subsequent IRC calculations confirm that the product of the C–Cl bond cleavage is complex $[(\text{ClCs})(\text{CsCO}_3)]\text{Pd}^{\text{II}}\text{P}(\eta^1\text{-C}_6\text{H}_4\text{Ph})$, **INT2_Cs**. Thus, while the C–Cl cleavage at the **TS1_Cs** leads to two-electron, i.e. Pd(0)/Pd(II), oxidation of Pd-center, it results in the formation of Pd–C(aryl), Pd–O(from CO_3) and Cs–Cl bonds, but Pd–Cl bond. The resulted Pd^{II} intermediate **INT2_Cs** is metastable: It releases CsCl molecule and rearranges to product complex $[\text{CsCO}_3]\text{Pd}^{\text{II}}\text{P}(\eta^1\text{-C}_6\text{H}_4\text{Ph})$, **B_Cs**.¹⁴ The overall reaction



is highly (by 49.5 kcal/mol) exergonic.

In summary, if Cs-carbonate is soluble at the utilized reaction conditions, then the chlorophenylene C–Cl addition in the mixture of **PdP2**, **1a** and Cs_2CO_3 is a highly exergonic process, proceeds via the “base-assisted oxidative addition” mechanism (which resembles the concerted nucleophilic aromatic substitution $\text{S}_{\text{N}}\text{Ar}$ mechanism¹⁵) and leads to intermediate

$[(\text{CsCO}_3)]\text{Pd}^{\text{II}}\text{P}(\eta^1\text{-C}_6\text{H}_4\text{Ph})$, **B_Cs**. Importantly, the presence of Cs_2CO_3 in the reaction mixture is critical for success of this step of the studied Pd-catalyzed annulative coupling reaction. It not only facilitates the active catalyst generation, but also directly participates in the C–Cl bond cleavage, and introduces mechanistic switch of Pd(0)/Pd(II) oxidation from the traditional oxidative addition to the “base-assisted oxidative addition.”

B. Formation of the Palladacycle and Pd-aryne intermediates. Previously,⁴ the activation of either C–H^B (i.e. “bay”) or C–H^O (i.e. “ortho”) bonds – leading to the formation of palladacycle and Pd-aryne intermediates, respectively – were proposed to be next, but alternative, steps of the studied Pd-catalyzed annulative chlorophenylene dimerization reaction. However, our extensive calculations have convincingly shown that the next step of this reaction, initiated from the intermediate **B_Cs** can be very complex and is subject to the chemical nature of both the used base and its aggregation state (i.e. full or partial solubility), as well as the electronic properties of the intermediate species (for example, complex **B_Cs**). Indeed, if the base molecule has a low aggregation capability (i.e. high solubility), then the Pd-aryne and palladacycle formation can be directly initiated from the complex **B_Cs**. In contrast, if the base molecule has a relatively higher aggregation capability in the presence of intermediate **B_Cs** (i.e. if it is prone to the aggregate formation), then prior the C–H bond activation complex **B_Cs** may add one (or several, which were not pursued) more Cs_2CO_3 molecule(s) to form “Cs-cluster-complex”. For example, calculations show that the addition of one molecule of Cs_2CO_3 to intermediate **B_Cs**, i.e. reaction **B_Cs** + $\text{Cs}_2\text{CO}_3 \rightarrow [\text{Cs}_3(\text{CO}_3)_2]\text{Pd}^{\text{II}}\text{P}(\eta^1\text{-C}_6\text{H}_4\text{Ph})$, **C_Cs**, is exergonic by 11.4 kcal/mol. As seen in Figure 3, the generated $[\text{Cs}_3(\text{CO}_3)_2]$ fragment of **C_Cs** has a well-defined “cage-type” of structure and is bidentately coordinated to Pd-center with the Pd–O¹ = 2.159 Å and Pd–O² = 2.159 Å bonds. Previously, we have reported similar “Cs-cluster-complex” in the study of Ni-*dcype* catalyzed C–H/C–O coupling of benzoxazole and naphthalen-2-yl pivalate in the presence of Cs_2CO_3 .¹⁶

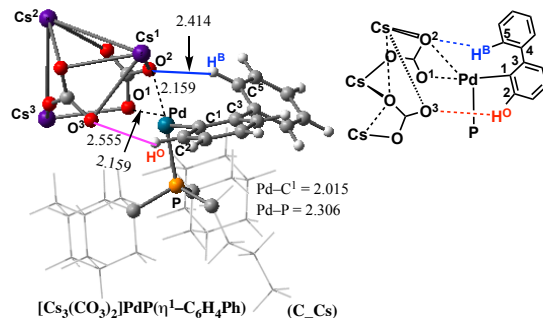


Figure 3. The proposed “Cs-cluster-complex” $[\text{Cs}_3(\text{CO}_3)_2]\text{PdP}(\eta^1\text{-C}_6\text{H}_4\text{Ph})$ (i.e. **C_Cs**) with its important geometry parameters (distances are in Å).

Thus, next step of the studied Pd-catalyzed annulative chlorophenylene dimerization reaction can be initiated from either **B_Cs** or **C_Cs** intermediates with CsCO_3 or $\text{Cs}_3(\text{CO}_3)_2$ fragments, respectively. Below, we discuss mechanism of the reaction initiated from the “Cs-cluster-complex” $[\text{Cs}_3(\text{CO}_3)_2]\text{Pd}^{\text{II}}\text{P}(\eta^1\text{-C}_6\text{H}_4\text{Ph})$, **C_Cs**. Nevertheless, we also studied mechanism of the Pd-catalyzed annulative chlorophenylene dimerization reaction directly initiated from the complex **B_Cs** with the CsCO_3 fragment, and included all data and related discussion into the Supporting Information (Figure S1). Here, we will compare differences of these two sets of reactions if that would be critically important.

Close examination of **C_Cs** shows that the O²-center of the bidentately coordinated CO₃-group and O³-center of another CO₃-group are within hydrogen bonding distances (O²-H^B = 2.414 Å and O³-H^O = 2.555 Å) from the phenyl groups of the di-phenyl ligand. Thus, these atoms can act as proton acceptors either from the C⁵-H^B (leading to the palladacycle intermediate) or C²-H^O (leading to the Pd-aryne formation) bonds. Therefore, below, we study the palladacycle and Pd-aryne formation in the cluster-complex **C_Cs**. Here, we wish to mention that the calculations (see Figure S2 in Supporting Information) have discounted the second C-Cl bond activation by intermediate **C_Cs** because of the required extremely large energy barrier.

B.1. Palladacycle formation. In intermediate **C_Cs**, the palladacycle formation occurs via the concerted-metalation-deprotonation (CMD)¹⁷ of the C⁵-H^B bond by the O²-center of the CO₃-unit at the transition state **TS2_Cs** (see Figure 4). Consistently, in **TS2_Cs** the weak Pd-O² bond is completely broken (see Figures 3 and 4), the activated C⁵-H^B bond is elongated to 1.393 Å, and, consequently, the emerging O²-H^B and Pd-C⁵ bonds are formed with 1.297 and 2.317 Å bond distances, respectively. The calculated free energy barrier is 31.4 kcal/mol, relative to pre-reaction complex **C_Cs**.

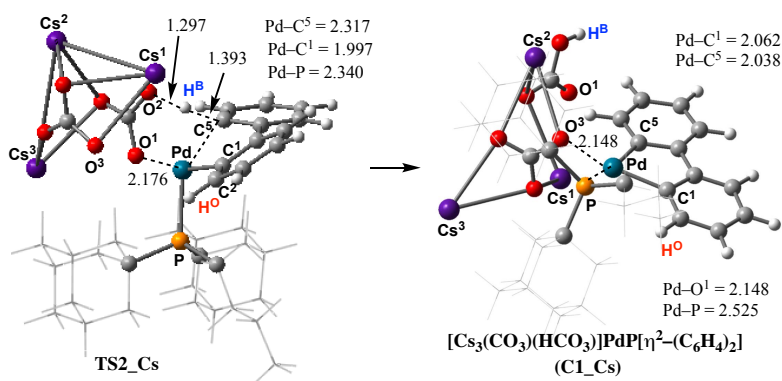


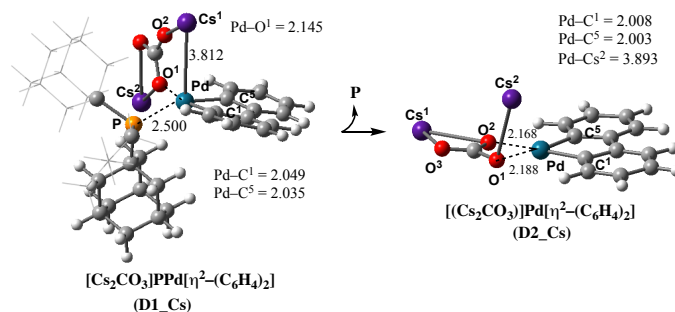
Figure 4. Transition state and product of the palladacycle formation in [Cs₃(CO₃)₂]**PdP**(η¹-C₆H₄Ph) with their important geometry parameters (distances are in Å).

The IRC calculations from the transition state **TS2_Cs** led to intermediate [Cs₃(CO₃)(HCO₃)]Pd^{II}P[η²-(C₆H₄)₂] (**C1_Cs_cf1**, see Figure S3 of Supporting Information), which later isomerized to its most stable conformer **C1_Cs**. The overall cyclopalladation reaction is found to be endergonic by only 4.2 kcal/mol, relative to complex **C_Cs**. In order for the reaction to proceed further the resulting palladacycle **C1_Cs** should either react with another equivalent of substrate with less than 27.2 kcal/mol energy barrier (this energy is required for the reverse reaction) or undergo another kinetically and thermodynamically favorable transformations. Calculations show that reaction of **C1_Cs** with the second equivalent of substrate **1a** requires a significant free energy barrier and cannot be next step of the reaction (see Figure S3 of Supporting Information).

Satisfyingly, we have identified multiple potentially enabling transformations (see Scheme S1 of Supporting Information) leading to the thermodynamically most favorable products [Cs₂CO₃]**PPd**^{II}[η²-(C₆H₄)₂], **D1_Cs**, and [Cs₂CO₃]**Pd**^{II}[η²-(C₆H₄)₂], **D2_Cs** (see Figure 5), both of them are result of replacement of the protonated base, i.e. the [Cs₃(CO₃)(HCO₃)] fragment, by another equivalent of Cs₂CO₃ [this can be considered as one of the possible ways of proton (or acid) removal from the catalytic mixture which previously was proposed to facilitate forward reaction¹⁸]. Calculations show that regardless of their formation pathways (dissociative or

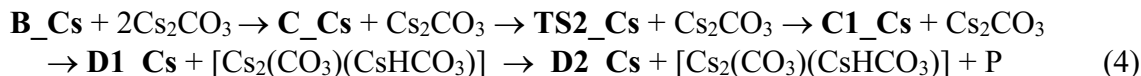
associative) the resulting intermediates **D1_Cs** and **D2_Cs** are thermodynamically favorable by 6.6 and 10.4 kcal/mol, respectively (relative to the initial complex **C1_Cs**): thus, the $[\text{Cs}_3(\text{CO}_3)(\text{HCO}_3)]$ -to- Cs_2CO_3 ligand exchange in complex **C1_Cs** is a facile and thermodynamically favorable process and provides much needed driving force to the palladacycle formation in course of the Cs-carbonate mediated and Pd-catalyzed annulative chlorophenylene dimerization reaction.

Figure 5. The calculated thermodynamically most favorable $[\text{Cs}_2\text{CO}_3]\text{PPd}^{\text{II}}[\eta^2-(\text{C}_6\text{H}_4)_2]$, **D1_Cs**, and $[\text{Cs}_2\text{CO}_3]\text{Pd}^{\text{II}}[\eta^2-(\text{C}_6\text{H}_4)_2]$, **D2_Cs**, palladacycles resulted by the $[\text{Cs}_3(\text{CO}_3)(\text{HCO}_3)]$ -to- Cs_2CO_3 ligand exchange in the complex **C1_Cs**.



Comparison of these intermediates shows that dissociation of **P** ligand from $[\text{Cs}_2\text{CO}_3]\text{PPd}^{\text{II}}[\eta^2-(\text{C}_6\text{H}_4)_2]$, **D1_Cs**, to form complex $[\text{Cs}_2\text{CO}_3]\text{Pd}^{\text{II}}[\eta^2-(\text{C}_6\text{H}_4)_2]$, **D2_Cs**, is thermodynamically slightly favorable and may proceed via a lower energy barrier (which was not identified). A close examination shows that the entropy is a major factor in this favorable phosphine dissociation.

In summary (see Figure 6), the palladacycle formation in **B_Cs**, i.e. reaction:



is kinetically and thermodynamically feasible: indeed, the **D1_Cs** and **D2_Cs** formations are 13.8 and 17.6 kcal/mol exergonic and proceed via overall 31.4 kcal/mol free energy barrier at the transition state **TS2_Cs**. Thus, the **D1_Cs** and **D2_Cs** complexes are the products of the cyclopalladation process.

Data presented in the Supporting Information (Figure S1) for the palladacycle formation directly from intermediate **B_Cs** (i.e. without the “Cs-cluster complex” formation) show that it proceeds via a very similar mechanism with a 30.5 kcal/mol free energy barrier for the C–H activation and is exergonic by 7.7 kcal/mol. Comparison of these data with those (i.e. with 31.4 and 17.6 kcal/mol, respectively) for the reaction occurring via the “Cs-cluster complex” formation pathway shows that the proposed “Cs-cluster complex” formation has no critical impact to the palladacycle formation from the product of the first C–Cl activation, i.e. intermediate **B_Cs**. *Thus, if Cs-carbonate is soluble under the used experimental conditions to drive the first C–Cl activation in the Pd-catalyzed annulative chlorophenylene dimerization reaction, the following palladacycle formation is independent from the aggregation state of base.*

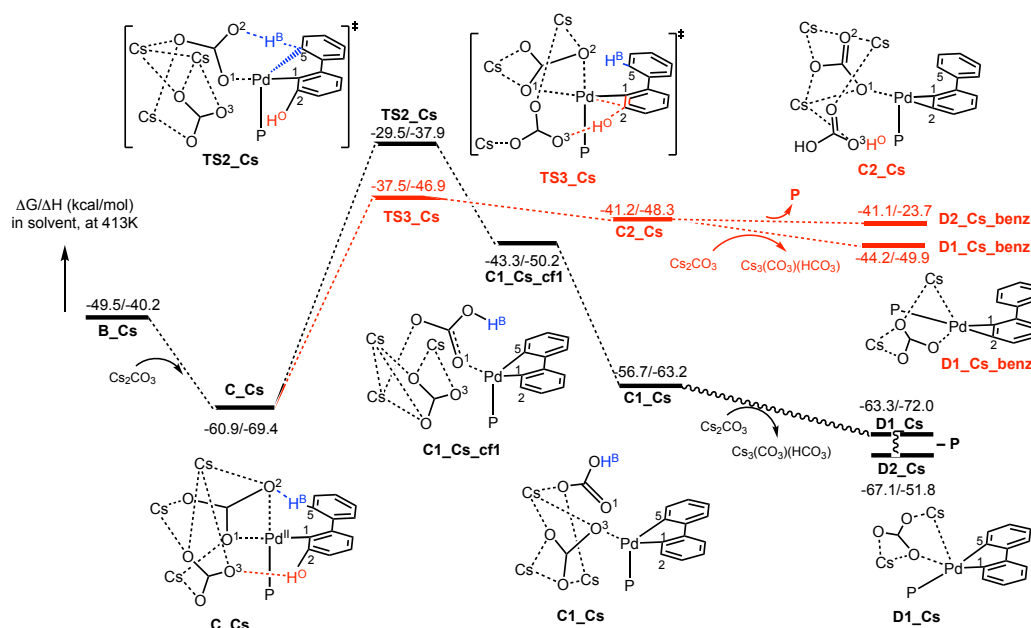


Figure 6. Free energy surfaces of the palladacycle (in black) and Pd-aryne (in red) formation.

B.2. Palladium-aryne formation. As discussed above, the alternative pathway initiated from **C_Cs** (or **B_Cs**, see above) is the formation of Pd-aryne complex $[\text{Cs}_2(\text{CO}_3)(\text{CsHCO}_3)]\text{PdP}(\eta^2\text{-C}_6\text{H}_3\text{Ph})$, **C2_Cs**, that occurs by deprotonation of the $\text{C}^2\text{-H}^0$ bond by O^3 -center of another (i.e. second) CO_3 -group of the $\text{Cs}_3(\text{CO}_3)_2$ fragment (see Figures 3 and 7, as well as Scheme 4). Pd-aryne is not a common intermediate in the Pd(II)-catalyzed C–H functionalization chemistry but has been extensively studied and proposed in various organic and organometallic transformations.¹⁹ The performed IRC calculations from the associated transition state **TS3_Cs** confirmed that the Pd-aryne formation occurs via an asymmetric (i.e. “proton abstraction then Pd–C bond formation”) mechanism (see Scheme 4 for proposed concept of the aryne formation based on the performed calculations) with 23.4 kcal/mol free energy barrier, calculated relative to **C_Cs**. At the transition state **TS3_Cs**, the $\text{C}^2\text{-H}^0$ bond is elongated (to 1.495 Å) and the nascent $\text{O}^3\text{-H}^0$, Pd– C^2 and $\text{C}^1\equiv\text{C}^2$ bonds are formed with 1.144, 2.918 and 1.391 Å bond distances, respectively. In the product complex **C2_Cs**, the aryne ligand (i.e. $\text{C}_6\text{H}_3\text{Ph}$) is coordinated to Pd-center via its $\text{C}^1\equiv\text{C}^2$ bond (with $\text{C}^1\text{-C}^2 = 1.354\text{ Å}$). Based on the analyses (see Scheme 4) we conclude that complex **C2_Cs** is a Pd(0)-aryne complex, the calculated geometry parameters of which are in good agreement with those $[\text{Pd}-\text{C}^1=2.042(6)\text{ Å}$, $\text{Pd}-\text{C}^2=2.032(6)\text{ Å}$, and $\text{C}^1\text{-C}^2=1.324(8)\text{ Å}$] reported previously for the $\text{Pd}(\eta^2\text{-C}_6\text{H}_4)(\text{PCy}_3)_2$ complex in X-ray studies.^{19a}

As shown in Figure 6, the Pd-aryne formation is 19.7 kcal/mol endergonic (relative to pre-reaction complex **C_Cs**). All our efforts to identify transformation that can provide additional thermodynamic stability (i.e. driving force) to the formed Pd-aryne intermediate were unsuccessful. The dissociation of phosphine ligand from $[\text{Cs}_3(\text{CO}_3)(\text{HCO}_3)]\text{PdP}(\eta^2\text{-C}_6\text{H}_3\text{Ph})$ to generate **D2_Cs_benz** is a thermoneutral process, and the $[\text{Cs}_3(\text{CO}_3)(\text{HCO}_3)]$ -to- Cs_2CO_3 exchange to form **D1_Cs_benz** is only 3.0 kcal/mol exergonic. Furthermore, moderate (with a 47.5 kcal/mol free energy) stability of the formed **D1_Cs_benz** complex relative to the aryne dissociation [i.e. relative to the $[\text{Cs}_2(\text{CO}_3)]\text{PdP} + \text{C}_6\text{H}_3\text{Ph}$ dissociation limit], also excludes the formation of free aryne molecule during this reaction. Thus, it is conceivable to conclude that participation of the Pd-aryne complex, or its derivatives, in the studied Pd-catalyzed and Cs-carbonate mediated

annulative chlorophenylene dimerization is less likely: even though it occurs with a lower (23.4 vs 31.4 kcal/mol) free energy barrier than the competing palladacycle formation, it lacks the driving force to proceed.

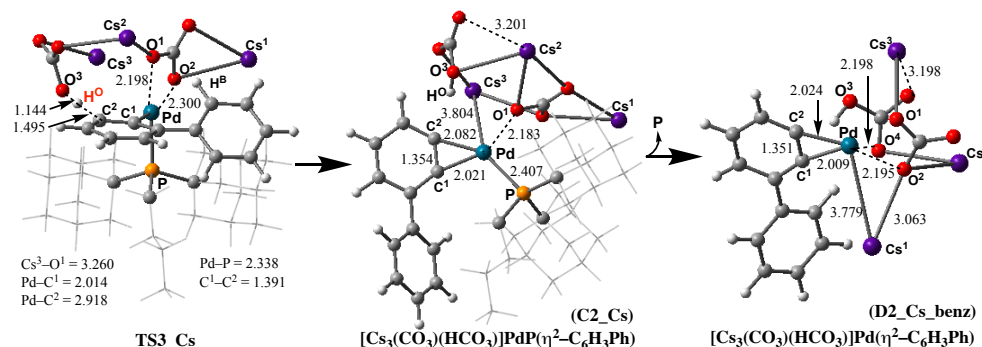


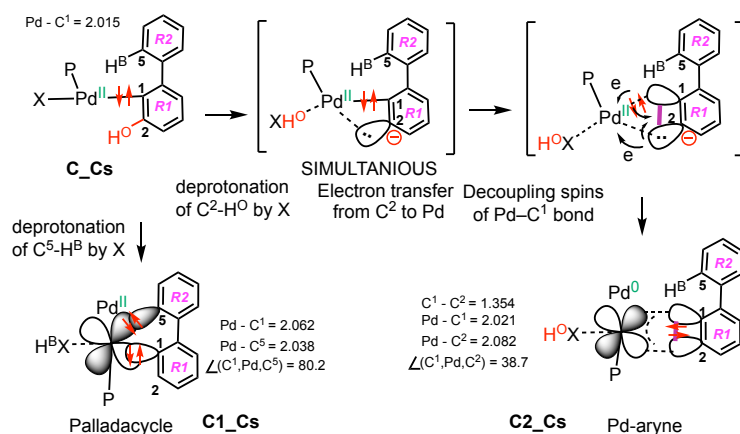
Figure 7. Transition state and intermediates of the Pd-aryne formation in $[\text{Cs}_3(\text{CO}_3)_2]\text{PdP}(\eta^1\text{-C}_6\text{H}_4\text{Ph})$ with their important geometry parameters (distances are in Å).

In order to rationalize the difference in the calculated energy barriers and thermodynamicity of the palladacycle and Pd-aryne formation reactions in the Pd-catalyzed and Cs-carbonate mediated annulative chlorophenylene dimerization, we closely compare the structures of the associated intermediates, products and transition states. Analyses shown that these differences are due to several major factors. First, C-H^{O} bond is more activated than C-H^{B} bond because of direct bonding of cationic Pd(II) to the phenyl ring R1 of **C_Cs** with the C-H^{O} bond (see Scheme 4). Second, in order to participate in the C-H^{B} activation, O^2 -center has to be dissociated from the Pd(II)-center which introduces large distortion to the well-defined square-planar geometry of the Pd(II)-center (see Figures 4 and 7, and Figure S6 in Supporting Information). Third, difference of the Pd-ligand bonding in the **D1_Cs** and **D1_Cs_benz** products: as shown in Scheme 4, although the Pd - C bond distances are very similar in **D1_Cs** and **D1_Cs_benz**, the much shorter $\text{C}^1 - \text{C}^2$ bond distance (and smaller $[\text{C}^1, \text{Pd}, \text{C}^2]$ bond angle) in **D1_Cs_benz** induces a ring-strength and destabilizes Pd-C bonds.

Data presented in Supporting Information (Figure S4) for the Pd-aryne formation directly from the intermediate **B_Cs** (i.e. without the “Cs-cluster complex” formation) show that it proceeds with a 38.6 kcal/mol energy barrier and is endergonic by 26.4 kcal/mol. Comparison of these data with those (23.4 and 19.7 kcal/mol, respectively) for the reaction initiated from the “Cs-cluster complex” **C_Cs** shows that the “Cs-cluster complex” formation may significantly facilitate the Pd-aryne formation process. *Thus, based on the above presented findings, while the palladacycle formation in intermediate C_Cs is independent from the aggregation state of base, the Pd-aryne formation turns to be facilitated by the “Cs-cluster complex” formation (i.e aggregation state of base).*

In summary, above presented data clearly show that the Pd-catalyzed and Cs-carbonated mediated chlorophenylene C-Cl and C-H bond activation leads to the thermodynamically more favorable palladacycle intermediates **D1_Cs** and **D2_Cs**.

Scheme 4. Selected Geometry Parameters (distances are in Å, and angles are in deg.) and Schematic Presentation of the Stable Palladacycle (**C1_Cs**) and Pd-aryne (**C2_Cs**) Complexes, as well as a Concept of the Pd-aryne Formation. Here X Stands for the $[\text{Cs}_3(\text{CO}_3)_2]$ Fragment.



C. The second equivalent of substrate addition to the palladacycle or competing $Pd^{II}/Pd^{II} \rightarrow Pd^0/Pd^{IV}$ transmetalation. As anticipated, the next step of the reaction is the formation of intermediate $[CsCO_3]Pd^{IV}[\eta^2-(C_6H_4)_2](\eta^1-C_6H_4Ph)$ (**INT4-Cs**). This, in general, can be achieved either via the second equivalent of substrate coordination to the energetically most stable palladacycle **D2-Cs** and following C-Cl bond activation or by the $Pd^{II}/Pd^{II} \rightarrow Pd^0/Pd^{IV}$ transmetalation.

Calculations show that the substrate coordination to **D2-Cs** leads to the formation of intermediate $[Cl-C_6H_4Ph]-(Cs_2CO_3)Pd^{II}[\eta^2-(C_6H_4)_2]$, **INT3-Cs**, which may have several isomers. Since **INT3-Cs** is only 0.9 kcal/mol stable relative to the reactants **D2-Cs** + **1a**, and unlikely to critically contribute to the reaction outcome, for the sake of simplicity, we report all of its calculated isomers in the Supporting Information (Figure S7). Briefly, in **INT3-Cs** (a) Cl-atom weakly interacts with one of the Cs-cations, and (b) the phosphine ligand dissociates with no (or insignificant) energy barrier.

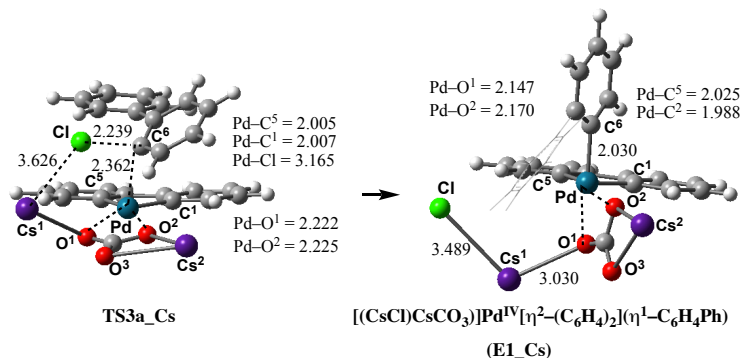


Figure 8. Structures along with important geometry parameters (distances are in Å) of the transition state **TS3a-Cs** and product **E1-Cs** of the second C-Cl bond activation by palladacycle **D2-Cs**.

The following C-Cl cleavage (i.e. in **INT3-Cs**) occurs, again, via the “*base-assisted oxidative addition*” mechanism at the transition state **TS3a-Cs** and leads to Pd^{IV} -complex $[(CsCl)CsCO_3]Pd^{IV}[\eta^2-(C_6H_4)_2](\eta^1-C_6H_4Ph)$ (**E1-Cs**) (see Figure 8). The associated free energy barrier with this process is 35.8 kcal/mol, and reaction **INT3-Cs** $\rightarrow$ **E1-Cs** is exergonic by 1.9 kcal/mol (Figure 9).²⁰ Comparison of this barrier with 31.4 kcal/mol (or 30.5 kcal/mol for the pathway occurring without the “Cs-cluster complex” formation) free energy barrier required for the first C-Cl cleavage (i.e. for the $Pd(0)/Pd(II)$ oxidation) show that the second C-Cl bond

addition (*i.e.* the Pd(II)/Pd(IV) oxidation) is more energy demanding process. From the Pd(IV)-complex **E1_Cs**, the CsCl dissociation occurs with only 0.9 kcal/mol free energy and leads to the **INT4_Cs** intermediate.²¹

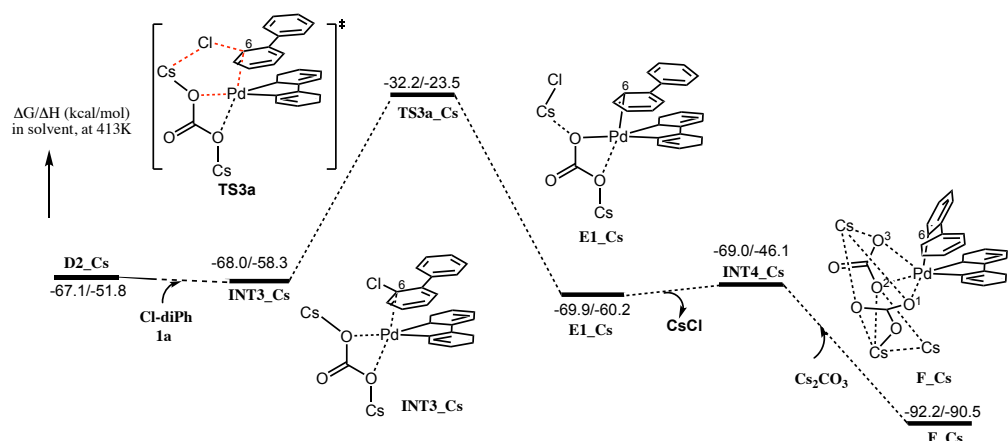
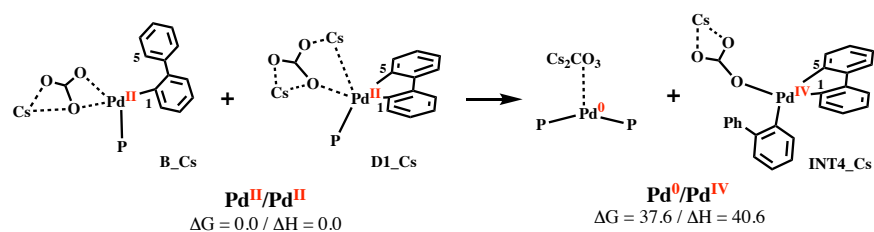


Figure 9. Free energy surface for the second C–Cl activation by the **D2_Cs** intermediate.

The energetically most favorable, among the alternative Pd^{II}/Pd^{II} → Pd⁰/Pd^{IV} transmetalation processes, is presented in Scheme 5. Calculations show that even this process is thermodynamically more demanding than the substrate coordination to **D2_Cs** and following C–Cl bond cleavage pathway discussed above. Therefore, below we will not discuss the Pd^{II}/Pd^{II} → Pd⁰/Pd^{IV} transmetalation in more details, while we include all related structures to Supporting Information together with their energies.

Scheme 5. Schematic Presentation of the Energetically Most Favorable Pd^{II}/Pd^{II} → Pd⁰/Pd^{IV} Transmetalation Reaction. Energies Are Given in kcal/mol.

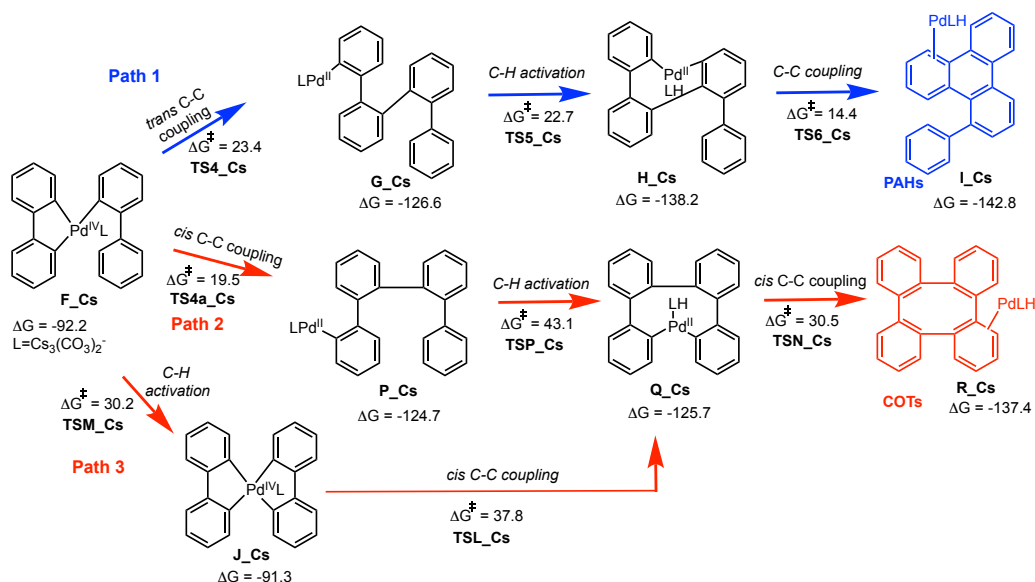


D. Product Formation.

In the presence of base with a relatively higher aggregation capability, intermediate **INT4_Cs** may rearrange to the complex [Cs₃(CO₃)₂]Pd^{IV}[η²-(C₆H₄)₂](η¹-C₆H₄Ph) (**F_Cs**): the reaction **INT4_Cs** + Cs₂CO₃ → **F_Cs** is calculated to be exergonic by 23.2 kcal/mol. Thus, product formation, either cyclooctatetraene (COT) or polycyclic aromatic hydrocarbon (PAH) (see structures **4** and **5** in Scheme 2a), can be initiated from either intermediate **INT4_Cs** (if the base has a *low* aggregation capability) or complex **F_Cs** (if the existing base molecules *can* form higher-level aggregates).

Scheme 6. Comparison of Three Different Reaction Pathways Leading to the PAH (path-1, blue) and COT (path-2 and path-3, red) Products. Energies (given in kcal/mol) Are Calculated Relative

to the (a) **PdP2** + 2xCs₂CO₃ + 2x[Cl-C₆H₄Ph] Limit for Intermediates and Products, and (b) Corresponding Pre-reaction Complexes for the Transition States.



Our extensive studies have shown that PAH formation in **F_Cs** (we also studied PAH and COT formations initiated from the complex **INT4_Cs**, see Figure S10 in Supporting Information) proceeds via path-1 (see Scheme 6, also see PES of this reaction in Figure S11 of Supporting Information) that includes reductive elimination (i.e. *trans* C–C coupling at the transition state **TS4_Cs**), C–H bond activation (at the transition state **TS5_Cs**), and the second C–C coupling (at the transition state **TS6_Cs**) steps. The first C–C coupling, i.e. **F_Cs** $\rightarrow$ **TS4_Cs** $\rightarrow$ **G_Cs** or Pd(IV)/Pd(II) 2-electron reduction, requires 23.4 kcal/mol free energy barrier and is exergonic by 12.1 kcal/mol. [These values are 18.3 kcal/mol and 28.0 kcal/mol, respectively, if this process will be initiated directly from the **INT4_Cs**]. The following C–H bond activation and the second C–C coupling occur with the 22.7 and 14.4 kcal/mol energy barriers and lead to the final product **I_Cs** [These values are 31.8 and 5.8 kcal/mol, respectively, if this process is initiated directly from the **INT4_Cs**]. As shown in Figure 10, in the product complex **I_Cs**, Pd(0)-center is only loosely coordinated to the formed PAH molecule. Overall PAH formation from intermediate **F_Cs** is exergonic by 50.6 kcal/mol (57.5 kcal/mol, if this process is initiated directly from the **INT4_Cs**).

The above presented data show that (a) if the reaction proceeded via the “Cs-cluster complex” formation pathway (initiated from intermediate **F_Cs**), it would require a 7-8 kcal/mol smaller energy barrier and would be *ca* 7 kcal/mol less exergonic than if that will proceed via the “no Cs-cluster complex” pathway (initiated from directly from the intermediate **INT4_Cs**). Regardless, the second C–Cl activation step remains the rate-limiting step of entire Cs-carbonate mediated and Pd-catalyzed annulative chlorophenylene dimerization reaction.

Alternative product of the studied annulative chlorophenylene dimerization reaction could be cyclooctatetraene (called as product **R_Cs**), which, in general, is formed from intermediate **F_Cs** (with “Cs-cluster complex”) or **INT4_Cs** (if reaction proceeds via without “Cs-cluster complex” formation mechanism) via paths 2 and 3, as shown in Scheme 6. Path-2 follows via the *cis* C–C coupling (at the transition state **TS4a_Cs**), the C–H bond activation (at the transition state **TSP_Cs**), and the second *cis* C–C coupling (at the transition state **TSN_Cs**). An alternative pathway, i.e. path-3, starts with the C–H bond activation (at the transition state **TSM_Cs**), and

follows via the two consequent *cis* C–C coupling steps (at the transition states **TSL_Cs** and **TSN_Cs**). Calculations show that paths 2 and 3 occur with very high free energy barriers at the C–H activation (with 43.1 and 40.5 kcal/mol energy barriers, if the reaction is initiated from **F_Cs** and **INT4_Cs**, respectively) and the second reductive elimination (37.8 and 36.2 kcal/mol, if the reaction will be initiated from **F_Cs** and **INT4_Cs**, respectively) steps, respectively.

Based on the above presented data it is conceivable to conclude: the COT formation cannot compete with the PAH formation in the studied Pd-catalyzed annulative chlorophenylene dimerization in the presence of Cs_2CO_3 , regardless of aggregation states of the base. This finding is consistent with experiments showing no COT products at the utilized conditions (see Supporting Information for more details).

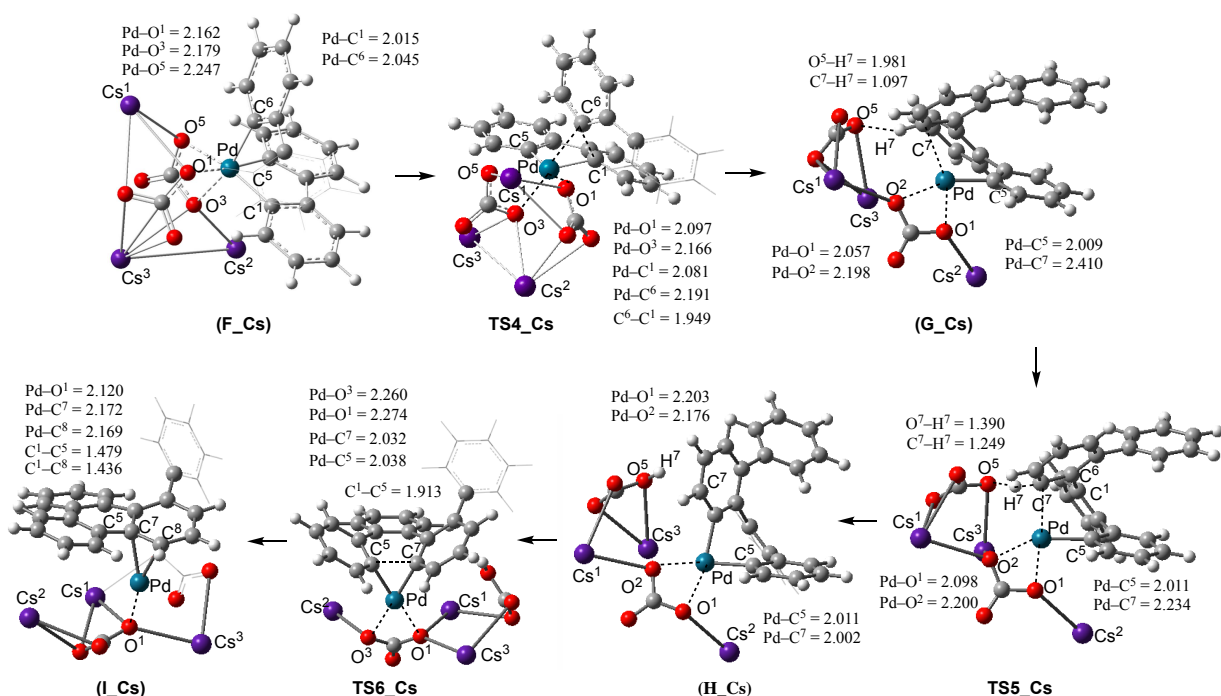


Figure 10. Structures and important geometry parameters (distances are in Å) of reactants, intermediates, transition states and products of the energetically most favorable polyaromatic hydrocarbons (PAHs) formation pathway, i. e. path-1.

E. Impact of the $\text{Cs}_2\text{CO}_3 \rightarrow \text{Na}_2\text{CO}_3$ substitution on the reaction outcome. To validate, once again, the role of base in the Pd-catalyzed annulative chlorophenylene dimerization, we calculated free energy surfaces of all elementary reactions, reported above, also in the presence of Na_2CO_3 . Here, we chose Na_2CO_3 because experiments have shown that the yield of the reaction reduces from 82% to 0% upon the $\text{Cs}_2\text{CO}_3 \rightarrow \text{Na}_2\text{CO}_3$ substitution. In our computational modeling, at first, we assumed the Na-carbonate to be soluble and studied the impact of the presence of Na_2CO_3 in the reaction mixture to the reaction outcome.

Briefly, we found that while the coordination of Na_2CO_3 to complex **PdP2**, unlike Cs_2CO_3 (for comparison, see Figure 2a) is endergonic (by 9.5 kcal/mol), it also facilitates the phosphine dissociation from **PdP2**, and consequently, the formation of active catalyst (See Figure S14 in Supporting Information). Indeed, the free energy required for one of phosphine ligands dissociation from **PdP2** is almost two times smaller in the presence of Na_2CO_3 than in the absence of Na_2CO_3 , 10.4 kcal/mol vs 21.1 kcal/mol, respectively. Thus, as in the Cs_2CO_3 case, in the

presence of Na_2CO_3 the active catalyst of the reaction is intermediate $[\text{Na}_2\text{CO}_3]\text{PdP}$ (below called as **A_Na**). The following oxidative addition of C–Cl bond of **1a** to intermediate **A_Na** proceeds with a moderate (11.7 kcal/mol) energy barrier at the “base-assisted oxidative addition” transition state and leads to the complex $[\text{NaCO}_3]\text{PdP}$ (below called as **B_Na**). Thus, if the sodium-carbonate were soluble under the utilized experimental conditions, then the catalytic active species formation and following C–Cl addition (or Pd(0)/Pd(II) oxidation), like in the presence of Cs_2CO_3 , would occur with a moderate (22.1 kcal/mol) free energy barrier and would be exergonic (by 25.5 kcal/mol, see Supporting Information). *In other words, the observed dramatic difference in the reaction yield upon the Cs_2CO_3 to Na_2CO_3 substitution can be explained neither by the active catalyst formation nor the first C–Cl oxidative addition, while it could be result of poor solubility of the Na-carbonate.*

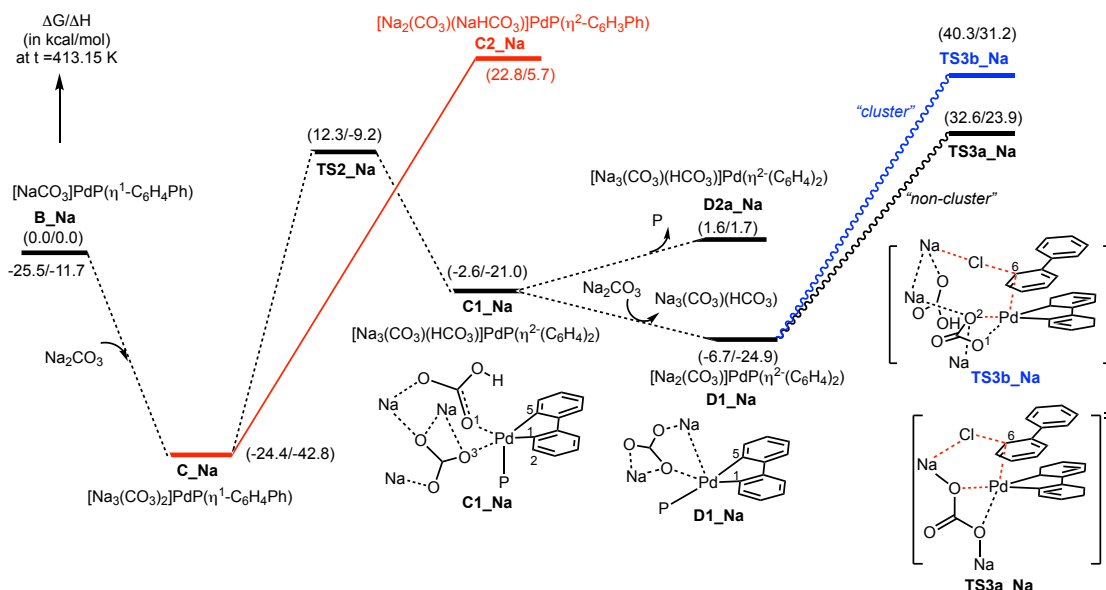


Figure 11. Free energy surfaces of the palladacycle (in black) and Pd-benzyne (in red) formation in the complex **B_Na**. For details of the reactions initiated from intermediates **D1_Na** and **D2a_Na** see Supporting Information.

Next, we investigated palladacycle and Pd-aryne formation in the presence of Na_2CO_3 (see Figure 11). Similar to the case with Cs_2CO_3 , these steps of the Pd-catalyzed annulative chlorophenylene dimerization in the presence of Na_2CO_3 can be initiated either directly from complex **B_Na** (if the base molecule has a low aggregation capability, i.e. is highly soluble) or from the “Na-cluster-complex” $[\text{Na}_3(\text{CO}_3)_2]\text{PdP}(\eta^1\text{-C}_6\text{H}_4\text{Ph})$, **C_Na**, (if the base molecule were prone to form a highly aggregated Na-carbonate species). Again, here, we studied both mechanistic scenarios, while below we discuss only the reaction initiated from the complex **C_Na**. Calculated data for the reaction from **B_Na** are included into the Supporting Information (Figure S15), and will be compared when it becomes important.

Compared with the Cs_2CO_3 case (see Figure 6), we found (see Supporting Information for more details) that (a) the coordination of the second equivalent of Na_2CO_3 to **B_Na** and formation of the “Na-cluster complex” **C_Na** is highly exergonic (by 24.4 kcal/mol), more so than the same reaction in the presence of Cs_2CO_3 : *this finding indicates that Na-carbonate is prone to form high aggregation species, i.e. is less soluble, than Cs-carbonate*, (b) the palladacycle (**C1_Na**)

formation in **C_Na** has *ca* 5-6 kcal/mol more energy barrier (36.7 kcal/mol) and is endergonic by 21.8 kcal/mol, and (c) the Pd-aryne formation in **C_Na** is highly (by 47.2 kcal/mol) endergonic (therefore, we did not calculate the Pd-aryne formation transition state). Most importantly, neither the following (from the palladacycle **C1_Na**) $[\text{Na}_3(\text{CO}_3)(\text{HCO}_3)]$ -to- Na_2CO_3 exchange nor phosphine dissociation leading to the **D1_Na** and **D2a_Na** complexes, respectively, are thermodynamically feasible. *Thus, the palladacycle formation (we also expect the Pd-aryne formation) initiated from the “Na-cluster complex” C_Na occurs over a much higher energy barrier and is more endergonic than that initiated from the “Cs-cluster complex” C_Cs. These findings could be explained by larger stability of the “Na-cluster complex” C_Na compared to the “Cs-cluster complex” C_Cs, i.e. by weaker solubility of Na_2CO_3 compared to Cs_2CO_3 .*

As expected, the second C–Cl oxidative addition to the thermodynamically unfavorable palladacycles, either **D1_Na** or **D2_Na**, is going to be a highly energy demanding process. Indeed, the calculated C–Cl activation barriers (relative **C_Na**) are as high as 57.0 and 64.7 kcal/mol, for the following “cluster” and “non-cluster” pathways, respectively (see Figure 11 and Figure S17 in Supporting Information). Thus, the second C–Cl addition in the presence of Na_2CO_3 requires a prohibitively high energy barrier and is unlikely to proceed. This conclusion is consistent with our previous experiments showing zero yield in the presence of Na_2CO_3 .

Conclusion

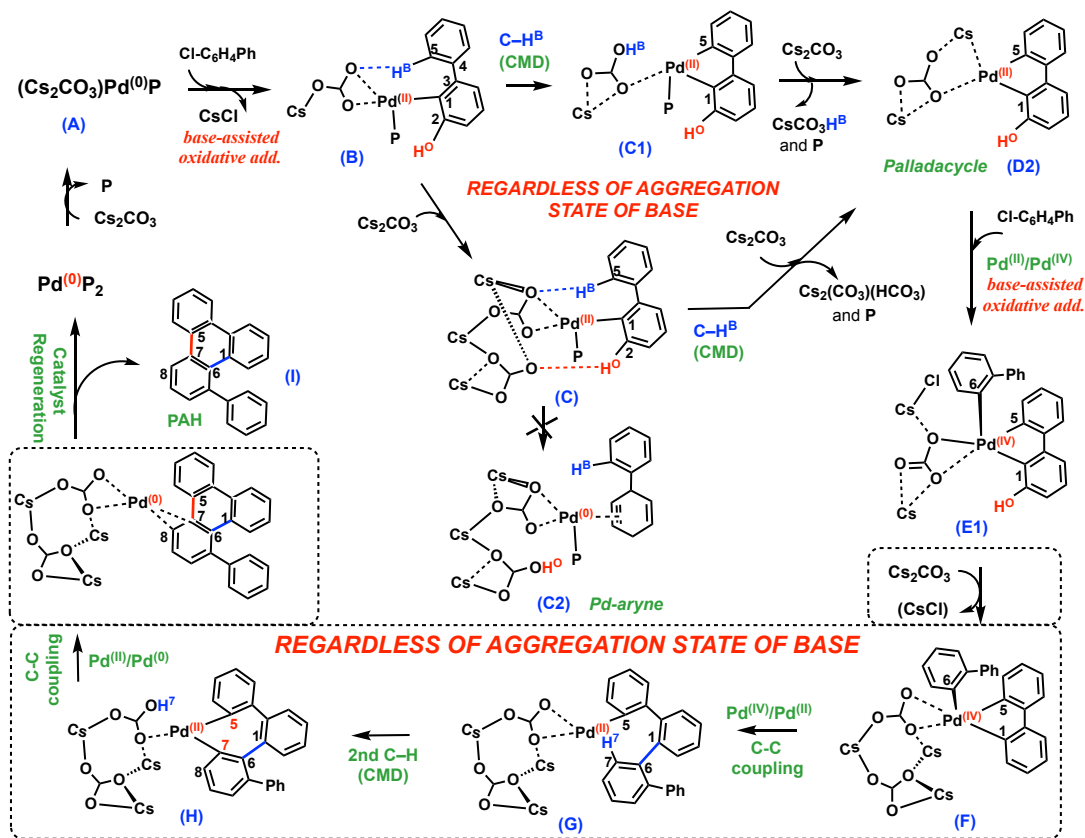
Based on the rigorous computations presented here, a modified mechanism of the Pd-catalyzed annulative chlorophenylene dimerization was proposed (see Scheme 7, here for the sake of clarity we omit suffix “_Cs” of the labels of the presented structures):

1. Initial steps of this reaction are: (a) the active catalyst **A** formation, (b) the first C–Cl bond activation via the “base-assisted oxidative addition” mechanism, and (c) the formation of intermediate **B**. Overall, these steps of the reaction proceed via 16.2 kcal/mol free energy barrier for the C–Cl bond activation and are highly exergonic. Importantly, the presence of base molecules (i.e. Cs_2CO_3) in the reaction mixture is critical for success of these steps of the studied reaction: *Base directly participates in the C–Cl bond cleavage, introduces mechanistic switch of the Pd(0)/Pd(II) oxidation, and makes reaction more exergonic.*

2. Among the following palladacycle and Pd-aryne formation pathways, the palladacycle formation is favorable: it proceeds with a moderate C–H activation free energy barrier (~30-31 kcal/mol) and is slightly exergonic. Although the Pd-aryne formation may require slightly lower C–H activation barrier, it is a highly endergonic process and lacks the driving force to proceed: thus, the participation of the Pd-aryne complex, or its derivatives, in the studied Pd-catalyzed annulative chlorophenylene dimerization in the presence of Cs_2CO_3 is unlikely. Again, the presence of the base molecule (i.e. Cs_2CO_3) in the reaction mixture is important for the palladacycle formation: it (a) participates in the “bay” C–H bond activation, and (b) facilitates the driving of the reaction forward by removal of proton to the solution via the cesium(bicarbonate)-to-cesium(carbonate) exchange mechanism. We show that *if base is soluble under the used experimental conditions to drive the first C–Cl activation, the following palladacycle formation is independent from the aggregation state (or solubility) of base;*

3. The next step of the reaction is the second C–Cl bond addition to palladacycle **D2** via another “base-assisted oxidative addition” mechanism and formation of intermediate **F**. Overall, this step, i.e. Pd(II)→Pd(IV) oxidation, is a rate-limiting step of entire Pd-catalyzed and Cs-carbonate mediated annulative chlorophenylene dimerization: it occurs over a 35.8 kcal/mol free energy barrier and is exergonic by 25.1 kcal/mol.

Scheme 7. The Proposed Mechanism of the Pd(0)-catalyzed and Cs₂CO₃-mediated Annulative Chlorophenylene Dimerization.



4. The final stage of the reaction is the product formation from intermediate F. Calculations show that polycyclic aromatic hydrocarbon (PAH) formation via the subsequent *trans* C–C coupling, C–H bond activation, and the second C–C coupling steps, requires lower free energy barriers. This process is exergonic by 50.6 kcal/mol. Alternative pathway, namely, cyclooctatetraene (COT) formation from F requires a higher free energy barrier and is not feasible. This finding is consistent with experiments shown no COT product in the utilized conditions.

5. Calculations indicate that the observed dramatic change in the yield of the Pd-catalyzed annulative chlorophenylene dimerization reaction (from 82 % to 0%) upon use of Na-carbonate instead of Cs-carbonate is result of not only poor solubility of Na-carbonate in the used experimental conditions, but also a prohibitively large free energy barrier required for the second C–Cl activation, i.e. Pd(II)-to-Pd(IV) oxidation.

ASSOCIATED CONTENT

Supporting Information. Energies and Cartesian coordinates for all reported structures. This material is available free of charge via the Internet at <http://pubs.acs.org>

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Notes

The authors declare no competing financial interests.

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14. We were not able to locate a transition state associated with this process but expect the barrier to be small.

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20. We have also investigated the second C–Cl activation from **INT3_Cs_P**, in which the phosphine ligand binds with palladium (compared to **INT3_Cs** in which no phosphine ligand). However, the activation barrier for this pathway is 5.4 kcal/mol higher than from **INT3_Cs**. See Figure S8 in Supporting Information for details.

21. We have also studied the second C–Cl activation from **D2a_Cs** (this complex comes after phosphine ligand dissociation on **C1_Cs**) but the activation barrier is 1.2 kcal/mol higher than that from **D1_Cs** (see Figure S9 in Supporting Information).

Table of Context Use

Roles of base in the Pd-Catalyzed Annulative Chlorophenylene Dimerization

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